

tion program (as identified in section 1769f(b) of title 42); and

(E) conclude operations at such time as the Secretary determines appropriate.

(3) Multiple recalls

The Secretary may establish multiple or concurrent incident command operations or similar operations in the event of multiple recalls or foodborne illness outbreaks necessitating such action by the Department of Health and Human Services.

(June 25, 1938, ch. 675, §423, as added Pub. L. 111-353, title II, §206(a), Jan. 4, 2011, 124 Stat. 3939.)

REFERENCES IN TEXT

The Public Health Service Act, referred to in subsec. (i), is act July 1, 1944, ch. 373, 58 Stat. 682, which is classified generally to chapter 6A (§201 et seq.) of Title 42, The Public Health and Welfare. For complete classification of this Act to the Code, see Short Title note set out under section 201 of Title 42 and Tables.

CONSTRUCTION

Nothing in this section to be construed to alter jurisdiction and authorities established under certain other Acts or in a manner inconsistent with international agreements to which the United States is a party, see sections 2251 and 2252 of this title.

SEARCH ENGINE

Pub. L. 111-353, title II, §206(b), Jan. 4, 2011, 124 Stat. 3942, provided that: “Not later than 90 days after the date of enactment of this Act [Jan. 4, 2011], the Secretary shall modify the Internet Web site of the Food and Drug Administration to include a search engine that—

“(1) is consumer-friendly, as determined by the Secretary; and

“(2) provides a means by which an individual may locate relevant information regarding each article of food subject to a recall under section 423 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 350f] and the status of such recall (such as whether a recall is ongoing or has been completed).”

§ 350f-1. Annual report to Congress

(1) In general

Not later than 2 years after January 4, 2011, and annually thereafter, the Secretary of Health and Human Services (referred to in this section as the “Secretary”) shall submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on the use of recall authority under section 350f of this title (as added by subsection (a))¹ and any public health advisories issued by the Secretary that advise against the consumption of an article of food on the ground that the article of food is adulterated and poses an imminent danger to health.

(2) Content

The report under paragraph (1) shall include, with respect to the report year—

(A) the identity of each article of food that was the subject of a public health advisory described in paragraph (1), an opportunity to cease distribution and recall under subsection

(a) of section 350f of this title, or a mandatory recall order under subsection (b) of such section;

(B) the number of responsible parties, as defined in section 350f of this title, formally given the opportunity to cease distribution of an article of food and recall such article, as described in section 350f(a) of such title;

(C) the number of responsible parties described in subparagraph (B) who did not cease distribution of or recall an article of food after given the opportunity to cease distribution or recall under section 350f(a) of this title;

(D) the number of recall orders issued under section 350f(b) of this title; and

(E) a description of any instances in which there was no testing that confirmed adulteration of an article of food that was the subject of a recall under section 350f(b) of this title or a public health advisory described in paragraph (1).

(Pub. L. 111-353, title II, §206(f), Jan. 4, 2011, 124 Stat. 3943.)

REFERENCES IN TEXT

Subsection (a), referred to in par. (1), means subsec. (a) of section 206 of Pub. L. 111-353.

CODIFICATION

Section was enacted as part of the FDA Food Safety Modernization Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

CONSTRUCTION

Nothing in this section to be construed to alter jurisdiction and authorities established under certain other Acts or in a manner inconsistent with international agreements to which the United States is a party, see sections 2251 and 2252 of this title.

SUBCHAPTER V—DRUGS AND DEVICES

PART A—DRUGS AND DEVICES

§ 351. Adulterated drugs and devices

A drug or device shall be deemed to be adulterated—

(a) Poisonous, insanitary, etc., ingredients; adequate controls in manufacture

(1) If it consists in whole or in part of any filthy, putrid, or decomposed substance; or (2)(A) if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; or (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the

¹ See References in Text note below.

positron emission tomography compounding standards and the official monographs of the United States Pharmacopoeia to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess; or (3) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) if (A) it bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 379e(a) of this title, or (B) it is a color additive the intended use of which in or on drugs or devices is for purposes of coloring only and is unsafe within the meaning of section 379e(a) of this title; or (5) if it is a new animal drug which is unsafe within the meaning of section 360b of this title; or (6) if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 360b of this title.

(b) Strength, quality, or purity differing from official compendium

If it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium. Such determination as to strength, quality, or purity shall be made in accordance with the tests or methods of assay set forth in such compendium, except that whenever tests or methods of assay have not been prescribed in such compendium, or such tests or methods of assay as are prescribed are, in the judgment of the Secretary, insufficient for the making of such determination, the Secretary shall bring such fact to the attention of the appropriate body charged with the revision of such compendium, and if such body fails within a reasonable time to prescribe tests or methods of assay which, in the judgment of the Secretary, are sufficient for purposes of this paragraph, then the Secretary shall promulgate regulations prescribing appropriate tests or methods of assay in accordance with which such determination as to strength, quality, or purity shall be made. No drug defined in an official compendium shall be deemed to be adulterated under this paragraph because it differs from the standard of strength, quality, or purity therefor set forth in such compendium, if its difference in strength, quality, or purity from such standard is plainly stated on its label. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homoeopathic Pharmacopoeia of the United States it shall be subject to the requirements of the United States Pharmacopoeia unless it is labeled and offered for sale as a homoeopathic drug, in which case it shall be subject to the provisions of the Homoeopathic Pharmacopoeia of the United States and not to those of the United States Pharmacopoeia.

(c) Misrepresentation of strength, etc., where drug is unrecognized in compendium

If it is not subject to the provisions of paragraph (b) of this section and its strength differs from, or its purity or quality falls below, that which it purports or is represented to possess.

(d) Mixture with or substitution of another substance

If it is a drug and any substance has been (1) mixed or packed therewith so as to reduce its quality or strength or (2) substituted wholly or in part therefor.

(e) Devices not in conformity with performance standards

(1) If it is, or purports to be or is represented as, a device which is subject to a performance standard established under section 360d of this title unless such device is in all respects in conformity with such standard.

(2) If it is declared to be, purports to be, or is represented as, a device that is in conformity with any standard recognized under section 360d(c) of this title unless such device is in all respects in conformity with such standard.

(f) Certain class III devices

(1) If it is a class III device—

(A)(i) which is required by an order issued under subsection (b) of section 360e of this title to have an approval under such section of an application for premarket approval and which is not exempt from section 360e of this title under section 360j(g) of this title, and

(ii)(I) for which an application for premarket approval or a notice of completion of a product development protocol was not filed with the Secretary within the ninety-day period beginning on the date of the issuance of such order, or

(II) for which such an application was filed and approval of the application has been denied, suspended, or withdrawn, or such a notice was filed and has been declared not completed or the approval of the device under the protocol has been withdrawn;

(B)(i) which was classified under section 360c(f) of this title into class III, which under section 360e(a) of this title is required to have in effect an approved application for premarket approval, and which is not exempt from section 360e of this title under section 360j(g) of this title, and

(ii) which has an application which has been suspended or is otherwise not in effect; or

(C) which was classified under section 360j(l) of this title into class III, which under such section is required to have in effect an approved application under section 360e of this title, and which has an application which has been suspended or is otherwise not in effect.

(2)(A) In the case of a device classified under section 360c(f) of this title into class III and intended solely for investigational use, paragraph¹ (1)(B) shall not apply with respect to such device during the period ending on the ninetieth day after the date of the promulgation of the regulations prescribing the procedures and conditions required by section 360j(g)(2) of this title.

(B) In the case of a device subject to an order issued under subsection (b) of section 360e of this title, paragraph¹ (1) shall not apply with respect to such device during the period ending—

(i) on the last day of the thirtieth calendar month beginning after the month in which the

¹ So in original. Probably should be "subparagraph".

classification of the device in class III became effective under section 360c of this title, or

(ii) on the ninetieth day after the date of the issuance of such order,

whichever occurs later.

(3) In the case of a device with respect to which a regulation was promulgated under section 360e(b) of this title prior to July 9, 2012, a reference in this subsection to an order issued under section 360e(b) of this title shall be deemed to include such regulation.

(g) Banned devices

If it is a banned device.

(h) Manufacture, packing, storage, or installation of device not in conformity with applicable requirements or conditions

If it is a device and the methods used in, or the facilities or controls used for, its manufacture, packing, storage, or installation are not in conformity with applicable requirements under section 360j(f)(1) of this title or an applicable condition prescribed by an order under section 360j(f)(2) of this title.

(i) Failure to comply with requirements under which device was exempted for investigational use

If it is a device for which an exemption has been granted under section 360j(g) of this title for investigational use and the person who was granted such exemption or any investigator who uses such device under such exemption fails to comply with a requirement prescribed by or under such section.

(j) Delayed, denied, or limited inspection; refusal to permit entry or inspection

If it is a drug and it has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection.

For purposes of paragraph (a)(2)(B), the term “current good manufacturing practice” includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products.

(June 25, 1938, ch. 675, § 501, 52 Stat. 1049; Pub. L. 86-618, title I, § 102(b)(1), July 12, 1960, 74 Stat. 398; Pub. L. 87-781, title I, § 101, Oct. 10, 1962, 76 Stat. 780; Pub. L. 90-399, § 101(a), July 13, 1968, 82 Stat. 343; Pub. L. 94-295, §§ 3(d), 9(b)(1), May 28, 1976, 90 Stat. 576, 583; Pub. L. 101-629, § 9(b), Nov. 28, 1990, 104 Stat. 4521; Pub. L. 102-571, title I, § 107(8), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 105-115, title I, § 121(b)(1), title II, § 204(c), Nov. 21, 1997, 111 Stat. 2320, 2336; Pub. L. 112-144, title VI, § 608(b)(2), title VII, §§ 707(a), 711, July 9, 2012, 126 Stat. 1058, 1068, 1071.)

AMENDMENTS

2012—Pub. L. 112-144, § 711, inserted concluding provisions.

Par. (f)(1)(A)(i). Pub. L. 112-144, § 608(b)(2)(A)(i), substituted “an order issued” for “a regulation promulgated”.

Par. (f)(1)(A)(ii)(I). Pub. L. 112-144, § 608(b)(2)(A)(ii), substituted “issuance of such order” for “promulgation of such regulation”.

Par. (f)(2)(B). Pub. L. 112-144, § 608(b)(2)(B), substituted “an order issued” for “a regulation promulgated” in introductory provisions and “issuance of such order” for “promulgation of such regulation” in subcl. (ii).

Par. (f)(3). Pub. L. 112-144, § 608(b)(2)(C), added subpar. (3).

Par. (j). Pub. L. 112-144, § 707(a), added par. (j).

1997—Par. (a)(2)(C). Pub. L. 105-115, § 121(b)(1), inserted “; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopoeia to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess;” before “or (3)”.

Par. (e). Pub. L. 105-115, § 204(c), designated existing provisions as subpar. (1) and added subpar. (2).

1992—Par. (a)(4). Pub. L. 102-571 substituted “379e(a)” for “376(a)” in cls. (A) and (B).

1990—Par. (f)(1). Pub. L. 101-629, § 9(b), which directed the amendment of subpars. (A) to (C) of par. (f), was executed by making the amendments in cls. (A) to (C) of subpar. (1) of par. (f) as follows to reflect the probable intent of Congress: in cl. (A)(ii)(II), substituted “; suspended, or withdrawn” for “or withdrawn”; in cl. (B)(ii), substituted “which has an application which has been suspended or is otherwise not in effect” for “which does not have such an application in effect”; and in cl. (C), substituted “which has an application which has been suspended or is otherwise not in effect” for “which does not have such an application in effect”.

1976—Par. (a). Pub. L. 94-295, § 9(b)(1), substituted “(3) if its” for “(3) if it is a drug and its” in cl. (3), substituted “(4) if (A) it bears or contains” for “(4) if (A) it is a drug which bears or contains” in cl. (4)(A), and substituted “drugs or devices” for “drugs” in cl. (4)(B).

Pars. (e) to (i). Pub. L. 94-295, § 3(d), added pars. (e) to (i).

1968—Par. (a). Pub. L. 90-399 added cls. (5) and (6).

1962—Par. (a). Pub. L. 87-781 designated existing provisions of cl. (2) as (A) and added (B).

1960—Par. (a). Pub. L. 86-618 substituted provisions in cl. (4) relating to unsafe color additives for provisions which related to a coal-tar color other than one from a batch that has been certified in accordance with regulations as provided by section 354 of this title.

EFFECTIVE AND TERMINATION DATES OF 1997 AMENDMENT

Pub. L. 105-115, title I, § 121(b)(2), Nov. 21, 1997, 111 Stat. 2320, provided that: “Section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) shall not apply 4 years after the date of enactment of this Act [Nov. 21, 1997] or 2 years after the date on which the Secretary of Health and Human Services establishes the requirements described in subsection (c)(1)(B) [section 121(c)(1)(B) of Pub. L. 105-115, set out as a note under section 355 of this title], whichever is later.”

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

EFFECTIVE DATE OF 1968 AMENDMENT

Amendment by Pub. L. 90-399 effective on first day of thirteenth calendar month after July 13, 1968, see section 108(a) of Pub. L. 90-399, set out as an Effective Date and Transitional Provisions note under section 360b of this title.

EFFECTIVE DATE OF 1962 AMENDMENT; EXCEPTIONS

Amendment by Pub. L. 87-781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87-781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1960 AMENDMENT

Amendment by Pub. L. 86-618 effective July 12, 1960, subject to the provisions of section 203 of Pub. L. 86-618, see section 202 of Pub. L. 86-618, set out as a note under section 379e of this title.

EFFECTIVE DATE; POSTPONEMENT

Par. (a)(4) effective Jan. 1, 1940, see act June 23, 1939, ch. 242, 53 Stat. 853, set out as an Effective Date; Postponement in Certain Cases note under section 301 of this title.

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

APPROVAL BY REGULATION PRIOR TO JULY 9, 2012

Pub. L. 112-144, title VI, §608(b)(3), July 9, 2012, 126 Stat. 1059, provided that: "The amendments made by this subsection [amending this section and section 360e of this title] shall have no effect on a regulation that was promulgated prior to the date of enactment of this Act [July 9, 2012] requiring that a device have an approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e) of an application for pre-market approval."

GUIDANCE

Pub. L. 112-144, title VII, §707(b), July 9, 2012, 126 Stat. 1068, provided that: "Not later than 1 year after the date of enactment of this section [July 9, 2012], the Secretary of Health and Human Services shall issue guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection, or refusing to permit entry or inspection, for purposes of section 501(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 351(j)] (as added by subsection (a))."

§ 352. Misbranded drugs and devices

A drug or device shall be deemed to be misbranded—

(a) False or misleading label

If its labeling is false or misleading in any particular. Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 355 of this title or under section 262(a) of title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 355(a) of this title or in section 262(a) of title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term "health

care economic information" means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.

(b) Package form; contents of label

If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count: *Provided*, That under clause (2) of this paragraph reasonable variations shall be permitted, and exemptions as to small packages shall be established, by regulations prescribed by the Secretary.

(c) Prominence of information on label

If any word, statement, or other information required by or under authority of this chapter to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

(d) Repealed. Pub. L. 105-115, title I, § 126(b), Nov. 21, 1997, 111 Stat. 2327**(e) Designation of drugs or devices by established names**

(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

(ii) the established name and quantity or, if determined to be appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if determined to be appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if determined to be appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, except that nothing in this subclause shall be deemed to require that any trade secret be divulged, and except that the requirements of this subclause with respect to alpha-

betical order shall apply only to nonprescription drugs that are not also cosmetics and that this subclause shall not apply to nonprescription drugs not intended for human use.

(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of subclause (ii) or (iii) of clause (A) or this clause is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(2) If it is a device and it has an established name, unless its label bears, to the exclusion of any other nonproprietary name, its established name (as defined in subparagraph (4)) prominently printed in type at least half as large as that used thereon for any proprietary name or designation for such device, except that to the extent compliance with the requirements of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

(3) As used in subparagraph (1), the term “established name”, with respect to a drug or ingredient thereof, means (A) the applicable official name designated pursuant to section 358 of this title, or (B), if there is no such name and such drug, or such ingredient, is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug or of such ingredient, except that where clause (B) of this subparagraph applies to an article recognized in the United States Pharmacopoeia and in the Homoeopathic Pharmacopoeia under different official titles, the official title used in the United States Pharmacopoeia shall apply unless it is labeled and offered for sale as a homoeopathic drug, in which case the official title used in the Homoeopathic Pharmacopoeia shall apply.

(4) As used in subparagraph (2), the term “established name” with respect to a device means (A) the applicable official name of the device designated pursuant to section 358 of this title, (B) if there is no such name and such device is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then any common or usual name of such device.

(f) Directions for use and warnings on label

Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users, except that where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting

such drug or device from such requirement. Required labeling for prescription devices intended for use in health care facilities or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments may be made available solely by electronic means, provided that the labeling complies with all applicable requirements of law, and that the manufacturer affords such users the opportunity to request the labeling in paper form, and after such request, promptly provides the requested information without additional cost.

(g) Representations as recognized drug; packing and labeling; inconsistent requirements for designation of drug

If it purports to be a drug the name of which is recognized in an official compendium, unless it is packaged and labeled as prescribed therein. The method of packing may be modified with the consent of the Secretary. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homoeopathic Pharmacopoeia of the United States, it shall be subject to the requirements of the United States Pharmacopoeia with respect to packaging and labeling unless it is labeled and offered for sale as a homoeopathic drug, in which case it shall be subject to the provisions of the Homoeopathic Pharmacopoeia of the United States, and not those of the United States Pharmacopoeia, except that in the event of inconsistency between the requirements of this paragraph and those of paragraph (e) as to the name by which the drug or its ingredients shall be designated, the requirements of paragraph (e) shall prevail.

(h) Deteriorative drugs; packing and labeling

If it has been found by the Secretary to be a drug liable to deterioration, unless it is packaged in such form and manner, and its label bears a statement of such precautions, as the Secretary shall by regulations require as necessary for the protection of the public health. No such regulation shall be established for any drug recognized in an official compendium until the Secretary shall have informed the appropriate body charged with the revision of such compendium of the need for such packaging or labeling requirements and such body shall have failed within a reasonable time to prescribe such requirements.

(i) Drug; misleading container; imitation; offer for sale under another name

(1) If it is a drug and its container is so made, formed, or filled as to be misleading; or (2) if it is an imitation of another drug; or (3) if it is offered for sale under the name of another drug.

(j) Health-endangering when used as prescribed

If it is dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.

(k), (l) Repealed. Pub. L. 105-115, title I, § 125(a)(2)(B), (b)(2)(D), Nov. 21, 1997, 111 Stat. 2325

(m) Color additives; packing and labeling

If it is a color additive the intended use of which is for the purpose of coloring only, unless

its packaging and labeling are in conformity with such packaging and labeling requirements applicable to such color additive, as may be contained in regulations issued under section 379e of this title.

(n) Prescription drug advertisements: established name; quantitative formula; side effects, contraindications, and effectiveness; prior approval; false advertising; labeling; construction of the Convention on Psychotropic Substances

In the case of any prescription drug distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug a true statement of (1) the established name as defined in paragraph (e) of this section, printed prominently and in type at least half as large as that used for any trade or brand name thereof, (2) the formula showing quantitatively each ingredient of such drug to the extent required for labels under paragraph (e) of this section, and (3) such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with section 371(a) of this title, and in the case of published direct-to-consumer advertisements the following statement printed in conspicuous text: "You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.", except that (A) except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement, and (B) no advertisement of a prescription drug, published after the effective date of regulations issued under this paragraph applicable to advertisements of prescription drugs, shall with respect to the matters specified in this paragraph or covered by such regulations, be subject to the provisions of sections 52 to 57 of title 15. This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title. Nothing in the Convention on Psychotropic Substances, signed at Vienna, Austria, on February 21, 1971, shall be construed to prevent drug price communications to consumers. In the case of an advertisement for a drug subject to section 353(b)(1) of this title presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner.

(o) Drugs or devices from nonregistered establishments

If it was manufactured, prepared, propagated, compounded, or processed in an establishment not duly registered under section 360 of this title, if it is a drug and was imported or offered for import by a commercial importer of drugs not duly registered under section 381(s) of this title, if it was not included in a list required by section 360(j) of this title, if a notice or other in-

formation respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires.

(p) Packaging or labeling of drugs in violation of regulations

If it is a drug and its packaging or labeling is in violation of an applicable regulation issued pursuant to section 1472 or 1473 of title 15.

(q) Restricted devices using false or misleading advertising or used in violation of regulations

In the case of any restricted device distributed or offered for sale in any State, if (1) its advertising is false or misleading in any particular, or (2) it is sold, distributed, or used in violation of regulations prescribed under section 360j(e) of this title.

(r) Restricted devices not carrying requisite accompanying statements in advertisements and other descriptive printed matter

In the case of any restricted device distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that device (1) a true statement of the device's established name as defined in subsection (e) of this section, printed prominently and in type at least half as large as that used for any trade or brand name thereof, and (2) a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications and, in the case of specific devices made subject to a finding by the Secretary after notice and opportunity for comment that such action is necessary to protect the public health, a full description of the components of such device or the formula showing quantitatively each ingredient of such device to the extent required in regulations which shall be issued by the Secretary after an opportunity for a hearing. Except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement and no advertisement of a restricted device, published after the effective date of this paragraph shall, with respect to the matters specified in this paragraph or covered by regulations issued hereunder, be subject to the provisions of sections 52 through 55 of title 15. This paragraph shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title.

(s) Devices subject to performance standards not bearing requisite labeling

If it is a device subject to a performance standard established under section 360d of this title, unless it bears such labeling as may be prescribed in such performance standard.

(t) Devices for which there has been a failure or refusal to give required notification or to furnish required material or information

If it is a device and there was a failure or refusal (1) to comply with any requirement pre-

scribed under section 360h of this title respecting the device, (2) to furnish any material or information required by or under section 360i of this title respecting the device, or (3) to comply with a requirement under section 360l of this title.

(u) Identification of manufacturer

(1) Subject to paragraph (2), if it is a reprocessed single-use device, unless it, or an attachment thereto, prominently and conspicuously bears the name of the manufacturer of the reprocessed device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer.

(2) If the original device or an attachment thereto does not prominently and conspicuously bear the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, a reprocessed device may satisfy the requirements of paragraph (1) through the use of a detachable label on the packaging that identifies the manufacturer and is intended to be affixed to the medical record of a patient.

(v) Reprocessed single-use devices

If it is a reprocessed single-use device, unless all labeling of the device prominently and conspicuously bears the statement “Reprocessed device for single use. Reprocessed by ____.” The name of the manufacturer of the reprocessed device shall be placed in the space identifying the person responsible for reprocessing.

(w) New animal drugs

If it is a new animal drug—

(1) that is conditionally approved under section 360ccc of this title and its labeling does not conform with the approved application or section 360ccc(f) of this title, or that is not conditionally approved under section 360ccc of this title and its label bears the statement set forth in section 360ccc(f)(1)(A) of this title; or

(2) that is indexed under section 360ccc-1 of this title and its labeling does not conform with the index listing under section 360ccc-1(e) of this title or 360ccc-1(h) of this title, or that has not been indexed under section 360ccc-1 of this title and its label bears the statement set forth in section 360ccc-1(h) of this title.

(x) Nonprescription drugs

If it is a nonprescription drug (as defined in section 379aa of this title) that is marketed in the United States, unless the label of such drug includes a domestic address or domestic phone number through which the responsible person (as described in section 379aa of this title) may receive a report of a serious adverse event (as defined in section 379aa of this title) with such drug.

(y) Drugs subject to approved risk evaluation and mitigation strategy

If it is a drug subject to an approved risk evaluation and mitigation strategy pursuant to section 355(p) of this title and the responsible person (as such term is used in section 355-1 of this title) fails to comply with a requirement of such strategy provided for under subsection (d), (e), or (f) of section 355-1 of this title.

(z) Postmarket studies and clinical trials; new safety information in labeling

If it is a drug, and the responsible person (as such term is used in section 355(o) of this title) is in violation of a requirement established under paragraph (3) (relating to postmarket studies and clinical trials) or paragraph (4) (relating to labeling) of section 355(o) of this title with respect to such drug.

(aa) Unpaid fees; failure to submit identifying information

If it is a drug, or an active pharmaceutical ingredient, and it was manufactured, prepared, propagated, compounded, or processed in a facility for which fees have not been paid as required by section 379j-42(a)(4) of this title or for which identifying information required by section 379j-42(f) of this title has not been submitted, or it contains an active pharmaceutical ingredient that was manufactured, prepared, propagated, compounded, or processed in such a facility.

(bb) False or misleading advertisement or promotion of compounded drug

If the advertising or promotion of a compounded drug is false or misleading in any particular.

(cc) Failure to bear product identifier

If it is a drug and it fails to bear the product identifier as required by section 360eee-1 of this title.

(June 25, 1938, ch. 675, § 502, 52 Stat. 1050; June 23, 1939, ch. 242, § 3, 53 Stat. 854; Dec. 22, 1941, ch. 613, § 2, 55 Stat. 851; July 6, 1945, ch. 281, § 2, 59 Stat. 463; Mar. 10, 1947, ch. 16, § 2, 61 Stat. 11; July 13, 1949, ch. 305, § 1, 63 Stat. 409; Aug. 5, 1953, ch. 334, § 1, 67 Stat. 389; Pub. L. 86-618, title I, § 102(b)(2), July 12, 1960, 74 Stat. 398; Pub. L. 87-781, title I, §§ 105(c), 112(a), (b), 131(a), title III, § 305, Oct. 10, 1962, 76 Stat. 785, 790, 791, 795; Pub. L. 90-399, § 105(a), July 13, 1968, 82 Stat. 352; Pub. L. 91-601, § 6(d), formerly § 7(d), Dec. 30, 1970, 84 Stat. 1673, renumbered Pub. L. 97-35, title XII, § 1205(c), Aug. 13, 1981, 95 Stat. 716; Pub. L. 94-295, §§ 3(e), 4(b)(2), 5(a), 9(b)(2), May 28, 1976, 90 Stat. 577, 580, 583; Pub. L. 95-633, title I, § 111, Nov. 10, 1978, 92 Stat. 3773; Pub. L. 102-300, § 3(a)(2), June 16, 1992, 106 Stat. 239; Pub. L. 102-571, title I, § 107(9), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 103-80, § 3(m), Aug. 13, 1993, 107 Stat. 777; Pub. L. 105-115, title I, §§ 114(a), 125(a)(2)(B), (b)(2)(D), 126(b), title IV, § 412(c), Nov. 21, 1997, 111 Stat. 2312, 2325, 2327, 2375; Pub. L. 107-250, title II, § 206, title III, §§ 301(a), 302(a)(1), Oct. 26, 2002, 116 Stat. 1613, 1616; Pub. L. 108-214, § 2(b)(2)(B), Apr. 1, 2004, 118 Stat. 575; Pub. L. 108-282, title I, § 102(b)(5)(E), Aug. 2, 2004, 118 Stat. 902; Pub. L. 109-43, § 2(c)(1), Aug. 1, 2005, 119 Stat. 441; Pub. L. 109-462, § 2(d), Dec. 22, 2006, 120 Stat. 3472; Pub. L. 110-85, title IX, §§ 901(d)(3)(A), (6), 902(a), 906(a), Sept. 27, 2007, 121 Stat. 940, 942, 943, 949; Pub. L. 112-144, title III, § 306, title VII, §§ 702(a), 714(c), July 9, 2012, 126 Stat. 1024, 1065, 1074; Pub. L. 112-193, § 2(a), Oct. 5, 2012, 126 Stat. 1443; Pub. L. 113-54, title I, § 103(b), title II, § 206(b), Nov. 27, 2013, 127 Stat. 597, 639.)

AMENDMENTS

2013—Par. (bb). Pub. L. 113-54, § 103(b), added par. (bb).

Par. (cc). Pub. L. 113-54, §206(b), added par. (cc).

2012—Par. (o). Pub. L. 112-144, §714(c), inserted “if it is a drug and was imported or offered for import by a commercial importer of drugs not duly registered under section 381(s) of this title,” after “not duly registered under section 360 of this title.”

Pub. L. 112-144, §702(a), struck out “in any State” after “establishment”.

Par. (aa). Pub. L. 112-193 substituted “379j-42(a)(4)” for “379j-41(a)(4)”.

Pub. L. 112-144, §306, added par. (aa).

2007—Par. (n). Pub. L. 110-85, §906(a), inserted “and in the case of published direct-to-consumer advertisements the following statement printed in conspicuous text: ‘You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.’” after “section 371(a) of this title.”

Pub. L. 110-85, §901(d)(6), substituted “section 371(a) of this title” for “the procedure specified in section 371(e) of this title”.

Pub. L. 110-85, §901(d)(3)(A), inserted at end “In the case of an advertisement for a drug subject to section 353(b)(1) of this title presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner.”

Pars. (y), (z). Pub. L. 110-85, §902(a), added pars. (y) and (z).

2006—Par. (x). Pub. L. 109-462 added par. (x).

2005—Par. (u). Pub. L. 109-43 amended par. (u) generally. Prior to amendment, par. (u) read as follows: “If it is a device, unless it, or an attachment thereto, prominently and conspicuously bears the name of the manufacturer of the device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, except that the Secretary may waive any requirement under this paragraph for the device if the Secretary determines that compliance with the requirement is not feasible for the device or would compromise the provision of reasonable assurance of the safety or effectiveness of the device.”

2004—Par. (f). Pub. L. 108-214, in last sentence, inserted “or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments” after “in health care facilities”, inserted comma after “means”, substituted “requirements of law, and that the manufacturer affords such users the opportunity” for “requirements of law and, that the manufacturer affords health care facilities the opportunity”, and struck out “the health care facility” after “promptly provides”.

Par. (w). Pub. L. 108-282 added par. (w).

2002—Par. (f). Pub. L. 107-250, §206, inserted at end “Required labeling for prescription devices intended for use in health care facilities may be made available solely by electronic means provided that the labeling complies with all applicable requirements of law and, that the manufacturer affords health care facilities the opportunity to request the labeling in paper form, and after such request, promptly provides the health care facility the requested information without additional cost.”

Par. (u). Pub. L. 107-250, §301(a), which directed amendment of section by adding par. (u) at end, was executed by adding par. (u) before par. (v) to reflect the probable intent of Congress.

Par. (v). Pub. L. 107-250, §302(a)(1), added par. (v).

1997—Par. (a). Pub. L. 105-115, §114(a), inserted at end “Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 355 of this title

or under section 262(a) of title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 355(a) of this title or in section 262(a) of title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term ‘health care economic information’ means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.”

Par. (d). Pub. L. 105-115, §126(b), struck out par. (d) which read as follows: “If it is for use by man and contains any quantity of the narcotic or hypnotic substance alpha eucaine, barbituric acid, betaeucaine, bromal, cannabis, carbromal, chloral, coca, cocaine, codeine, heroin, marihuana, morphine, opium, paraldehyde, peyote, or sulphonmethane; or any chemical derivative of such substance, which derivative has been by the Secretary, after investigation, found to be, and by regulations designated as, habit forming; unless its label bears the name and quantity or proportion of such substance or derivative and in juxtaposition therewith the statement ‘Warning—May be habit forming.’”

Par. (e)(1). Pub. L. 105-115, §412(c), amended subpar. (1) generally. Prior to amendment, subpar. (1) read as follows: “If it is a drug, unless (A) its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (3)) of the drug, if such there be, and (ii), in case it is fabricated from two or more ingredients, the established name and quantity of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including, whether active or not, the established name and quantity or proportion of any bromides, ether, chloroform, acetanilid, acetphenetidin, amidopyrine, antipyrine, atropine, hyoscyne, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury ouabain strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein; *Provided*, That the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this paragraph, shall apply only to prescription drugs; and (B) for any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) is printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient: *Provided*, That to the extent that compliance with the requirements of clause (A)(ii) or clause (B) of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.”

Par. (k). Pub. L. 105-115, §125(a)(2)(B), struck out par. (k) which read as follows: “If it is, or purports to be, or is represented as a drug composed wholly or partly of insulin, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 356 of this title, and (2) such certificate or release is in effect with respect to such drug.”

Par. (l). Pub. L. 105-115, §125(b)(2)(D), struck out par. (l) which read as follows: “If it is, or purports to be, or is represented as a drug (except a drug for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 357 of this title, and (2) such certificate or release is in effect with respect to such drug: *Provided*, That this paragraph shall not

apply to any drug or class of drugs exempted by regulations promulgated under section 357(c) or (d) of this title.”

1993—Par. (e)(3). Pub. L. 103–80, §3(m)(1), substituted “of such ingredient, except that” for “of such ingredient: *Provided, That*”.

Par. (f). Pub. L. 103–80, §3(m)(2), substituted “users, except that where” for “users: *Provided, That where*”.

Par. (g). Pub. L. 103–80, §3(m)(3), substituted “prescribed therein. The method” for “prescribed therein: *Provided, That the method*” and “Pharmacopoeia, except that” for “Pharmacopoeia: *Provided further, That,*”.

Par. (n). Pub. L. 103–80, §3(m)(4), substituted “, except that (A)” for “: *Provided, That (A)*”.

1992—Par. (m). Pub. L. 102–571 substituted “379e” for “376”.

Par. (t)(3). Pub. L. 102–300 added cl. (3).

1978—Par. (n). Pub. L. 95–633 inserted provision relating to the construction of the Convention on Psychotropic Substances.

1976—Par. (e). Pub. L. 94–295, §5(a), substituted “subparagraph (3)” for “subparagraph (2)” in subpar. (1), added subpar. (2), redesignated former subpar. (2) as (3) and in subpar. (3) as so redesignated substituted “subparagraph (1)” for “this paragraph (e)”, and added subpar. (4).

Par. (j). Pub. L. 94–295, §3(e)(2), substituted “dosage or manner.” for “dosage.”.

Par. (m). Pub. L. 94–295, §9(b)(2), substituted “the intended use of which is for” for “the intended use of which in or on drugs is for”.

Par. (o). Pub. L. 94–295, §4(b)(2), substituted “If it was manufactured” for “If it is a drug and was manufactured” and inserted “, if it was not included in a list required by section 360(j) of this title, if a notice or other information respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires”.

Pars. (q) to (t). Pub. L. 94–295, §3(e)(1), added pars. (q) to (t).

1970—Par. (p). Pub. L. 91–601 added par. (p).

1968—Par. (l). Pub. L. 90–399 inserted “(except a drug for use in animals other than man)” after “represented as a drug”.

1962—Par. (e). Pub. L. 87–781, §112(a), designated existing provisions as subpar. (1), substituted “, unless (A) its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (2) of this subsection) of the drug, if such there be, and (ii), in case it is fabricated from two or more ingredients, the established name and quantity” for “and is not designated solely by a name recognized in an official compendium unless its label bears (1) the common or usual name of the drug, if such there be; and (2), in case it is fabricated from two or more ingredients, the common or usual name”, and “the established name” for “the name”, provided that the requirement for stating the quantity of active ingredients, other than those specified in this par., applies only to prescription drugs, and that the established name of a drug on a label is to be printed prominently and in type at least half as large as used for any proprietary designation, and added subpar. (2) defining “established name”.

Par. (g). Pub. L. 87–781, §112(b), provided that if there is an inconsistency between the provisions of this par. and those of par. (e), as to the name of a drug, the requirements of par. (e) should prevail.

Par. (l). Pub. L. 87–781, §105(c), substituted “bacitracin, or any other antibiotic drug” for “or bacitracin.”

Par. (n). Pub. L. 87–781, §131(a), added par. (n).

Par. (o). Pub. L. 87–781, §305, added par. (o).

1960—Par. (m). Pub. L. 86–618 added par. (m).

1953—Par. (l). Act Aug. 5, 1953, substituted “chlorotetracycline” for “aureomycin”.

1949—Par. (l). Act July 13, 1949, inserted “, aureomycin, chloramphenicol, or bacitracin” after “streptomycin”.

1947—Par. (l). Act Mar. 10, 1947, inserted “or streptomycin” after “penicillin”.

1945—Par. (l). Act July 6, 1945, added par. (l).

1941—Par. (k). Act Dec. 22, 1941, added par. (k).

1939—Par. (d). Act June 29, 1939, substituted “name, and quality or proportion” for “name, quantity, and percentage”.

EFFECTIVE DATE OF 2012 AMENDMENT

Amendment by section 306 of Pub. L. 112–144 effective Oct. 1, 2012, see section 305 of Pub. L. 112–144, set out as an Effective and Termination Dates note under section 379j–41 of this title.

EFFECTIVE DATE OF 2007 AMENDMENT

Amendment by Pub. L. 110–85 effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110–85, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 2006 AMENDMENT

Pub. L. 109–462, §2(e)(1), (2), Dec. 22, 2006, 120 Stat. 3472, provided that:

“(1) IN GENERAL.—Except as provided in paragraph (2), the amendments made by this section [enacting section 379aa of this title and amending this section and section 331 of this title] shall take effect 1 year after the date of enactment of this Act [Dec. 22, 2006].

“(2) MISBRANDING.—Section 502(x) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(x)] (as added by this section) shall apply to any nonprescription drug (as defined in such section 502(x)) labeled on or after the date that is 1 year after the date of enactment of this Act [Dec. 22, 2006].”

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–250, title III, §301(b), Oct. 26, 2002, 116 Stat. 1616, as amended by Pub. L. 108–214, §2(c)(1), Apr. 1, 2004, 118 Stat. 575; Pub. L. 109–43, §2(d), Aug. 1, 2005, 119 Stat. 441, provided that: “Section 502(u) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(u)] (as amended by section 2(c) of the Medical Device User Fee Stabilization Act of 2005 [Pub. L. 109–43])—

“(1) shall be effective—

“(A) with respect to devices described under paragraph (1) of such section, 12 months after the date of enactment of the Medical Device User Fee Stabilization Act of 2005 [Aug. 1, 2005], or the date on which the original device first bears the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, whichever is later; and

“(B) with respect to devices described under paragraph (2) of such section 502(u), 12 months after such date of enactment; and

“(2) shall apply only to devices reprocessed and introduced or delivered for introduction in interstate commerce after such applicable effective date.”

Pub. L. 107–250, title III, §302(a)(2), Oct. 26, 2002, 116 Stat. 1616, provided that: “The amendment made by paragraph (1) [amending this section] takes effect 15 months after the date of the enactment of this Act [Oct. 26, 2002], and only applies to devices introduced or delivered for introduction into interstate commerce after such effective date.”

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 114(a), 126(b), and 412(c) of Pub. L. 105–115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1978 AMENDMENT

Amendment by Pub. L. 95–633 effective on date the Convention on Psychotropic Substances enters into

force in the United States [July 15, 1980], see section 112 of Pub. L. 95-633, set out as an Effective Date note under section 801a of this title.

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91-601 effective Dec. 30, 1970, and regulations establishing special packaging standards effective no sooner than 180 days or later than one year from date regulations are final, or an earlier date published in Federal Register, see section 8 of Pub. L. 91-601, set out as an Effective Date note under section 1471 of Title 15, Commerce and Trade.

EFFECTIVE DATE OF 1968 AMENDMENT

Amendment by Pub. L. 90-399 effective on first day of thirteenth calendar month after July 13, 1968, see section 108(a) of Pub. L. 90-399, set out as an Effective Date and Transitional Provisions note under section 360b of this title.

EFFECTIVE DATE OF 1962 AMENDMENT

Pub. L. 87-781, title I, §112(c), Oct. 10, 1962, 76 Stat. 791, provided that: "This section [amending this section] shall take effect on the first day of the seventh calendar month following the month in which this Act is enacted [October 1962]."

Pub. L. 87-781, title I, §131(b), Oct. 10, 1962, 76 Stat. 792, provided that: "No drug which was being commercially distributed prior to the date of enactment of this Act [Oct. 10, 1962] shall be deemed to be misbranded under paragraph (n) of section 502 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(n)], as added by this section, until the earlier of the following dates: (1) the first day of the seventh month following the month in which this Act is enacted; or (2) the effective date of regulations first issued under clause (3) of such paragraph (n) in accordance with the procedure specified in section 701(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371(e)]."

Amendment by Pub. L. 87-781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87-781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1960 AMENDMENT

Amendment by Pub. L. 86-618 effective July 12, 1960, subject to the provisions of section 203 of Pub. L. 86-618, see section 202 of Pub. L. 86-618, set out as a note under section 379e of this title.

EFFECTIVE DATE; POSTPONEMENT

Pars. (b) and (d) to (h) effective Jan. 1, 1940, and such paragraphs effective July 1, 1940, as provided by regulations for certain lithographed labeling and containers bearing certain labeling, see act June 23, 1939, ch. 242, 53 Stat. 853, set out as an Effective Date: Postponement in Certain Cases note under section 301 of this title.

REGULATIONS

Pub. L. 110-85, title IX, §901(d)(3)(B), Sept. 27, 2007, 121 Stat. 940, provided that: "Not later than 30 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007 [Sept. 27, 2007], the Secretary of Health and Human Services shall by regulation establish standards for determining whether a major statement relating to side effects and contraindications of a drug, described in section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)) (as amended by subparagraph (A)) is presented in the manner required under such section."

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

PRESENTATION OF PRESCRIPTION DRUG BENEFIT AND RISK INFORMATION

Pub. L. 111-148, title III, §3507, Mar. 23, 2010, 124 Stat. 530, provided that:

"(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the 'Secretary'), acting through the Commissioner of Food and Drugs, shall determine whether the addition of quantitative summaries of the benefits and risks of prescription drugs in a standardized format (such as a table or drug facts box) to the promotional labeling or print advertising of such drugs would improve health care decisionmaking by clinicians and patients and consumers.

"(b) REVIEW AND CONSULTATION.—In making the determination under subsection (a), the Secretary shall review all available scientific evidence and research on decisionmaking and social and cognitive psychology and consult with drug manufacturers, clinicians, patients and consumers, experts in health literacy, representatives of racial and ethnic minorities, and experts in women's and pediatric health.

"(c) REPORT.—Not later than 1 year after the date of enactment of this Act [Mar. 23, 2010], the Secretary shall submit to Congress a report that provides—

"(1) the determination by the Secretary under subsection (a); and

"(2) the reasoning and analysis underlying that determination.

"(d) AUTHORITY.—If the Secretary determines under subsection (a) that the addition of quantitative summaries of the benefits and risks of prescription drugs in a standardized format (such as a table or drug facts box) to the promotional labeling or print advertising of such drugs would improve health care decisionmaking by clinicians and patients and consumers, then the Secretary, not later than 3 years after the date of submission of the report under subsection (c), shall promulgate proposed regulations as necessary to implement such format.

"(e) CLARIFICATION.—Nothing in this section shall be construed to restrict the existing authorities of the Secretary with respect to benefit and risk information."

GUIDANCE; MISBRANDED DEVICES

Pub. L. 109-43, §2(c)(2), Aug. 1, 2005, 119 Stat. 441, provided that: "Not later than 180 days after the date of enactment of this Act [Aug. 1, 2005], the Secretary of Health and Human Services shall issue guidance to identify circumstances in which the name of the manufacturer of the original device, a generally recognized abbreviation of such name, or a unique and generally recognized symbol identifying such manufacturer, is not 'prominent and conspicuous', as used in section 502(u) of Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(u)] (as amended by paragraph (1))."

STUDIES

Pub. L. 110-85, title IX, §906(b), Sept. 27, 2007, 121 Stat. 950, provided that:

"(1) IN GENERAL.—In the case of direct-to-consumer television advertisements, the Secretary of Health and Human Services, in consultation with the Advisory Committee on Risk Communication under section 567 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360bbb-6] (as added by section 917), shall, not later than 6 months after the date of the enactment of this Act [Sept. 27, 2007], conduct a study to determine if the statement in section 502(n) of such Act [21 U.S.C. 352(n)] (as added by subsection (a)) required with respect to published direct-to-consumer advertisements is appropriate for inclusion in such television advertisements.

"(2) CONTENT.—As part of the study under paragraph (1), such Secretary shall consider whether the information in the statement described in paragraph (1) would detract from the presentation of risk information in a direct-to-consumer television advertisement. If such Secretary determines the inclusion of such statement

is appropriate in direct-to-consumer television advertisements, such Secretary shall issue regulations requiring the implementation of such statement in direct-to-consumer television advertisements, including determining a reasonable length of time for displaying the statement in such advertisements. The Secretary shall report to the appropriate committees of Congress the findings of such study and any plans to issue regulations under this paragraph."

Pub. L. 108-173, title I, §107(f), Dec. 8, 2003, 117 Stat. 2171, directed the Secretary of Health and Human Services to undertake a study of how to make prescription pharmaceutical information, including drug labels and usage instructions, accessible to blind and visually-impaired individuals, and to submit a report to Congress not later than 18 months after Dec. 8, 2003.

Pub. L. 105-115, title I, §114(b), Nov. 21, 1997, 111 Stat. 2312, provided that: "The Comptroller General of the United States shall conduct a study of the implementation of the provisions added by the amendment made by subsection (a) [amending this section]. Not later than 4 years and 6 months after the date of enactment of this Act [Nov. 21, 1997], the Comptroller General of the United States shall prepare and submit to Congress a report containing the findings of the study."

COUNTERFEITING OF DRUGS; CONGRESSIONAL FINDINGS AND DECLARATION OF POLICY

Pub. L. 89-74, §9(a), July 15, 1965, 79 Stat. 234, provided that: "The Congress finds and declares that there is a substantial traffic in counterfeit drugs simulating the brand or other identifying mark or device of the manufacturer of the genuine article; that such traffic poses a serious hazard to the health of innocent consumers of such drugs because of the lack of proper qualifications, facilities, and manufacturing controls on the part of the counterfeiter, whose operations are clandestine; that, while such drugs are deemed misbranded within the meaning of section 502(i) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 352(i)], the controls for the suppression of the traffic in such drugs are inadequate because of the difficulty of determining the place of interstate origin of such drugs and, if that place is discovered, the fact that the implements for counterfeiting are not subject to seizure, and that these factors require enactment of additional controls with respect to such drugs without regard to their interstate or intrastate origins."

Provisions as effective Feb. 1, 1966, see section 11 of Pub. L. 89-74, set out as an Effective Date of 1965 Amendment note under section 321 of this title.

§ 353. Exemptions and consideration for certain drugs, devices, and biological products

(a) Regulations for goods to be processed, labeled, or repacked elsewhere

The Secretary is directed to promulgate regulations exempting from any labeling or packaging requirement of this chapter drugs and devices which are, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantities at establishments other than those where originally processed or packed, on condition that such drugs and devices are not adulterated or misbranded under the provisions of this chapter upon removal from such processing, labeling, or repackaging establishment.

(b) Prescription by physician; exemption from labeling and prescription requirements; misbranded drugs; compliance with narcotic and marihuana laws

(1) A drug intended for use by man which—

(A) because of its toxicity or other potentiality for harmful effect, or the method of its

use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

(B) is limited by an approved application under section 355 of this title to use under the professional supervision of a practitioner licensed by law to administer such drug;

shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug, or (ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist. The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

(2) Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 352 of this title, except paragraphs (a), (i)(2) and (3), (k), and (l), and the packaging requirements of paragraphs (g), (h), and (p), if the drug bears a label containing the name and address of the dispenser, the serial number and date of the prescription or of its filling, the name of the prescriber, and, if stated in the prescription, the name of the patient, and the directions for use and cautionary statements, if any, contained in such prescription. This exemption shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail, or to a drug dispensed in violation of paragraph (1) of this subsection.

(3) The Secretary may by regulation remove drugs subject to section 355 of this title from the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health.

(4)(A) A drug that is subject to paragraph (1) shall be deemed to be misbranded if at any time prior to dispensing the label of the drug fails to bear, at a minimum, the symbol "Rx only".

(B) A drug to which paragraph (1) does not apply shall be deemed to be misbranded if at any time prior to dispensing the label of the drug bears the symbol described in subparagraph (A).

(5) Nothing in this subsection shall be construed to relieve any person from any requirement prescribed by or under authority of law with respect to drugs now included or which may hereafter be included within the classifications stated in sections 4721, 6001, and 6151 of title 26, or to marihuana as defined in section 4761 of title 26.

(c) Sales restrictions

(1) No person may sell, purchase, or trade or offer to sell, purchase, or trade any drug sample. For purposes of this paragraph and subsection (d) of this section, the term "drug sample" means a unit of a drug, subject to subsection (b) of this section, which is not intended to be sold and is intended to promote the sale of the drug. Nothing in this paragraph shall subject an offi-

cer or executive of a drug manufacturer or distributor to criminal liability solely because of a sale, purchase, trade, or offer to sell, purchase, or trade in violation of this paragraph by other employees of the manufacturer or distributor.

(2) No person may sell, purchase, or trade, offer to sell, purchase, or trade, or counterfeit any coupon. For purposes of this paragraph, the term “coupon” means a form which may be redeemed, at no cost or at a reduced cost, for a drug which is prescribed in accordance with subsection (b) of this section.

(3)(A) No person may sell, purchase, or trade, or offer to sell, purchase, or trade, any drug—

(i) which is subject to subsection (b) of this section, and

(ii)(I) which was purchased by a public or private hospital or other health care entity, or

(II) which was donated or supplied at a reduced price to a charitable organization described in section 501(c)(3) of title 26.

(B) Subparagraph (A) does not apply to—

(i) the purchase or other acquisition by a hospital or other health care entity which is a member of a group purchasing organization of a drug for its own use from the group purchasing organization or from other hospitals or health care entities which are members of such organization,

(ii) the sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by an organization described in subparagraph (A)(ii)(II) to a nonprofit affiliate of the organization to the extent otherwise permitted by law,

(iii) a sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug among hospitals or other health care entities which are under common control,

(iv) a sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug for emergency medical reasons, or

(v) a sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug pursuant to a prescription executed in accordance with subsection (b) of this section.

For purposes of this paragraph, the term “entity” does not include a wholesale distributor of drugs or a retail pharmacy licensed under State law and the term “emergency medical reasons” includes transfers of a drug between health care entities or from a health care entity to a retail pharmacy undertaken to alleviate temporary shortages of the drug arising from delays in or interruptions of regular distribution schedules.

(d) Distribution of drug samples

(1) Except as provided in paragraphs (2) and (3), no person may distribute any drug sample. For purposes of this subsection, the term “distribute” does not include the providing of a drug sample to a patient by a—

(A) practitioner licensed to prescribe such drug,

(B) health care professional acting at the direction and under the supervision of such a practitioner, or

(C) pharmacy of a hospital or of another health care entity that is acting at the direc-

tion of such a practitioner and that received such sample pursuant to paragraph (2) or (3).

(2)(A) The manufacturer or authorized distributor of record of a drug subject to subsection (b) of this section may, in accordance with this paragraph, distribute drug samples by mail or common carrier to practitioners licensed to prescribe such drugs or, at the request of a licensed practitioner, to pharmacies of hospitals or other health care entities. Such a distribution of drug samples may only be made—

(i) in response to a written request for drug samples made on a form which meets the requirements of subparagraph (B), and

(ii) under a system which requires the recipient of the drug sample to execute a written receipt for the drug sample upon its delivery and the return of the receipt to the manufacturer or authorized distributor of record.

(B) A written request for a drug sample required by subparagraph (A)(i) shall contain—

(i) the name, address, professional designation, and signature of the practitioner making the request,

(ii) the identity of the drug sample requested and the quantity requested,

(iii) the name of the manufacturer of the drug sample requested, and

(iv) the date of the request.

(C) Each drug manufacturer or authorized distributor of record which makes distributions by mail or common carrier under this paragraph shall maintain, for a period of 3 years, the request forms submitted for such distributions and the receipts submitted for such distributions and shall maintain a record of distributions of drug samples which identifies the drugs distributed and the recipients of the distributions. Forms, receipts, and records required to be maintained under this subparagraph shall be made available by the drug manufacturer or authorized distributor of record to Federal and State officials engaged in the regulation of drugs and in the enforcement of laws applicable to drugs.

(3) The manufacturer or authorized distributor of record of a drug subject to subsection (b) of this section may, by means other than mail or common carrier, distribute drug samples only if the manufacturer or authorized distributor of record makes the distributions in accordance with subparagraph (A) and carries out the activities described in subparagraphs (B) through (F) as follows:

(A) Drug samples may only be distributed—

(i) to practitioners licensed to prescribe such drugs if they make a written request for the drug samples, or

(ii) at the written request of such a licensed practitioner, to pharmacies of hospitals or other health care entities.

A written request for drug samples shall be made on a form which contains the practitioner's name, address, and professional designation, the identity of the drug sample requested, the quantity of drug samples requested, the name of the manufacturer or authorized distributor of record of the drug sample, the date of the request and signature of the practitioner making the request.

(B) Drug manufacturers or authorized distributors of record shall store drug samples under conditions that will maintain their stability, integrity, and effectiveness and will assure that the drug samples will be free of contamination, deterioration, and adulteration.

(C) Drug manufacturers or authorized distributors of record shall conduct, at least annually, a complete and accurate inventory of all drug samples in the possession of representatives of the manufacturer or authorized distributor of record. Drug manufacturers or authorized distributors of record shall maintain lists of the names and address of each of their representatives who distribute drug samples and of the sites where drug samples are stored. Drug manufacturers or authorized distributors of record shall maintain records for at least 3 years of all drug samples distributed, destroyed, or returned to the manufacturer or authorized distributor of record, of all inventories maintained under this subparagraph, of all thefts or significant losses of drug samples, and of all requests made under subparagraph (A) for drug samples. Records and lists maintained under this subparagraph shall be made available by the drug manufacturer or authorized distributor of record to the Secretary upon request.

(D) Drug manufacturers or authorized distributors of record shall notify the Secretary of any significant loss of drug samples and any known theft of drug samples.

(E) Drug manufacturers or authorized distributors of record shall report to the Secretary any conviction of their representatives for violations of subsection (c)(1) of this section or a State law because of the sale, purchase, or trade of a drug sample or the offer to sell, purchase, or trade a drug sample.

(F) Drug manufacturers or authorized distributors of record shall provide to the Secretary the name and telephone number of the individual responsible for responding to a request for information respecting drug samples.

(e) Wholesale distributors; guidelines for licensing; definitions

(1)(A) Each person who is engaged in the wholesale distribution of a drug subject to subsection (b) of this section and who is not the manufacturer or an authorized distributor of record of such drug shall, before each wholesale distribution of such drug (including each distribution to an authorized distributor of record or to a retail pharmacy), provide to the person who receives the drug a statement (in such form and containing such information as the Secretary may require) identifying each prior sale, purchase, or trade of such drug (including the date of the transaction and the names and addresses of all parties to the transaction).

(B) Each manufacturer of a drug subject to subsection (b) of this section shall maintain at its corporate offices a current list of the authorized distributors of record of such drug.

(2)(A) No person may engage in the wholesale distribution in interstate commerce of drugs subject to subsection (b) of this section in a State unless such person is licensed by the State in accordance with the guidelines issued under subparagraph (B).

(B) The Secretary shall by regulation issue guidelines establishing minimum standards, terms, and conditions for the licensing of persons to make wholesale distributions in interstate commerce of drugs subject to subsection (b) of this section. Such guidelines shall prescribe requirements for the storage and handling of such drugs and for the establishment and maintenance of records of the distributions of such drugs.

(3) For the purposes of this subsection and subsection (d) of this section—

(A) the term “authorized distributors of record” means those distributors with whom a manufacturer has established an ongoing relationship to distribute such manufacturer’s products, and

(B) the term “wholesale distribution” means distribution of drugs subject to subsection (b) of this section to other than the consumer or patient but does not include intracompany sales and does not include distributions of drugs described in subsection (c)(3)(B) of this section.

(f) Veterinary prescription drugs

(1)(A) A drug intended for use by animals other than man, other than a veterinary feed directive drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug, which—

(i) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary for its use, is not safe for animal use except under the professional supervision of a licensed veterinarian, or

(ii) is limited by an approved application under subsection (b) of section 360b of this title, a conditionally-approved application under section 360ccc of this title, or an index listing under section 360ccc-1 of this title to use under the professional supervision of a licensed veterinarian,

shall be dispensed only by or upon the lawful written or oral order of a licensed veterinarian in the course of the veterinarian’s professional practice.

(B) For purposes of subparagraph (A), an order is lawful if the order—

(i) is a prescription or other order authorized by law,

(ii) is, if an oral order, promptly reduced to writing by the person lawfully filling the order, and filed by that person, and

(iii) is refilled only if authorized in the original order or in a subsequent oral order promptly reduced to writing by the person lawfully filling the order, and filed by that person.

(C) The act of dispensing a drug contrary to the provisions of this paragraph shall be deemed to be an act which results in the drug being misbranded while held for sale.

(2) Any drug when dispensed in accordance with paragraph (1) of this subsection—

(A) shall be exempt from the requirements of section 352 of this title, except subsections (a), (g), (h), (i)(2), (i)(3), and (p) of such section, and

(B) shall be exempt from the packaging requirements of subsections (g), (h), and (p) of such section, if—

(i) when dispensed by a licensed veterinarian, the drug bears a label containing the name and address of the practitioner and any directions for use and cautionary statements specified by the practitioner, or

(ii) when dispensed by filling the lawful order of a licensed veterinarian, the drug bears a label containing the name and address of the dispenser, the serial number and date of the order or of its filling, the name of the licensed veterinarian, and the directions for use and cautionary statements, if any, contained in such order.

The preceding sentence shall not apply to any drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail.

(3) The Secretary may by regulation exempt drugs for animals other than man subject to section 360b, 360ccc, or 360ccc-1 of this title from the requirements of paragraph (1) when such requirements are not necessary for the protection of the public health.

(4) A drug which is subject to paragraph (1) shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.". A drug to which paragraph (1) does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the statement specified in the preceding sentence.

(g) Regulation of combination products

(1) The Secretary shall in accordance with this subsection assign an agency center to regulate products that constitute a combination of a drug, device, or biological product. The Secretary shall determine the primary mode of action of the combination product. If the Secretary determines that the primary mode of action is that of—

(A) a drug (other than a biological product), the agency center charged with premarket review of drugs shall have primary jurisdiction,

(B) a device, the agency center charged with premarket review of devices shall have primary jurisdiction, or

(C) a biological product, the agency center charged with premarket review of biological products shall have primary jurisdiction.

(2) Nothing in this subsection shall prevent the Secretary from using any agency resources of the Food and Drug Administration necessary to ensure adequate review of the safety, effectiveness, or substantial equivalence of an article.

(3) The Secretary shall promulgate regulations to implement market clearance procedures in accordance with paragraphs (1) and (2) not later than 1 year after November 28, 1990.

(4)(A) Not later than 60 days after October 26, 2002, the Secretary shall establish within the Office of the Commissioner of Food and Drugs an office to ensure the prompt assignment of combination products to agency centers, the timely and effective premarket review of such products, and consistent and appropriate postmarket regulation of like products subject to the same statutory requirements to the extent permitted

by law. Additionally, the office shall, in determining whether a product is to be designated a combination product, consult with the component within the Office of the Commissioner of Food and Drugs that is responsible for such determinations. Such office (referred to in this paragraph as the "Office") shall have appropriate scientific and medical expertise, and shall be headed by a director.

(B) In carrying out this subsection, the Office shall, for each combination product, promptly assign an agency center with primary jurisdiction in accordance with paragraph (1) for the premarket review of such product.

(C)(i) In carrying out this subsection, the Office shall ensure timely and effective premarket reviews by overseeing the timeliness of and coordinating reviews involving more than one agency center.

(ii) In order to ensure the timeliness of the premarket review of a combination product, the agency center with primary jurisdiction for the product, and the consulting agency center, shall be responsible to the Office with respect to the timeliness of the premarket review.

(D) In carrying out this subsection, the Office shall ensure the consistency and appropriateness of postmarket regulation of like products subject to the same statutory requirements to the extent permitted by law.

(E)(i) Any dispute regarding the timeliness of the premarket review of a combination product may be presented to the Office for resolution, unless the dispute is clearly premature.

(ii) During the review process, any dispute regarding the substance of the premarket review may be presented to the Commissioner of Food and Drugs after first being considered by the agency center with primary jurisdiction of the premarket review, under the scientific dispute resolution procedures for such center. The Commissioner of Food and Drugs shall consult with the Director of the Office in resolving the substantive dispute.

(F) The Secretary, acting through the Office, shall review each agreement, guidance, or practice of the Secretary that is specific to the assignment of combination products to agency centers and shall determine whether the agreement, guidance, or practice is consistent with the requirements of this subsection. In carrying out such review, the Secretary shall consult with stakeholders and the directors of the agency centers. After such consultation, the Secretary shall determine whether to continue in effect, modify, revise, or eliminate such agreement, guidance, or practice, and shall publish in the Federal Register a notice of the availability of such modified or revised agreement, guidance or practice. Nothing in this paragraph shall be construed as preventing the Secretary from following each agreement, guidance, or practice until continued, modified, revised, or eliminated.

(G) Not later than one year after October 26, 2002, and annually thereafter, the Secretary shall report to the appropriate committees of Congress on the activities and impact of the Office. The report shall include provisions—

(i) describing the numbers and types of combination products under review and the timeli-

ness in days of such assignments, reviews, and dispute resolutions;

(ii) identifying the number of premarket reviews of such products that involved a consulting agency center; and

(iii) describing improvements in the consistency of postmarket regulation of combination products.

(H) Nothing in this paragraph shall be construed to limit the regulatory authority of any agency center.

(5) As used in this subsection:

(A) The term “agency center” means a center or alternative organizational component of the Food and Drug Administration.

(B) The term “biological product” has the meaning given the term in section 262(i) of title 42.

(C) The term “market clearance” includes—

(i) approval of an application under section 355, 357,¹ 360e, or 360j(g) of this title,

(ii) a finding of substantial equivalence under this part, and

(iii) approval of a biologics license application under subsection (a) of section 262 of title 42.

(June 25, 1938, ch. 675, § 503, 52 Stat. 1051; Oct. 26, 1951, ch. 578, § 1, 65 Stat. 648; Pub. L. 87-781, title I, § 104(e)(2), Oct. 10, 1962, 76 Stat. 785; Pub. L. 91-601, § 6(e), formerly § 7(e), Dec. 30, 1970, 84 Stat. 1673, renumbered Pub. L. 97-35, title XII, § 1205(c), Aug. 13, 1981, 95 Stat. 716; Pub. L. 100-293, §§ 4-6, Apr. 22, 1988, 102 Stat. 96-98; Pub. L. 100-670, title I, § 105, Nov. 16, 1988, 102 Stat. 3983; Pub. L. 101-629, § 16(a), Nov. 28, 1990, 104 Stat. 4526; Pub. L. 102-108, § 2(d), Aug. 17, 1991, 105 Stat. 550; Pub. L. 102-300, § 6(d), June 16, 1992, 106 Stat. 240; Pub. L. 102-353, §§ 2(a)-(c), 4, Aug. 26, 1992, 106 Stat. 941, 942; Pub. L. 104-250, § 5(a), Oct. 9, 1996, 110 Stat. 3155; Pub. L. 105-115, title I, §§ 123(e), 126(a), (c)(1), (2), Nov. 21, 1997, 111 Stat. 2324, 2327, 2328; Pub. L. 107-250, title II, § 204, Oct. 26, 2002, 116 Stat. 1611; Pub. L. 108-282, title I, § 102(b)(5)(F), Aug. 2, 2004, 118 Stat. 903; Pub. L. 113-54, title II, § 204(a)(1)-(4), (b), Nov. 27, 2013, 127 Stat. 630-635.)

AMENDMENT OF SUBSECTIONS (d) AND (e)

Pub. L. 113-54, title II, § 204(a)(1)-(4), (b), (c), Nov. 27, 2013, 127 Stat. 630-636, provided that, effective Jan. 1, 2015, this section is amended as follows:

(1) in subsection (d), by adding at the end the following:

(4) In this subsection, the term “authorized distributors of record” means those distributors with whom a manufacturer has established an ongoing relationship to distribute such manufacturer’s products.; and

(2) in subsection (e), by striking paragraphs

(1) to (3) and adding the following:

(1) Requirement.—Subject to section 360eee-2 of this title:

(A) In general.—No person may engage in wholesale distribution of a drug subject to subsection (b)(1) in any State unless such person—

(i)(I) is licensed by the State from which the drug is distributed; or

(II) if the State from which the drug is distributed has not established a licensure requirement, is licensed by the Secretary; and

(ii) if the drug is distributed interstate, is licensed by the State into which the drug is distributed if the State into which the drug is distributed requires the licensure of a person that distributes drugs into the State.

(B) Standards.—Each Federal and State license described in subparagraph (A) shall meet the standards, terms, and conditions established by the Secretary under section 360eee-2 of this title.

(2) Reporting and database.—

(A) Reporting.—Beginning January 1, 2015, any person who owns or operates an establishment that engages in wholesale distribution shall—

(i) report to the Secretary, on an annual basis pursuant to a schedule determined by the Secretary—

(I) each State by which the person is licensed and the appropriate identification number of each such license; and

(II) the name, address, and contact information of each facility at which, and all trade names under which, the person conducts business; and

(ii) report to the Secretary within a reasonable period of time and in a reasonable manner, as determined by the Secretary, any significant disciplinary actions, such as the revocation or suspension of a wholesale distributor license, taken by a State or the Federal Government during the reporting period against the wholesale distributor.

(B) Database.—Not later than January 1, 2015, the Secretary shall establish a database of authorized wholesale distributors. Such database shall—

(i) identify each authorized wholesale distributor by name, contact information, and each State where such wholesale distributor is appropriately licensed to engage in wholesale distribution;

(ii) be available to the public on the Internet Web site of the Food and Drug Administration; and

(iii) be regularly updated on a schedule determined by the Secretary.

(C) Coordination.—The Secretary shall establish a format and procedure for appropriate State officials to access the information provided pursuant to subparagraph (A) in a prompt and secure manner.

(D) Confidentiality.—Nothing in this paragraph shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(3) Costs.—

(A) Authorized fees of secretary.—If a State does not establish a licensing program for persons engaged in the wholesale distribution of a drug subject to subsection (b), the Secretary shall license a person engaged in wholesale distribution located in such State and may collect a reasonable fee in such amount necessary to reimburse the Secretary for costs associated with establishing and administering the licensure program and

¹ See References in Text note below.

conducting periodic inspections under this section. The Secretary shall adjust fee rates as needed on an annual basis to generate only the amount of revenue needed to perform this service. Fees authorized under this paragraph shall be collected and available for obligation only to the extent and in the amount provided in advance in appropriations Acts. Such fees are authorized to remain available until expended. Such sums as may be necessary may be transferred from the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation.

(B) *State licensing fees.*—Nothing in this chapter shall prohibit States from collecting fees from wholesale distributors in connection with State licensing of such distributors.

(4) For the purposes of this subsection and subsection (d), the term “wholesale distribution” means the distribution of a drug subject to subsection (b) to a person other than a consumer or patient, or receipt of a drug subject to subsection (b) by a person other than the consumer or patient, but does not include—

(A) intracompany distribution of any drug between members of an affiliate or within a manufacturer;

(B) the distribution of a drug, or an offer to distribute a drug among hospitals or other health care entities which are under common control;

(C) the distribution of a drug or an offer to distribute a drug for emergency medical reasons, including a public health emergency declaration pursuant to section 247d of title 42, except that, for purposes of this paragraph, a drug shortage not caused by a public health emergency shall not constitute an emergency medical reason;

(D) the dispensing of a drug pursuant to a prescription executed in accordance with subsection (b)(1);

(E) the distribution of minimal quantities of drug by a licensed retail pharmacy to a licensed practitioner for office use;

(F) the distribution of a drug or an offer to distribute a drug by a charitable organization to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

(G) the purchase or other acquisition by a dispenser, hospital, or other health care entity of a drug for use by such dispenser, hospital, or other health care entity;

(H) the distribution of a drug by the manufacturer of such drug;

(I) the receipt or transfer of a drug by an authorized third-party logistics provider provided that such third-party logistics provider does not take ownership of the drug;

(J) a common carrier that transports a drug, provided that the common carrier does not take ownership of the drug;

(K) the distribution of a drug, or an offer to distribute a drug by an authorized repackager that has taken ownership or possession of the drug and repacks it in accordance with section 360eee-1(e) of this title;

(L) salable drug returns when conducted by a dispenser;

(M) the distribution of a collection of finished medical devices, which may include a product or biological product, assembled in kit form strictly

for the convenience of the purchaser or user (referred to in this subparagraph as a “medical convenience kit”) if—

(i) the medical convenience kit is assembled in an establishment that is registered with the Food and Drug Administration as a device manufacturer in accordance with section 360(b)(2) of this title;

(ii) the medical convenience kit does not contain a controlled substance that appears in a schedule contained in the Comprehensive Drug Abuse Prevention and Control Act of 1970;

(iii) in the case of a medical convenience kit that includes a product, the person that manufactures the kit—

(I) purchased such product directly from the pharmaceutical manufacturer or from a wholesale distributor that purchased the product directly from the pharmaceutical manufacturer; and

(II) does not alter the primary container or label of the product as purchased from the manufacturer or wholesale distributor; and

(iv) in the case of a medical convenience kit that includes a product, the product is—

(I) an intravenous solution intended for the replenishment of fluids and electrolytes;

(II) a product intended to maintain the equilibrium of water and minerals in the body;

(III) a product intended for irrigation or reconstitution;

(IV) an anesthetic;

(V) an anticoagulant;

(VI) a vasopressor; or

(VII) a sympathomimetic;

(N) the distribution of an intravenous drug that, by its formulation, is intended for the replenishment of fluids and electrolytes (such as sodium, chloride, and potassium) or calories (such as dextrose and amino acids);

(O) the distribution of an intravenous drug used to maintain the equilibrium of water and minerals in the body, such as dialysis solutions;

(P) the distribution of a drug that is intended for irrigation, or sterile water, whether intended for such purposes or for injection;

(Q) the distribution of medical gas, as defined in section 360ddd of this title;

(R) facilitating the distribution of a product by providing solely administrative services, including processing of orders and payments; or

(S) the transfer of a product by a hospital or other health care entity, or by a wholesale distributor or manufacturer operating at the direction of the hospital or other health care entity, to a repackager described in section 360eee(16)(B) of this title and registered under section 360 of this title for the purpose of repackaging the drug for use by that hospital, or other health care entity and other health care entities that are under common control, if ownership of the drug remains with the hospital or other health care entity at all times.

(5) *Third-party logistics providers.*—Notwithstanding paragraphs (1) through (4), each entity that meets the definition of a third-party logistics provider under section 360eee(22) of this title shall obtain a license as a third-party logistics provider as described in section 360eee-3(a) of this title and

is not required to obtain a license as a wholesale distributor if the entity never assumes an ownership interest in the product it handles.

(6) *Affiliate*.—For purposes of this subsection, the term “affiliate” means a business entity that has a relationship with a second business entity if, directly or indirectly—

(A) one business entity controls, or has the power to control, the other business entity; or

(B) a third party controls, or has the power to control, both of the business entities.

See 2013 Amendment notes below.

REFERENCES IN TEXT

Section 357 of this title, referred to in subsec. (g)(5)(C)(i), was repealed by Pub. L. 105–115, title I, §125(b)(1), Nov. 21, 1997, 111 Stat. 2325.

CODIFICATION

In subsec. (b)(5), “sections 4721, 6001, and 6151 of title 26” and “section 4761 of title 26” substituted for “section 3220 of the Internal Revenue Code (26 U.S.C. 3220)” and “section 3238(b) of the Internal Revenue Code (26 U.S.C. 3238(b))”, respectively, on authority of section 7852(b) of Title 26, Internal Revenue Code.

AMENDMENTS

2013—Subsec. (d)(4). Pub. L. 113–54, §204(b), added par. (4).

Subsec. (e). Pub. L. 113–54, §204(a)(1)–(4), added pars. (1) to (6) and struck out former pars. (1) to (3). Prior to amendment, pars. (1) to (3) set out certain disclosure and licensing requirements for wholesale distributors and defined “authorized distributors of record” and “wholesale distribution”.

2004—Subsec. (f)(1)(A)(ii). Pub. L. 108–282, §102(b)(5)(F)(i), substituted “360b of this title, a conditionally-approved application under section 360ccc of this title, or an index listing under section 360ccc–1 of this title” for “360b of this title”.

Subsec. (f)(3). Pub. L. 108–282, §102(b)(5)(F)(ii), substituted “section 360b, 360ccc, or 360ccc–1” for “section 360b”.

2002—Subsec. (g)(1). Pub. L. 107–250, §204(1)(A), substituted “shall in accordance with this subsection assign an agency center” for “shall designate a component of the Food and Drug Administration” in first sentence of introductory provisions.

Subsec. (g)(1)(A) to (C). Pub. L. 107–250, §204(1)(B), substituted “the agency center charged” for “the persons charged”.

Subsec. (g)(4). Pub. L. 107–250, §204(3), added par. (4). Former par. (4) redesignated (5).

Subsec. (g)(5). Pub. L. 107–250, §204(2), (4), redesignated par. (4) as (5), added subpar. (A), and redesignated former subpars. (A) and (B) as (B) and (C), respectively.

1997—Subsec. (b)(1)(A) to (C). Pub. L. 105–115, §126(c)(1), redesignated subpars. (B) and (C) as (A) and (B), respectively, and struck out former subpar. (A), which read as follows: “is a habit-forming drug to which section 352(d) of this title applies; or”.

Subsec. (b)(3). Pub. L. 105–115, §126(c)(2), struck out reference to section 352(d) of this title before “355”.

Subsec. (b)(4). Pub. L. 105–115, §126(a), amended par. (4) generally. Prior to amendment, par. (4) read as follows: “A drug which is subject to paragraph (1) of this subsection shall be deemed to be misbranded if at any time prior to dispensing its label fails to bear the statement ‘Caution: Federal law prohibits dispensing without prescription’. A drug to which paragraph (1) of this subsection does not apply shall be deemed to be misbranded if at any time prior to dispensing its label bears the caution statement quoted in the preceding sentence.”

Subsec. (g)(4)(A). Pub. L. 105–115, §123(e)(1), substituted “section 262(i) of title 42” for “section 262(a) of title 42”.

Subsec. (g)(4)(B)(iii). Pub. L. 105–115, §123(e)(2), substituted “biologics license application under subsection (a)” for “product or establishment license under subsection (a) or (d)”.

1996—Subsec. (f)(1)(A). Pub. L. 104–250 inserted “, other than a veterinary feed directive drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug,” after “other than man” in introductory provisions.

1992—Subsec. (d)(1). Pub. L. 102–353, §4(1), amended par. (1) generally. Prior to amendment, par. (1) read as follows: “Except as provided in paragraphs (2) and (3), no representative of a drug manufacturer or distributor may distribute any drug sample.”

Subsec. (d)(2). Pub. L. 102–353, §4(2), substituted “authorized distributor of record” for “distributor” wherever appearing.

Subsec. (d)(3). Pub. L. 102–353, §4(2), substituted “authorized distributor of record” for “distributor” and “authorized distributors of record” for “distributors” wherever appearing.

Subsec. (e)(1). Pub. L. 102–353, §4(3), amended par. (1) generally. Prior to amendment, par. (1) read as follows: “Each person who is engaged in the wholesale distribution of drugs subject to subsection (b) of this section and who is not an authorized distributor of record of such drugs shall provide to each wholesale distributor of such drugs a statement identifying each sale of the drug (including the date of the sale) before the sale to such wholesale distributor. Each manufacturer shall maintain at its corporate offices a current list of such authorized distributors.”

Subsec. (e)(2)(A). Pub. L. 102–353, §2(a), (d), temporarily inserted “or has registered with the Secretary in accordance with paragraph (3)”. See Termination Date of 1992 Amendment note below.

Subsec. (e)(3). Pub. L. 102–353, §2(b), (d), temporarily added par. (3). Former par. (3) redesignated (4). See Termination Date of 1992 Amendment note below.

Subsec. (e)(4). Pub. L. 102–353, §4(4), inserted “and subsection (d) of this section” after “For the purposes of this subsection”.

Pub. L. 102–353, §2(b), (d), temporarily redesignated par. (3) as (4). See Termination Date of 1992 Amendment note below.

Subsec. (f)(1)(B). Pub. L. 102–353, §2(c), which directed the substitution of “an order” for “and order”, could not be executed because “and order” did not appear in subpar. (B).

Subsec. (g)(3). Pub. L. 102–300 substituted “clearance” for “approval”.

1991—Subsec. (c). Pub. L. 102–108, §2(d)(3), redesignated subsec. (c), relating to veterinary prescription drugs, as (f). Former subsec. (f) redesignated (g).

Subsec. (c)(2), (3)(B)(v). Pub. L. 102–108, §2(d)(1), made technical amendment to reference to subsection (b) of this section involving corresponding provision of original act.

Subsec. (d)(3)(E). Pub. L. 102–108, §2(d)(2), made technical amendment to reference to subsection (c)(1) of this section involving corresponding provision of original act.

Subsec. (f). Pub. L. 102–108, §2(d)(4), redesignated subsec. (f), relating to regulation of combination products, as (g).

Pub. L. 102–108, §2(d)(3), redesignated subsec. (c), relating to veterinary prescription drugs, as (f).

Subsec. (g). Pub. L. 102–108, §2(d)(4), redesignated subsec. (f), relating to regulation of combination products, as (g).

1990—Pub. L. 101–629, §16(a)(1), substituted “Exemptions and consideration for certain drugs, devices, and biological products” for “Exemptions in case of drugs and devices” in section catchline.

Subsec. (f). Pub. L. 101–629, §16(a)(2), added subsec. (f). 1988—Subsec. (c). Pub. L. 100–670 added subsec. (c) relating to veterinary prescription drugs.

Pub. L. 100–293, §4, added subsec. (c) relating to sales restrictions.

Subsec. (d). Pub. L. 100–293, §5, added subsec. (d).

Subsec. (e). Pub. L. 100-293, § 6, added subsec. (e).
1970—Subsec. (b)(2). Pub. L. 91-601 included exemption from packaging requirements of subsec. (p) of section 352 of this title.

1962—Subsec. (b)(1)(C). Pub. L. 87-781 substituted “approved” for “effective”.

1951—Subsec. (b). Act Oct. 26, 1951, amended subsec. (b) generally to protect the public from abuses in the sale of potent prescription drugs, and to relieve retail pharmacists and the public from unnecessary restrictions on the dispensation of drugs that are safe to use without supervision of a doctor.

EFFECTIVE DATE OF 2013 AMENDMENT

Pub. L. 113-54, title II, § 204(c), Nov. 27, 2013, 127 Stat. 636, provided that: “The amendments made by subsections (a) and (b) [enacting section 360eee-2 of this title and amending this section] shall take effect on January 1, 2015.”

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

TERMINATION DATE OF 1992 AMENDMENT

Pub. L. 102-353, § 2(d), Aug. 26, 1992, 106 Stat. 941, provided that: “Effective September 14, 1994, the amendments made by subsections (a) and (b) [amending this section] shall no longer be in effect.”

EFFECTIVE DATE OF 1988 AMENDMENT

Pub. L. 100-293, § 8, Apr. 22, 1988, 102 Stat. 100, provided that:

“(a) GENERAL RULE.—Except as provided in subsection (b), this Act and the amendments made by this Act [amending this section and sections 331, 333, and 381 of this title and enacting provisions set out as notes under this section and section 301 of this title] shall take effect upon the expiration of 90 days after the date of the enactment of this Act [Apr. 22, 1988].

“(b) EXCEPTION.—

“(1) Section 503(d) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353(d)] (as added by section 5 of this Act) shall take effect upon the expiration of 180 days after the date of the enactment of this Act [Apr. 22, 1988].

“(2) The Secretary of Health and Human Services shall by regulation issue the guidelines required by section 503(e)(2)(B) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353(e)(2)(B)] (as added by section 6 of this Act) not later than 180 days after the date of the enactment of this Act. Section 503(e)(2)(A) of such Act shall take effect upon the expiration of 2 years after the date such regulations are promulgated and take effect.”

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91-601 effective Dec. 30, 1970, and regulations establishing special packaging standards effective no sooner than 180 days or later than one year from date regulations are final, or an earlier date published in Federal Register, see section 8 of Pub. L. 91-601, set out as an Effective Date note under section 1471 of Title 15, Commerce and Trade.

EFFECTIVE DATE OF 1962 AMENDMENT

Amendment by Pub. L. 87-781 effective Oct. 10, 1962, see section 107 of Pub. L. 87-781, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1951 AMENDMENT

Amendment by act Oct. 26, 1951, effective six months after Oct. 26, 1951, see section 3 of act Oct. 26, 1951, set out as a note under section 333 of this title.

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare

[now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

EFFECTIVE MEDICATION GUIDES

Pub. L. 104-180, title VI, § 601, Aug. 6, 1996, 110 Stat. 1593, provided that:

“(a) IN GENERAL.—Not later than 30 days after the date of enactment of this Act [Aug. 6, 1996], the Secretary of the Department of Health and Human Services shall request that national organizations representing health care professionals, consumer organizations, voluntary health agencies, the pharmaceutical industry, drug wholesalers, patient drug information database companies, and other relevant parties collaborate to develop a long-range comprehensive action plan to achieve goals consistent with the goals of the proposed rule of the Food and Drug Administration on ‘Prescription Drug Product Labeling: Medication Guide Requirements’ (60 Fed. Reg. 44182; relating to the provision of oral and written prescription information to consumers).

“(b) GOALS.—Goals consistent with the proposed rule described in subsection (a) are the distribution of useful written information to 75 percent of individuals receiving new prescriptions [sic] by the year 2000 and to 95 percent by the year 2006.

“(c) PLAN.—The plan described in subsection (a) shall—

“(1) identify the plan goals;

“(2) assess the effectiveness of the current private-sector approaches used to provide oral and written prescription information to consumers;

“(3) develop guidelines for providing effective oral and written prescription information consistent with the findings of any such assessment;

“(4) contain elements necessary to ensure the transmittal of useful information to the consuming public, including being scientifically accurate, non-promotional in tone and content, sufficiently specific and comprehensive as to adequately inform consumers about the use of the product, and in an understandable, legible format that is readily comprehensible and not confusing to consumers expected to use the product.[]

“(5) develop a mechanism to assess periodically the quality of the oral and written prescription information and the frequency with which the information is provided to consumers; and

“(6) provide for compliance with relevant State board regulations.

“(d) LIMITATION ON THE AUTHORITY OF THE SECRETARY.—The Secretary of the Department of Health and Human Services shall have no authority to implement the proposed rule described in subsection (a), or to develop any similar regulation, policy statement, or other guideline specifying a uniform content or format for written information voluntarily provided to consumers about prescription drugs if, (1) not later than 120 days after the date of enactment of this Act [Aug. 6, 1996], the national organizations described in subsection (a) develop and submit to the Secretary for Health and Human Services a comprehensive, long-range action plan (as described in subsection (a)) which shall be acceptable to the Secretary of Health and Human Services; (2) the aforementioned plan is submitted to the Secretary of Health and Human Services for review and acceptance: *Provided*, That the Secretary shall give due consideration to the submitted plan and that any such acceptance shall not be arbitrarily withheld; and (3) the implementation of (a) a plan accepted by the Secretary commences within 30 days of the Secretary’s acceptance of such plan, or (b) the plan submitted to the Secretary commences within 60 days of the submission of such plan if the Secretary fails to take any action on the plan within 30 days of the submission of the plan. The Secretary shall accept, reject or suggest modifications to the plan submitted within 30 days of its submission. The Secretary may confer

with and assist private parties in the development of the plan described in subsections (a) and (b).

“(e) SECRETARY REVIEW.—Not later than January 1, 2001, the Secretary of the Department of Health and Human Services shall review the status of private-sector initiatives designed to achieve the goals of the plan described in subsection (a), and if such goals are not achieved, the limitation in subsection (d) shall not apply, and the Secretary shall seek public comment on other initiatives that may be carried out to meet such goals.”

CONGRESSIONAL FINDINGS

Pub. L. 100-293, § 2, Apr. 22, 1988, 102 Stat. 95, provided that: “The Congress finds the following:

“(1) American consumers cannot purchase prescription drugs with the certainty that the products are safe and effective.

“(2) The integrity of the distribution system for prescription drugs is insufficient to prevent the introduction and eventual retail sale of substandard, ineffective, or even counterfeit drugs.

“(3) The existence and operation of a wholesale submarket, commonly known as the ‘diversion market’, prevents effective control over or even routine knowledge of the true sources of prescription drugs in a significant number of cases.

“(4) Large amounts of drugs are being reimported to the United States as American goods returned. These imports are a health and safety risk to American consumers because they may have become subpotent or adulterated during foreign handling and shipping.

“(5) The ready market for prescription drug reimports has been the catalyst for a continuing series of frauds against American manufacturers and has provided the cover for the importation of foreign counterfeit drugs.

“(6) The existing system of providing drug samples to physicians through manufacturer’s representatives has been abused for decades and has resulted in the sale to consumers of misbranded, expired, and adulterated pharmaceuticals.

“(7) The bulk resale of below wholesale priced prescription drugs by health care entities, for ultimate sale at retail, helps fuel the diversion market and is an unfair form of competition to wholesalers and retailers that must pay otherwise prevailing market prices.

“(8) The effect of these several practices and conditions is to create an unacceptable risk that counterfeit, adulterated, misbranded, subpotent, or expired drugs will be sold to American consumers.”

§ 353a. Pharmacy compounding

(a) In general

Sections 351(a)(2)(B), 352(f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding—

(1) is by—

(A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or

(B) a licensed physician,

on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

(2)(A) is by a licensed pharmacist or licensed physician in limited quantities before the re-

ceipt of a valid prescription order for such individual patient; and

(B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between—

(i) the licensed pharmacist or licensed physician; and

(ii)(I) such individual patient for whom the prescription order will be provided; or

(II) the physician or other licensed practitioner who will write such prescription order.

(b) Compounded drug

(1) Licensed pharmacist and licensed physician

A drug product may be compounded under subsection (a) of this section if the licensed pharmacist or licensed physician—

(A) compounds the drug product using bulk drug substances, as defined in regulations of the Secretary published at section 207.3(a)(4) of title 21 of the Code of Federal Regulations—

(i) that—

(I) comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(II) if such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or

(III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (c) of this section;

(ii) that are manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(iii) that are accompanied by valid certificates of analysis for each bulk drug substance;

(B) compounds the drug product using ingredients (other than bulk drug substances) that comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(C) does not compound a drug product that appears on a list published by the Secretary in the Federal Register of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective; and

(D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.

(2) Definition

For purposes of paragraph (1)(D), the term “essentially a copy of a commercially available drug product” does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.

(3) Drug product

A drug product may be compounded under subsection (a) only if—

(A) such drug product is not a drug product identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product; and

(B) such drug product is compounded in a State—

(i) that has entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or

(ii) that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician.

The Secretary shall, in consultation with the National Association of Boards of Pharmacy, develop a standard memorandum of understanding for use by the States in complying with subparagraph (B)(i).

(c) Regulations**(1) In general**

The Secretary shall issue regulations to implement this section. Before issuing regulations to implement subsections (b)(1)(A)(i)(III), (b)(1)(C), or (b)(3)(A) of this section, the Secretary shall convene and consult an advisory committee on compounding unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary.

(2) Limiting compounding

The Secretary, in consultation with the United States Pharmacopoeia Convention, Incorporated, shall promulgate regulations identifying drug substances that may be used in

compounding under subsection (b)(1)(A)(i)(III) of this section for which a monograph does not exist or which are not components of drug products approved by the Secretary. The Secretary shall include in the regulation the criteria for such substances, which shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify.

(d) Application

This section shall not apply to—

(1) compounded positron emission tomography drugs as defined in section 321(ii) of this title; or

(2) radiopharmaceuticals.

(e) “Compounding” defined

As used in this section, the term “compounding” does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling.

(June 25, 1938, ch. 675, §503A, as added Pub. L. 105-115, title I, §127(a), Nov. 21, 1997, 111 Stat. 2328; amended Pub. L. 113-54, title I, §106(a), Nov. 27, 2013, 127 Stat. 598.)

AMENDMENTS

2013—Subsec. (a). Pub. L. 113-54, §106(a)(1), struck out “unsolicited” before “receipt of a valid prescription” in introductory provisions.

Subsec. (b)(1)(A)(i)(III). Pub. L. 113-54, §106(a)(4), substituted “subsection (c)” for “subsection (d)”.

Subsecs. (c) to (f). Pub. L. 113-54, §106(a)(2), (3), redesignated subsecs. (d) to (f) as (c) to (e), respectively, and struck out former subsec. (c). Prior to amendment, subsec. (c) read as follows: “A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.”

EFFECTIVE DATE

Pub. L. 105-115, title I, §127(b), Nov. 21, 1997, 111 Stat. 2330, provided that: “Section 503A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 353a], added by subsection (a), shall take effect upon the expiration of the 1-year period beginning on the date of the enactment of this Act [Nov. 21, 1997].”

§ 353a-1. Enhanced communication**(a) Submissions from State boards of pharmacy**

In a manner specified by the Secretary of Health and Human Services (referred to in this section as the “Secretary”), the Secretary shall receive submissions from State boards of pharmacy—

(1) describing actions taken against compounding pharmacies, as described in subsection (b); or

(2) expressing concerns that a compounding pharmacy may be acting contrary to section 353a of this title.

(b) Content of submissions from State boards of pharmacy

An action referred to in subsection (a)(1) is, with respect to a pharmacy that compounds drugs, any of the following:

(1) The issuance of a warning letter, or the imposition of sanctions or penalties, by a State for violations of a State's pharmacy regulations pertaining to compounding.

(2) The suspension or revocation of a State-issued pharmacy license or registration for violations of a State's pharmacy regulations pertaining to compounding.

(3) The recall of a compounded drug due to concerns relating to the quality or purity of such drug.

(c) Consultation

The Secretary shall implement subsection (a) in consultation with the National Association of Boards of Pharmacy.

(d) Notifying State boards of pharmacy

The Secretary shall immediately notify State boards of pharmacy when—

(1) the Secretary receives a submission under subsection (a)(1); or

(2) the Secretary makes a determination that a pharmacy is acting contrary to section 353a of this title.

(Pub. L. 113-54, title I, §105, Nov. 27, 2013, 127 Stat. 597.)

CODIFICATION

Section was enacted as part of the Compounding Quality Act and also as part of the Drug Quality and Security Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 353b. Outsourcing facilities

(a) In general

Sections 352(f)(1), 355, and 360eee-1 of this title shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility if each of the following conditions is met:

(1) Registration and reporting

The drug is compounded in an outsourcing facility that is in compliance with the requirements of subsection (b).

(2) Bulk drug substances

The drug is compounded in an outsourcing facility that does not compound using bulk drug substances (as defined in section 207.3(a)(4) of title 21, Code of Federal Regulations (or any successor regulation)), unless—

(A)(i) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, by—

(I) publishing a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal;

(II) providing a period of not less than 60 calendar days for comment on the notice; and

(III) publishing a notice in the Federal Register designating bulk drug substances for inclusion on the list; or

(ii) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 356e of this title

at the time of compounding, distribution, and dispensing;

(B) if an applicable monograph exists under the United States Pharmacopeia, the National Formulary, or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substances each comply with the monograph;

(C) the bulk drug substances are each manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(D) the bulk drug substances are each accompanied by a valid certificate of analysis.

(3) Ingredients (other than bulk drug substances)

If any ingredients (other than bulk drug substances) are used in compounding the drug, such ingredients comply with the standards of the applicable United States Pharmacopeia or National Formulary monograph, if such monograph exists, or of another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph if any.

(4) Drugs withdrawn or removed because unsafe or not effective

The drug does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(5) Essentially a copy of an approved drug

The drug is not essentially a copy of one or more approved drugs.

(6) Drugs presenting demonstrable difficulties for compounding

The drug—

(A) is not identified (directly or as part of a category of drugs) on a list published by the Secretary, through the process described in subsection (c), of drugs or categories of drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs, taking into account the risks and benefits to patients; or

(B) is compounded in accordance with all applicable conditions identified on the list described in subparagraph (A) as conditions that are necessary to prevent the drug or category of drugs from presenting the demonstrable difficulties described in subparagraph (A).

(7) Elements to assure safe use

In the case of a drug that is compounded from a drug that is the subject of a risk evaluation and mitigation strategy approved with elements to assure safe use pursuant to section 355-1 of this title, or from a bulk drug substance that is a component of such drug, the outsourcing facility demonstrates to the Secretary prior to beginning compounding that such facility will utilize controls comparable to the controls applicable under the relevant risk evaluation and mitigation strategy.

(8) Prohibition on wholesaling

The drug will not be sold or transferred by an entity other than the outsourcing facility that compounded such drug. This paragraph does not prohibit administration of a drug in a health care setting or dispensing a drug pursuant to a prescription executed in accordance with section 353(b)(1) of this title.

(9) Fees

The drug is compounded in an outsourcing facility that has paid all fees owed by such facility pursuant to section 379j-62 of this title.

(10) Labeling of drugs**(A) Label**

The label of the drug includes—

(i) the statement “This is a compounded drug.” or a reasonable comparable alternative statement (as specified by the Secretary) that prominently identifies the drug as a compounded drug;

(ii) the name, address, and phone number of the applicable outsourcing facility; and (iii) with respect to the drug—

(I) the lot or batch number;

(II) the established name of the drug;

(III) the dosage form and strength;

(IV) the statement of quantity or volume, as appropriate;

(V) the date that the drug was compounded;

(VI) the expiration date;

(VII) storage and handling instructions;

(VIII) the National Drug Code number, if available;

(IX) the statement “Not for resale”, and, if the drug is dispensed or distributed other than pursuant to a prescription for an individual identified patient, the statement “Office Use Only”; and

(X) subject to subparagraph (B)(i), a list of active and inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

(B) Container

The container from which the individual units of the drug are removed for dispensing or for administration (such as a plastic bag containing individual product syringes) shall include—

(i) the information described under subparagraph (A)(iii)(X), if there is not space on the label for such information;

(ii) the following information to facilitate adverse event reporting: www.fda.gov/medwatch and 1-800-FDA-1088 (or any successor Internet Web site or phone number); and

(iii) directions for use, including, as appropriate, dosage and administration.

(C) Additional information

The label and labeling of the drug shall include any other information as determined necessary and specified in regulations promulgated by the Secretary.

(11) Outsourcing facility requirement

The drug is compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section.

(b) Registration of outsourcing facilities and reporting of drugs**(1) Registration of outsourcing facilities****(A) Annual registration**

Upon electing and in order to become an outsourcing facility, and during the period beginning on October 1 and ending on December 31 of each year thereafter, a facility—

(i) shall register with the Secretary its name, place of business, and unique facility identifier (which shall conform to the requirements for the unique facility identifier established under section 360 of this title), and a point of contact email address; and

(ii) shall indicate whether the outsourcing facility intends to compound a drug that appears on the list in effect under section 356e of this title during the subsequent calendar year.

(B) Availability of registration for inspection; list**(i) Registrations**

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this paragraph.

(ii) List

The Secretary shall make available on the public Internet Web site of the Food and Drug Administration a list of the name of each facility registered under this subsection as an outsourcing facility, the State in which each such facility is located, whether the facility compounds from bulk drug substances, and whether any such compounding from bulk drug substances is for sterile or nonsterile drugs.

(2) Drug reporting by outsourcing facilities**(A) In general**

Upon initially registering as an outsourcing facility, once during the month of June of each year, and once during the month of December of each year, each outsourcing facility that registers with the Secretary under paragraph (1) shall submit to the Secretary a report—

(i) identifying the drugs compounded by such outsourcing facility during the previous 6-month period; and

(ii) with respect to each drug identified under clause (i), providing the active ingredient, the source of such active ingredient, the National Drug Code number of the source drug or bulk active ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the National Drug Code number of the final product, if assigned.

(B) Form

Each report under subparagraph (A) shall be prepared in such form and manner as the Secretary may prescribe by regulation or guidance.

(C) Confidentiality

Reports submitted under this paragraph shall be exempt from inspection under paragraph (1)(B)(i), unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health.

(3) Electronic registration and reporting

Registrations and drug reporting under this subsection (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting waiver.

(4) Risk-based inspection frequency**(A) In general**

Outsourcing facilities—

- (i) shall be subject to inspection pursuant to section 374 of this title; and
- (ii) shall not be eligible for the exemption under section 374(a)(2)(A) of this title.

(B) Risk-based schedule

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect outsourcing facilities in accordance with a risk-based schedule established by the Secretary.

(C) Risk factors

In establishing the risk-based schedule, the Secretary shall inspect outsourcing facilities according to the known safety risks of such outsourcing facilities, which shall be based on the following factors:

- (i) The compliance history of the outsourcing facility.
- (ii) The record, history, and nature of recalls linked to the outsourcing facility.
- (iii) The inherent risk of the drugs compounded at the outsourcing facility.
- (iv) The inspection frequency and history of the outsourcing facility, including whether the outsourcing facility has been inspected pursuant to section 374 of this title within the last 4 years.
- (v) Whether the outsourcing facility has registered under this paragraph as an entity that intends to compound a drug that appears on the list in effect under section 356e of this title.
- (vi) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

(5) Adverse event reporting

Outsourcing facilities shall submit adverse event reports to the Secretary in accordance with the content and format requirements established through guidance or regulation under section 310.305 of title 21, Code of Federal Regulations (or any successor regulations).

(c) Regulations**(1) In general**

The Secretary shall implement the list described in subsection (a)(6) through regulations.

(2) Advisory committee on compounding

Before issuing regulations to implement subsection (a)(6), the Secretary shall convene and consult an advisory committee on compounding. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopeia, pharmacists with current experience and expertise in compounding, physicians with background and knowledge in compounding, and patient and public health advocacy organizations.

(3) Interim list**(A) In general**

Before the effective date of the regulations finalized to implement subsection (a)(6), the Secretary may designate drugs, categories of drugs, or conditions as described such¹ subsection by—

- (i) publishing a notice of such substances, drugs, categories of drugs, or conditions proposed for designation, including the rationale for such designation, in the Federal Register;
- (ii) providing a period of not less than 60 calendar days for comment on the notice; and
- (iii) publishing a notice in the Federal Register designating such drugs, categories of drugs, or conditions.

(B) Sunset of notice

Any notice provided under subparagraph (A) shall not be effective after the earlier of—

- (i) the date that is 5 years after November 27, 2013; or
- (ii) the effective date of the final regulations issued to implement subsection (a)(6).

(4) Updates

The Secretary shall review, and update as necessary, the regulations containing the lists of drugs, categories of drugs, or conditions described in subsection (a)(6) regularly, but not less than once every 4 years. Nothing in the previous sentence prohibits submissions to the Secretary, before or during any 4-year period described in such sentence, requesting updates to such lists.

(d)² Definitions

In this section:

- (1) The term “compounding” includes the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug.
- (2) The term “essentially a copy of an approved drug” means—

(A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 356e of this title at the

¹ So in original.

² So in original. Two subsecs. (d) have been enacted.

time of compounding, distribution, and dispensing; or

(B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

(3) The term “approved drug” means a drug that is approved under section 355 of this title and does not appear on the list described in subsection (a)(4) of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(4)(A) The term “outsourcing facility” means a facility at one geographic location or address that—

- (i) is engaged in the compounding of sterile drugs;
- (ii) has elected to register as an outsourcing facility; and
- (iii) complies with all of the requirements of this section.

(B) An outsourcing facility is not required to be a licensed pharmacy.

(C) An outsourcing facility may or may not obtain prescriptions for identified individual patients.

(5) The term “sterile drug” means a drug that is intended for parenteral administration, an ophthalmic or oral inhalation drug in aqueous format, or a drug that is required to be sterile under Federal or State law.

(d)² Obligation to pay fees

Payment of the fee under section 379j-62 of this title, as described in subsection (a)(9), shall not relieve an outsourcing facility that is licensed as a pharmacy in any State that requires pharmacy licensing fees of its obligation to pay such State fees.

(June 25, 1938, ch. 675, §503B, as added Pub. L. 113-54, title I, §102(a)(2), Nov. 27, 2013, 127 Stat. 588.)

PRIOR PROVISIONS

A prior section 503B of act June 25, 1938, ch. 675, was renumbered section 503C by Pub. L. 113-54, §102(a)(1), Nov. 27, 2013, 127 Stat. 587, and transferred to section 353c of this title.

§ 353c. Prereview of television advertisements

(a) In general

The Secretary may require the submission of any television advertisement for a drug (including any script, story board, rough, or a completed video production of the television advertisement) to the Secretary for review under this section not later than 45 days before dissemination of the television advertisement.

(b) Review

In conducting a review of a television advertisement under this section, the Secretary may

make recommendations with respect to information included in the label of the drug—

(1) on changes that are—

- (A) necessary to protect the consumer good and well-being; or
- (B) consistent with prescribing information for the product under review; and

(2) if appropriate and if information exists, on statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to specific population groups, including elderly populations, children, and racial and ethnic minorities.

(c) No authority to require changes

Except as provided by subsection (e), this section does not authorize the Secretary to make or direct changes in any material submitted pursuant to subsection (a).

(d) Elderly populations, children, racially and ethnically diverse communities

In formulating recommendations under subsection (b), the Secretary shall take into consideration the impact of the advertised drug on elderly populations, children, and racially and ethnically diverse communities.

(e) Specific disclosures

(1) Serious risk; safety protocol

In conducting a review of a television advertisement under this section, if the Secretary determines that the advertisement would be false or misleading without a specific disclosure about a serious risk listed in the labeling of the drug involved, the Secretary may require inclusion of such disclosure in the advertisement.

(2) Date of approval

In conducting a review of a television advertisement under this section, the Secretary may require the advertisement to include, for a period not to exceed 2 years from the date of the approval of the drug under section 355 of this title or section 262 of title 42, a specific disclosure of such date of approval if the Secretary determines that the advertisement would otherwise be false or misleading.

(f) Rule of construction

Nothing in this section may be construed as having any effect on requirements under section 352(n) of this title or on the authority of the Secretary under section 314.550, 314.640, 601.45, or 601.94 of title 21, Code of Federal Regulations (or successor regulations).

(June 25, 1938, ch. 675, §503C, formerly §503B, as added Pub. L. 110-85, title IX, §901(d)(2), Sept. 27, 2007, 121 Stat. 939, renumbered §503C, Pub. L. 113-54, title I, §102(a)(1), Nov. 27, 2013, 127 Stat. 587.)

CODIFICATION

Section was formerly classified to section 353b of this title prior to renumbering by Pub. L. 113-54.

EFFECTIVE DATE

Section effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110-85, set out as an Effective Date of 2007 Amendment note under section 331 of this title.

§ 354. Veterinary feed directive drugs

(a) Lawful veterinary feed directive requirement

(1) A drug intended for use in or on animal feed which is limited by an approved application filed pursuant to section 360b(b) of this title, a conditionally-approved application filed pursuant to section 360ccc of this title, or an index listing pursuant to section 360ccc-1 of this title to use under the professional supervision of a licensed veterinarian is a veterinary feed directive drug. Any animal feed bearing or containing a veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice. When labeled, distributed, held, and used in accordance with this section, a veterinary feed directive drug and any animal feed bearing or containing a veterinary feed directive drug shall be exempt from section 352(f) of this title.

(2) A veterinary feed directive is lawful if it—

(A) contains such information as the Secretary may by general regulation or by order require; and

(B) is in compliance with the conditions and indications for use of the drug set forth in the notice published pursuant to section 360b(i) of this title, or the index listing pursuant to section 360ccc-1(e) of this title.

(3)(A) Any persons involved in the distribution or use of animal feed bearing or containing a veterinary feed directive drug and the licensed veterinarian issuing the veterinary feed directive shall maintain a copy of the veterinary feed directive applicable to each such feed, except in the case of a person distributing such feed to another person for further distribution. Such person distributing the feed shall maintain a written acknowledgment from the person to whom the feed is shipped stating that that person shall not ship or move such feed to an animal production facility without a veterinary feed directive or ship such feed to another person for further distribution unless that person has provided the same written acknowledgment to its immediate supplier.

(B) Every person required under subparagraph (A) to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(C) Any person who distributes animal feed bearing or containing a veterinary feed directive drug shall upon first engaging in such distribution notify the Secretary of that person's name and place of business. The failure to provide such notification shall be deemed to be an act which results in the drug being misbranded.

(b) Labeling and advertising

A veterinary feed directive drug and any feed bearing or containing a veterinary feed directive drug shall be deemed to be misbranded if their labeling fails to bear such cautionary statement and such other information as the Secretary may by general regulation or by order prescribe, or their advertising fails to conform to the con-

ditions and indications for use published pursuant to section 360b(i) of this title, or the index listing pursuant to section 360ccc-1(e) of this title or fails to contain the general cautionary statement prescribed by the Secretary.

(c) Nonprescription status

Neither a drug subject to this section, nor animal feed bearing or containing such a drug, shall be deemed to be a prescription article under any Federal or State law.

(June 25, 1938, ch. 675, §504, as added Pub. L. 104-250, §5(b), Oct. 9, 1996, 110 Stat. 3155; amended Pub. L. 108-282, title I, §102(b)(5)(G), (H), Aug. 2, 2004, 118 Stat. 903.)

PRIOR PROVISIONS

A prior section 354, act June 25, 1938, ch. 675, §504, 52 Stat. 1052, which directed Secretary to promulgate regulations for listing of coal-tar colors, was repealed effective July 12, 1960, subject to provisions of section 203 of Pub. L. 86-618, by Pub. L. 86-618, title I, §103(a)(2), title II, §202, July 12, 1960, 74 Stat. 398, 404.

AMENDMENTS

2004—Subsec. (a)(1). Pub. L. 108-282, §102(b)(5)(G), substituted “360b(b) of this title, a conditionally-approved application filed pursuant to section 360ccc of this title, or an index listing pursuant to section 360ccc-1 of this title” for “360b(b) of this title”.

Subsecs. (a)(2)(B), (b). Pub. L. 108-282, §102(b)(5)(H), substituted “360b(i) of this title, or the index listing pursuant to section 360ccc-1(e) of this title” for “360b(i) of this title”.

§ 355. New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, and (G) any assessments required under section 355c of this title. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and

a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section—

- (i) that such patent information has not been filed,
- (ii) that such patent has expired,
- (iii) of the date on which such patent will expire, or
- (iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(A) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) TIMING OF NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph—

- (i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or
- (ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of

whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) RECIPIENTS OF NOTICE.—An applicant required under this paragraph to give notice shall give notice to—

- (i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and
- (ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) CONTENTS OF NOTICE.—A notice required under this paragraph shall—

- (i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and
- (ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) of this section prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size—

- (i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or
- (II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or
- (ii) with respect to an application for approval of a biological product under section 262(k) of title 42, of any necessary clinical study or studies.

The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 282(j)(5)(B) of title 42. Such certification shall not be considered an element of such application.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the op-

portunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A) of this section:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) of this section is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) of this section before the date on which the application (excluding an amendment or supplement to the application) was

submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) of this section or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed—

(I) if the judgment of the district court is appealed, the approval shall be made effective on—

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28 by an applicant referred to in subsection (b)(2) of this section for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) of this section for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other

terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) of this section and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) of this section or this subsection on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active

ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or non-infringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability¹ studies) essential to the approval of the supplement and conducted or sponsored by the person sub-

¹ So in original. Probably should be "bioavailability".

mitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under

such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b) of this section; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decision-making, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for premarket approval of a drug.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with re-

spect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order

under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section; and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including—

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a “clinical hold”) if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the

clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible or it is contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a “listed drug”);

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, informa-

tion to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(i) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) TIMING OF NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph—

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) RECIPIENTS OF NOTICE.—An applicant required under this subparagraph to give notice shall give notice to—

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) CONTENTS OF NOTICE.—A notice required under this subparagraph shall—

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of

a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term “listed drug” for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Sec-

retary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or

strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bio-equivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as

may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed—

(aa) if the judgment of the district court is appealed, the approval shall be made effective on—

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval

shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-DAY EXCLUSIVITY PERIOD.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) DEFINITIONS.—In this paragraph:

(aa) 180-DAY EXCLUSIVITY PERIOD.—The term “180-day exclusivity period” means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) FIRST APPLICANT.—As used in this subsection, the term “first applicant” means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) SUBSTANTIALLY COMPLETE APPLICATION.—As used in this subsection, the term “substantially complete application” means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) TENTATIVE APPROVAL.—

(AA) IN GENERAL.—The term “tentative approval” means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the

requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

(BB) LIMITATION.—A drug that is granted tentative approval by the Secretary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(C) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28 by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing

the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either—

- (aa) the drug for which the application was approved; or
- (bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) FORFEITURE OF 180-DAY EXCLUSIVITY PERIOD.—

(i) DEFINITION OF FORFEITURE EVENT.—In this subparagraph, the term “forfeiture event”, with respect to an application under this subsection, means the occurrence of any of the following:

- (I) FAILURE TO MARKET.—The first applicant fails to market the drug by the later of—
 - (aa) the earlier of the date that is—
 - (AA) 75 days after the date on which the approval of the application of the

first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

(II) WITHDRAWAL OF APPLICATION.—The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) AMENDMENT OF CERTIFICATION.—The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) FAILURE TO OBTAIN TENTATIVE APPROVAL.—The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER.—The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the

Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of title 15, except that the term includes section 45 of title 15 to the extent that that section applies to unfair methods of competition).

(VI) EXPIRATION OF ALL PATENTS.—All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) FORFEITURE.—The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) SUBSEQUENT APPLICANT.—If all first applicants forfeit the 180-day exclusivity period under clause (ii)—

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an applica-

tion may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn

from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(i) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(8) For purposes of this subsection:

(A)(i) The term “bioavailability” means the rate and extent to which the active ingredient

or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if—

(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the

listed drug has been approved by the Secretary within 60 days of such expiration;

(ii) the labeling revision described under clause (i) does not include a change to the “Warnings” section of the labeling;

(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

(A) DEFINITION.—In this paragraph, the term “data” refers to information with respect to a drug approved under this section or under section 262 of title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities—

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

(i) IN GENERAL.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355-1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) **TIMELINESS OF REPORTING.**—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) **PRIVATE SECTOR RESOURCES.**—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) **COMPLEMENTARY APPROACHES.**—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) **AUTHORITY FOR CONTRACTS.**—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) ADVANCED ANALYSIS OF DRUG SAFETY DATA.—

(A) **PURPOSE.**—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b-1 of title 42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) **PRIVACY.**—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals

and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) **PUBLIC PROCESS FOR PRIORITY QUESTIONS.**—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through—

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

(D) PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.—

(i) **IN GENERAL.**—Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including—

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs,² safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) **REQUEST FOR SPECIFIC METHODOLOGY.**—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) **USE OF ANALYSES.**—The Secretary shall provide the analyses described in this paragraph, including the methods and results of

² So in original. Probably should be “drug.”

such analyses, about a drug to the sponsor or sponsors of such drug.

(F) QUALIFIED ENTITIES.—

(i) IN GENERAL.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) QUALIFICATION.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) CONTRACT REQUIREMENTS.—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) ENSURING PRIVACY.—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) COMPONENT OF ANOTHER ORGANIZATION.—If a qualified entity is a component of another organization—

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) TERMINATION OR NONRENEWAL.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) CONFIDENTIALITY AND PRIVACY PROTECTIONS.—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) DISPOSITION OF DATA.—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) COMPETITIVE PROCEDURES.—The Secretary shall use competitive procedures (as defined in section 132 of title 41) to enter into contracts under subparagraph (G).

(I) REVIEW OF CONTRACT IN THE EVENT OF A MERGER OR ACQUISITION.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) COORDINATION.—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall—

(A) conduct regular, bi-weekly screening of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse³ Event Reporting System within the last quarter;

(B) report to Congress not later than 2 year⁴ after September 27, 2007, on procedures and processes of the Food and Drug Administration for addressing ongoing post market safety issues identified by the Office of Surveillance and Epidemiology and how recommendations of the Office of Surveillance and Epidemiology are handled within the agency; and

(C) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments.

(I) Public disclosure of safety and effectiveness data and action package

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

³ So in original. Probably should be preceded by “the”.

⁴ So in original. Probably should be “years”.

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.

(2) ACTION PACKAGE FOR APPROVAL.—

(A) ACTION PACKAGE.—The Secretary shall publish the action package for approval of an application under subsection (b) or section 262 of title 42 on the Internet Web site of the Food and Drug Administration—

(i) not later than 30 days after the date of approval of such application for a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5 for any other drug.

(B) IMMEDIATE PUBLICATION OF SUMMARY REVIEW.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) CONTENTS.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes—

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) REVIEW.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) CONFIDENTIAL INFORMATION.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

(n) Scientific advisory panels

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administra-

tive processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) Postmarket studies and clinical trials; labeling

(1) In general

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) Definitions

For purposes of this subsection:

(A) Responsible person

The term “responsible person” means a person who—

- (i) has submitted to the Secretary a covered application that is pending; or
- (ii) is the holder of an approved covered application.

(B) Covered application

The term “covered application” means—

- (i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and
- (ii) an application under section 262 of title 42.

(C) New safety information; serious risk

The terms “new safety information”, “serious risk”, and “signal of a serious risk” have the meanings given such terms in section 355-1(b) of this title.

(3) Studies and clinical trials

(A) In general

For any or all of the purposes specified in subparagraph (B), the Secretary may, sub-

ject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) Purposes of study or clinical trial

The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

- (i) To assess a known serious risk related to the use of the drug involved.
- (ii) To assess signals of serious risk related to the use of the drug.
- (iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) Establishment of requirement after approval of covered application

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) Determination by Secretary

(i) Postapproval studies

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) Postapproval clinical trials

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) Notification; timetables; periodic reports

(i) Notification

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) Timetable; periodic reports

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the respon-

sible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) Dispute resolution

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) Safety labeling changes requested by Secretary

(A) New safety information

If the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

(B) Response to notification

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) Review

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety information, and if so, the contents of such labeling changes.

(D) Discussions

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) Order

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety information. Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

(F) Dispute resolution

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) Violation

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) Public health threat

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) Rule of construction

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing require-

ments, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) Risk evaluation and mitigation strategy

(1) In general

A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355-1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355-1 of this title, including requirements regarding assessments of approved strategies.

(2) Certain postmarket studies

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) Petitions and civil actions regarding approval of certain applications

(1) In general

(A) Determination

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 262(k) of title 42 because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) Notification

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) Format

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

(i) a document; or

(ii) a meeting with the applicant involved.

(D) Public disclosure

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) Denial based on intent to delay

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) Final agency action

The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) Extension of 30-month period

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) Certification

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the fol-

lowing certification: “I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____ . If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons _____ or _____ organizations: _____ . I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.”, with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) Verification

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: “I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____ . If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____ . I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.”, with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) Exhaustion of administrative remedies

(A) Final agency action within 150 days

The Secretary shall be considered to have taken final agency action on a petition if—

- (i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or
- (ii) such period expires without the Secretary having made such a final decision.

(B) Dismissal of certain civil actions

If a civil action is filed against the Secretary with respect to any issue raised in the

petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) Administrative record

For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

- (i) the petition filed under paragraph (1) and any supplements and comments thereto;
- (ii) the Secretary’s response to such petition, if issued; and
- (iii) other information, as designated by the Secretary, related to the Secretary’s determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) Annual report on delays in approvals per petitions

The Secretary shall annually submit to the Congress a report that specifies—

- (A) the number of applications that were approved during the preceding 12-month period;
- (B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;
- (C) the number of days by which such applications were so delayed; and
- (D) the number of such petitions that were submitted during such period.

(4) Exceptions

(A) This subsection does not apply to—

- (i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or
- (ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an application submitted pursuant to section 262(k) of title 42.

(5) Definitions

(A) Application

For purposes of this subsection, the term “application” means an application submitted under subsection (b)(2) or (j) of the Act⁵ or 262(k)⁶ of title 42.

(B) Petition

For purposes of this subsection, other than paragraph (1)(A)(i), the term “petition”

⁵So in original. Probably should be “subsection (b)(2) or (j) of this section”.

⁶So in original. Probably should be preceded by “section”.

means a request described in paragraph (1)(A)(i).

(r) Postmarket drug safety information for patients and providers

(1) Establishment

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of title 42; and

(B) improves communication of drug safety information to patients and providers.

(2) Internet Web site

The Secretary shall carry out paragraph (1) by—

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing, by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports

received for the drug, including identification of any new risks not previously identified, potential new risks, or known risks reported in unusual number;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) Posting of drug labeling

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) Private sector resources

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) Review

The Advisory Committee on Risk Communication under section 360bbb-6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) Referral to advisory committee

Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42, the Secretary shall—

(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval.

(t) Database for authorized generic drugs**(1) In general****(A) Publication**

The Commissioner shall—

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) Notification

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) Inclusion

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) Authorized generic drug

In this section, the term “authorized generic drug” means a listed drug (as that term is used in subsection (j)) that—

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) Certain drugs containing single enantiomers**(1) In general**

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active ingredient (including any ester or salt of the active ingredient) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active ingredient as that contained in the approved racemic drug, if—

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug—

(I) includes full reports of new clinical investigations (other than bioavailability studies)—

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use—

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) Limitation**(A) No approval in certain therapeutic categories**

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) Labeling

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) Definition**(A) In general**

For purposes of this subsection, the term “therapeutic category” means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w-104(b)(3)(C)(ii) of title 42 and as in effect on September 27, 2007.

(B) Publication by Secretary

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) Availability

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2017.

(v) Antibiotic drugs submitted before November 21, 1997**(1) Antibiotic drugs approved before November 21, 1997****(A) In general**

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an appli-

cation described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

(2) Antibiotic drugs submitted before November 21, 1997, but not approved

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug—

(i) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(ii) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(iii) a patent term extension under section 156 of title 35, subject to the requirements of such section.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) Limitations

(A) Exclusivities and extensions

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in

subparagraphs⁷ (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) Conditions of use

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

(4) Application of certain provisions

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

(w) Deadline for determination on certain petitions

The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

(June 25, 1938, ch. 675, § 505, 52 Stat. 1052; Pub. L. 86-507, § 1(18), June 11, 1960, 74 Stat. 201; Pub. L. 87-781, title I, §§ 102(b)-(d), 103(a), (b), 104(a)-(d)(2), Oct. 10, 1962, 76 Stat. 781-783, 784, 785; Pub. L. 92-387, § 4(d), Aug. 16, 1972, 86 Stat. 562; Pub. L. 98-417, title I, §§ 101, 102(a)-(b)(5), 103, 104, Sept. 24, 1984, 98 Stat. 1585, 1592, 1593, 1597; Pub. L. 102-282, § 5, May 13, 1992, 106 Stat. 161; Pub. L. 103-80, § 3(n), Aug. 13, 1993, 107 Stat. 777; Pub. L. 105-115, title I, §§ 115, 117, 119, 120, 124(a), Nov. 21, 1997, 111 Stat. 2313, 2315, 2316, 2318, 2324; Pub. L. 106-113, div. B, § 1000(a)(9) [title IV, § 4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A-584; Pub. L. 107-109, § 15(c)(1), Jan. 4, 2002, 115 Stat. 1420; Pub. L. 108-155, § 2(b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108-173, title XI, §§ 1101(a), (b), 1102(a), 1103(a), Dec. 8, 2003, 117 Stat. 2448, 2452, 2457, 2460; Pub. L. 110-85, title VII, § 701(b), title VIII, § 801(b)(3)(A), (B), title IX, §§ 901(a), 903, 905(a), 914(a), 915, 916, 918, 920, 921, title XI, § 1113, Sept. 27, 2007, 121 Stat. 903, 921, 922, 943, 944, 953, 957, 958, 960-962, 976; Pub. L. 110-316, title III, § 301, Aug. 14, 2008, 122 Stat. 3524; Pub. L. 110-379, § 4(a), Oct. 8, 2008, 122 Stat. 4076; Pub. L. 111-31, div. A, title I, § 103(e), June 22, 2009, 123 Stat. 1837; Pub. L. 111-148, title VII, § 7002(d)(1), title X, § 10609, Mar. 23, 2010, 124 Stat. 816, 1014; Pub. L. 112-144, title IX, § 905, title XI, §§ 1101, 1134(a), 1135, July 9, 2012, 126 Stat. 1092, 1108, 1123; Pub. L. 113-5, title III, § 301, Mar. 13, 2013, 127 Stat. 179.)

REFERENCES IN TEXT

Section 264(c) of the Health Insurance Portability and Accountability Act of 1996, referred to in subsec. (k)(3)(C)(i)(I), (4)(G)(i)(D), is section 264(c) of Pub. L. 104-191, which is set out as a note under section 1320d-2 of Title 42, The Public Health and Welfare.

⁷ So in original. Probably should be "subparagraph".

The General Schedule, referred to in subsec. (n)(5), is set out under section 5332 of Title 5, Government Organization and Employees.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (o)(3)(E)(i), is section 101(c) of Pub. L. 110-85, which is set out as a note under section 379g of this title.

The Food and Drug Administration Modernization Act of 1997, referred to in subsec. (v)(1)(A), (2)(A), (4), is Pub. L. 105-115, Nov. 21, 1997, 111 Stat. 2296. Section 125 of the Act amended sections 321, 331, 335a, 352, 360, 360j, 360aa to 360cc, 360ee, 374, 379g, 381, and 382 of this title, section 45C of Title 26, Internal Revenue Code, section 156 of Title 35, Patents, and section 8126 of Title 38, Veterans' Benefits, repealed sections 356 and 357 of this title, and enacted provisions set out as a note under this section. For complete classification of this Act to the Code, see Short Title of 1997 Amendment note set out under section 301 of this title and Tables.

The Drug Price Competition and Patent Term Restoration Act of 1984, referred to in subsec. (v)(4), is Pub. L. 98-417, Sept. 24, 1984, 98 Stat. 1585. For complete classification of this Act to the Code, see Short Title of 1984 Amendment note set out under section 301 of this title and Tables.

CODIFICATION

In subsec. (k)(4)(H), “section 132 of title 41” substituted for “section 4(5) of the Federal Procurement Policy Act” on authority of Pub. L. 111-350, §6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

AMENDMENTS

2013—Subsec. (b)(5)(B). Pub. L. 113-5 substituted “size—” for “size of clinical trials intended to form the primary basis of an effectiveness claim or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies.”, added cls. (i) and (ii), and designated last two sentences as concluding provisions.

2012—Subsec. (d). Pub. L. 112-144, §905, inserted at end “The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for premarket approval of a drug.”

Subsec. (q)(1)(A). Pub. L. 112-144, §1135(1)(A), substituted “subsection (b)(2) or (j) of this section or section 262(k) of title 42” for “subsection (b)(2) or (j)” in introductory provisions.

Subsec. (q)(1)(F). Pub. L. 112-144, §1135(1)(B), substituted “150 days” for “180 days” in introductory provisions.

Subsec. (q)(2)(A). Pub. L. 112-144, §1135(2)(A), substituted “150” for “180” in heading.

Subsec. (q)(2)(i). Pub. L. 112-144, §1135(2)(B), substituted “150-day” for “180-day”.

Subsec. (q)(4). Pub. L. 112-144, §1135(3), designated existing provisions as subpar. (A), redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A), and added subpar. (B).

Subsec. (q)(5)(A). Pub. L. 112-144, §1135(4), substituted “subsection (b)(2) or (j) of the Act or 262(k) of title 42” for “subsection (b)(2) or (j)”.

Subsec. (u)(1)(A)(ii)(II). Pub. L. 112-144, §1101(b), inserted “clinical” after “any”.

Subsec. (u)(4). Pub. L. 112-144, §1101(a), substituted “2017” for “2012”.

Subsec. (w). Pub. L. 112-144, §1134(a), added subsec. (w).

2010—Subsec. (b)(5)(B). Pub. L. 111-148, §7002(d)(1), inserted “or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies” before period at end of first sentence.

Subsec. (j)(10). Pub. L. 111-148, §10609, added par. (10).
2009—Subsec. (n)(2). Pub. L. 111-31 made technical amendment to reference in original act which appears in text as reference to section 394 of this title.

2008—Subsec. (q)(1)(A). Pub. L. 110-316, §301, inserted concluding provisions.

Subsec. (v). Pub. L. 110-379 added subsec. (v).

2007—Subsec. (b)(6). Pub. L. 110-85, §801(b)(3)(B), added par. (6).

Subsec. (e). Pub. L. 110-85, §903, inserted at end “The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.”

Subsec. (i)(4). Pub. L. 110-85, §801(b)(3)(A), inserted at end “The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.”

Subsec. (k)(3), (4). Pub. L. 110-85, §905(a), added pars. (3) and (4).

Subsec. (k)(5). Pub. L. 110-85, §921, added par. (5).

Subsec. (l). Pub. L. 110-85, §916, designated existing provisions as par. (1), redesignated former pars. (1) to (5) as subpars. (A) to (E), respectively, of par. (1), and added par. (2).

Subsec. (n)(4) to (8). Pub. L. 110-85, §701(b), redesignated pars. (5) to (8) as (4) to (7), respectively, and struck out former par. (4) which read as follows: “Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member’s own scientific work is involved.”

Subsecs. (o), (p). Pub. L. 110-85, §901(a), added subsecs. (o) and (p).

Subsec. (q). Pub. L. 110-85, §914(a), added subsec. (q).

Subsec. (r). Pub. L. 110-85, §915, added subsec. (r).

Subsec. (s). Pub. L. 110-85, §918, added subsec. (s).

Subsec. (t). Pub. L. 110-85, §920, added subsec. (t).

Subsec. (u). Pub. L. 110-85, §1113, added subsec. (u).

2003—Subsec. (b)(1). Pub. L. 108-155, in second sentence, substituted “(F)” for “and (F)” and inserted “, and (G) any assessments required under section 355c of this title” before period at end.

Subsec. (b)(3). Pub. L. 108-173, §1101(b)(1)(A), added par. (3) and struck out former par. (3) which, in subpar. (A), required an applicant making a certification under par. (2)(A)(iv) to include statement that applicant will give notice to each owner of the patent which is the subject of the certification and to the holder of the approved application, in subpar. (B), directed that notice state that an application has been submitted and include a detailed statement of the applicant’s opinion that the patent is not valid or will not be infringed, and, in subpar. (C), provided that if an application is amended, notice shall be given when the amended application is submitted.

Subsec. (b)(4), (5). Pub. L. 108-173, §1101(b)(1)(B), added par. (4) and redesignated former par. (4) as (5).

Subsec. (c)(3). Pub. L. 108-173, §1101(b)(2)(A), substituted “by applying the following to each certification made under subsection (b)(2)(A) of this section” for “under the following” in introductory provisions.

Subsec. (c)(3)(C). Pub. L. 108-173, §1101(b)(2)(B)(iii), which directed the substitution of “subsection (b)(3) of this section” for “paragraph (3)(B)” in third sentence, could not be executed because such words do not appear. See note below.

Pub. L. 108-173, §1101(b)(2)(B)(ii)(VI), in concluding provisions, struck out “Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.” after “expediting the action.”

Pub. L. 108-173, §1101(b)(2)(B)(i), (ii)(I), in first sentence of introductory provisions, substituted “unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) of this section is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) of this section before the date on which the application (excluding an amendment or supplement to the application) was submitted” for “unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received” and, in second sentence of introductory provisions, substituted “subsection (b)(3) of this section” for “paragraph (3)(B)”.

Subsec. (c)(3)(C)(i). Pub. L. 108-173, §1101(b)(2)(B)(ii)(II), added cl. (i) and struck out former cl. (i) which read as follows: “if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision.”.

Subsec. (c)(3)(C)(ii). Pub. L. 108-173, §1101(b)(2)(B)(ii)(III), added cl. (ii) and struck out former cl. (ii) which read as follows: “if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or”.

Subsec. (c)(3)(C)(iii). Pub. L. 108-173, §1101(b)(2)(B)(ii)(IV), substituted “as provided in clause (i); or” for “on the date of such court decision.”

Subsec. (c)(3)(C)(iv). Pub. L. 108-173, §1101(b)(2)(B)(ii)(V), added cl. (iv).

Subsec. (c)(3)(D), (E). Pub. L. 108-173, §1101(b)(2)(C), (D), added subpar. (D) and redesignated former subpar. (D) as (E).

Subsec. (j)(2)(B). Pub. L. 108-173, §1101(a)(1)(A), added subpar. (B) and struck out former subpar. (B) which, in cl. (i), required that an applicant making a certification under subpar. (A)(vii)(IV) include in the application a statement that notice would be given to each owner of the patent and the holder of the approved application, in cl. (ii), required that notice would state that an application had been submitted and that it would include a detailed statement of the basis of the applicant's opinion, and, in cl. (iii), directed that notice of an amended application be given when the amended application had been submitted.

Subsec. (j)(2)(D). Pub. L. 108-173, §1101(a)(1)(B), added subpar. (D).

Subsec. (j)(5)(B). Pub. L. 108-173, §1101(a)(2)(A)(i), substituted “by applying the following to each certification made under paragraph (2)(A)(vii)” for “under the following” in introductory provisions.

Subsec. (j)(5)(B)(iii). Pub. L. 108-173, §1101(a)(2)(A)(ii)(II)(ee), which directed amendment of the second sentence of subsec. (j)(5)(B)(iii) by striking “Until the expiration” and all that follows in the matter after and below subclause (IV), was executed by striking “Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.” after “expediting the action.” in concluding provisions, to reflect the probable intent of Congress.

Pub. L. 108-173, §1101(a)(2)(A)(ii)(I), in introductory provisions, substituted “unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted” for “unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received”.

Subsec. (j)(5)(B)(iii)(I). Pub. L. 108-173, §1101(a)(2)(A)(ii)(II)(aa), added subcl. (I) and struck out former subcl. (I) which read as follows: “if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision.”.

Subsec. (j)(5)(B)(iii)(II). Pub. L. 108-173, §1101(a)(2)(A)(ii)(II)(bb), added subcl. (II) and struck out former subcl. (II) which read as follows: “if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or”.

Subsec. (j)(5)(B)(iii)(III). Pub. L. 108-173, §1101(a)(2)(A)(ii)(II)(cc), substituted “as provided in subclause (I); or” for “on the date of such court decision.”

Subsec. (j)(5)(B)(iii)(IV). Pub. L. 108-173, §1101(a)(2)(A)(ii)(II)(dd), added subcl. (IV).

Subsec. (j)(5)(B)(iv). Pub. L. 108-173, §1102(a)(1), added cl. (iv) and struck out former cl. (iv) which read as follows: “If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

“(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

“(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.”

Subsec. (j)(5)(C). Pub. L. 108-173, §1101(a)(2)(B), (C), added subpar. (C). Former subpar. (C) redesignated (E).

Subsec. (j)(5)(D). Pub. L. 108-173, §1102(a)(2), added subpar. (D).

Pub. L. 108-173, §1101(a)(2)(B), redesignated subpar. (D) as (F).

Subsec. (j)(5)(E), (F). Pub. L. 108-173, §1101(a)(2)(B), redesignated subpars. (C) and (D) as (E) and (F), respectively.

Subsec. (j)(8)(A). Pub. L. 108-173, §1103(a)(1), added subpar. (A) and struck out former subpar. (A) which read as follows: “The term ‘bioavailability’ means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.”

Subsec. (j)(8)(C). Pub. L. 108-173, §1103(a)(2), added subpar. (C).

2002—Subsec. (i)(1)(D). Pub. L. 107-109 added subpar. (D).

1999—Subsec. (m). Pub. L. 106-113 substituted “United States Patent and Trademark Office” for “Patent and Trademark Office of the Department of Commerce”.

1997—Subsec. (b)(1). Pub. L. 105-115, §115(b), inserted at end “The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).”

Subsec. (b)(4). Pub. L. 105-115, §119(a), added par. (4).
 Subsec. (c)(4). Pub. L. 105-115, §124(a), added par. (4).
 Subsec. (d). Pub. L. 105-115, §115(a), inserted at end
 "If the Secretary determines, based on relevant
 science, that data from one adequate and well-con-
 trolled clinical investigation and confirmatory evi-
 dence (obtained prior to or after such investigation) are
 sufficient to establish effectiveness, the Secretary may
 consider such data and evidence to constitute substan-
 tial evidence for purposes of the preceding sentence."
 Subsec. (i). Pub. L. 105-115, §117, inserted "(1)" after
 "(i)", redesignated former pars. (1) to (3) as subpars. (A)
 to (C), respectively, of par. (1), added pars. (2) to (4), and
 struck out closing provisions which read as follows:
 "Such regulations shall provide that such exemption
 shall be conditioned upon the manufacturer, or the
 sponsor of the investigation, requiring that experts
 using such drugs for investigational purposes certify to
 such manufacturer or sponsor that they will inform
 any human beings to whom such drugs, or any controls
 used in connection therewith, are being administered,
 or their representatives, that such drugs are being used
 for investigational purposes and will obtain the consent
 of such human beings or their representatives, except
 where they deem it not feasible or, in their professional
 judgment, contrary to the best interests of such human
 beings. Nothing in this subsection shall be construed to
 require any clinical investigator to submit directly to
 the Secretary reports on the investigational use of
 drugs."
 Subsec. (j)(2)(A)(i). Pub. L. 105-115, §119(b)(2)(A), sub-
 stituted "paragraph (7)" for "paragraph (6)".
 Subsec. (j)(3). Pub. L. 105-115, §119(b)(1)(B), added par.
 (3). Former par. (3) redesignated (4).
 Subsec. (j)(4). Pub. L. 105-115, §119(b)(1)(A), (2)(B), re-
 designated par. (3) as (4) and in introductory provisions
 substituted "paragraph (5)" for "paragraph (4)".
 Former par. (4) redesignated (5).
 Subsec. (j)(4)(I). Pub. L. 105-115, §119(b)(2)(C), sub-
 stituted "paragraph (6)" for "paragraph (5)".
 Subsec. (j)(5), (6). Pub. L. 105-115, §119(b)(1)(A), re-
 designated pars. (4) and (5) as (5) and (6), respectively.
 Former par. (6) redesignated (7).
 Subsec. (j)(7). Pub. L. 105-115, §119(b)(1)(A), (2)(D), re-
 designated par. (6) as (7) and in subpar. (C) substituted
 "paragraph (6)" for "paragraph (5)" in two places.
 Former par. (7) redesignated (8).
 Subsec. (j)(8), (9). Pub. L. 105-115, §119(b)(1)(A), re-
 designated pars. (7) and (8) as (8) and (9), respectively.
 Subsec. (n). Pub. L. 105-115, §120, added subsec. (n).
 1993—Subsec. (j)(6)(A)(ii). Pub. L. 103-80, §3(n)(1)(A),
 substituted "Secretary" for "Secretary".
 Subsec. (j)(6)(A)(iii). Pub. L. 103-80, §3(n)(1)(B), in-
 serted comma after "published by the Secretary".
 Subsec. (k)(1). Pub. L. 103-80, §3(n)(2), substituted
 "section. Regulations" for "section: *Provided, however,*
That regulations".
 1992—Subsec. (j)(8). Pub. L. 102-282 added par. (8).
 1984—Subsec. (a). Pub. L. 98-417, §102(b)(1), inserted
 "or (j)" after "subsection (b)".
 Subsec. (b). Pub. L. 98-417, §§102(a)(1), 103(a), de-
 signated existing provisions of subsec. (b) as par. (1)
 thereof and redesignated existing cls. (1) through (6) of
 such par. (1) as cls. (A) through (F) thereof, respec-
 tively, inserted requirement that the applicant file
 with the application the patent number and the expira-
 tion date of any patent which claims the drug for which
 the applicant submitted the application or which
 claims a method of using such drug and with respect to
 which a claim of patent infringement could reasonably
 be asserted if a person not licensed by the owner en-
 gaged in the manufacture, use, or sale of the drug, that
 the applicant amend the application to include such in-
 formation if an application is filed under this sub-
 section for a drug and a patent which claims such drug
 or a method of using such drug is issued after the filing
 date but before approval of the application, and that
 upon approval of the application, the Secretary publish
 the information submitted, and added pars. (2) and (3).
 Subsec. (c). Pub. L. 98-417, §§102(a)(2), (b)(2), 103(b),
 designated existing provisions of subsec. (c) as par. (1)

thereof and in par. (1) as so designated substituted
 "subsection (b) of this section" for "this subsection"
 and redesignated former pars. (1) and (2) as subpars. (A)
 and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(6), (7). Pub. L. 98-417, §102(a)(3)(A), added
 cl. (6) relating to the failure of the application to con-
 tain the patent information prescribed by subsec. (b) of
 this section, and redesignated former cl. (6) as (7).

Subsec. (e). Pub. L. 98-417, §102(a)(3)(B), in first sen-
 tence, added a new cl. (4) relating to the failure to file
 the patent information prescribed by subsec. (c) of this
 section within 30 days after the receipt of written no-
 tice from the Secretary specifying the failure to file
 such information, and redesignated former cl. (4) as (5).

Pub. L. 98-417, §102(b)(3), (4), in second sentence, in-
 serted in provisions preceding cl. (1) "submitted under
 subsection (b) or (j) of this section" and in cl. (1) sub-
 stituted "under subsection (k) of this section or to
 comply with the notice requirements of section
 360(k)(2) of this title" for "under subsection (j) of this
 section or to comply with the notice requirements of
 section 360(j)(2) of this title".

Subsecs. (j), (k). Pub. L. 98-417, §101, added subsec. (j)
 and redesignated former subsec. (j) as (k).

Subsec. (k)(1). Pub. L. 98-417, §102(b)(5), substituted
 "under subsection (b) or (j) of this section" for "pursu-
 ant to this section".

Subsecs. (l), (m). Pub. L. 98-417, §104, added subsecs.
 (l) and (m).

1972—Subsec. (e). Pub. L. 92-387 inserted "or to com-
 ply with the notice requirements of section 360(j)(2) of
 this title" in cl. (1) of second sentence relating to the
 maintenance of records.

1962—Subsec. (a). Pub. L. 87-781, §104(a), inserted "an
 approval of" before "an application".

Subsec. (b). Pub. L. 87-781, §102(b), inserted "and
 whether such drug is effective in use" after "is safe for
 use".

Subsec. (c). Pub. L. 87-781, §104(b), substituted provi-
 sions requiring the Secretary, within 180 days after fil-
 ing an application, or such additional period as the
 Secretary and the applicant agree upon, to either ap-
 prove the application, if meeting the requirements of
 subsec. (d) of this section, or give notice of opportunity
 for hearing on question of whether such application is
 approvable, and providing that if applicant requests
 hearing in writing within 30 days, the hearing shall
 begin within 90 days after expiration of said 30 days,
 unless the Secretary and applicant agree otherwise,
 that such hearing shall be expedited, and that the Sec-
 retary's order shall be issued within 90 days after date
 for filing final briefs, for provisions which had an appli-
 cation become effective on the sixtieth day after filing
 thereof unless prior thereto the Secretary postponed
 the date by written notice to such time, but not more
 than 180 days after filing, as the Secretary deemed nec-
 essary to study and investigate the application.

Subsec. (d). Pub. L. 87-781, §102(c), inserted refer-
 ences to subsec. (c), added cls. (5) and (6), provided that if
 after notice and opportunity for hearing, the Secretary
 finds that cls. (1) to (6) do not apply, he shall approve
 the application, and defined "substantial evidence" as
 used in this subsection and subsec. (e) of this section.

Subsec. (e). Pub. L. 87-781, §102(d), amended subsec.
 (e) generally, and among other changes, directed the
 Secretary to withdraw approval of an application if by
 tests, other scientific data or experience, or new evi-
 dence of clinical experience not contained in the appli-
 cation or available at the time of its approval, the drug
 is shown to be unsafe, or on the basis of new informa-
 tion, there is shown a lack of substantial evidence that
 the drug has the effect it is represented to have, and
 provided that if the Secretary, or acting Secretary,
 finds there is an imminent hazard to the public health,
 he may suspend approval immediately, notify the ap-
 plicant, and give him opportunity for an expedited
 hearing, that the Secretary may withdraw approval if
 the applicant fails to establish a system for maintain-
 ing required records, or has repeatedly or deliberately
 failed to maintain records and make reports, or has re-

fused access to, or copying or verification of such records, or if the Secretary finds on new evidence that the methods, facilities and controls in the manufacturing, processing, and packing are inadequate to assure and preserve the drugs' identity, strength, quality and purity, and were not made adequate within a reasonable time after receipt of written notice thereof, or finds on new evidence, that the labeling is false or misleading and was not corrected within a reasonable time after receipt of written notice thereof.

Subsec. (f). Pub. L. 87-781, §104(c), substituted provisions requiring the Secretary to revoke any previous order under subsecs. (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and to approve such application or reinstate such approval, for provisions which required him to revoke an order refusing effectiveness to an application.

Subsec. (h). Pub. L. 87-781, §104(d)(1), (2), inserted "as provided in section 2112 of title 28", and "except that until the filing of the record the Secretary may modify or set aside his order", substituted "or withdrawing approval of an application under this section" for "to permit the application to become effective, or suspending the effectiveness of the application", "United States court of appeals for the circuit" for "district court of the United States within any district", "Court of Appeals for the District of Columbia Circuit" for "District Court for the District of Columbia", "transmitted by the clerk of the court to" for "served upon", and "by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28" for "as provided in sections 225, 346, and 347 of title 28, as amended, and in section 7, as amended, of the Act entitled 'An Act to establish a Court of Appeals for the District of Columbia', approved February 9, 1893", and eliminated "upon" before "any officer designated", "a transcript of" before "the record" and "and decree" before "of the court affirming".

Subsec. (i). Pub. L. 87-781, §103(b), inserted "the foregoing subsections of" after "operation of", and "and effectiveness" after "safety", and provided that the regulations may condition exemptions upon the submission of reports of preclinical tests to justify the proposed clinical testing, upon the obtaining by the manufacturer or sponsor of the investigation of a new drug of a signed agreement from each of the investigators that patients to whom the drug is administered will be under his supervision or under investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings, or upon the establishment and maintenance of records and reports of data obtained by the investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug, and provided that the regulations shall condition an exemption upon the manufacturer or sponsor of the investigation requiring that experts using such drugs certify that they will inform humans to whom such drugs or any controls connected therewith are administered, or their representatives, and will obtain the consent of such people where feasible and not contrary to the best interests of such people, and that reports on the investigational use of drugs are not required to be submitted directly to the Secretary.

Subsec. (j). Pub. L. 87-781, §103(a), added subsec. (j).
1960—Subsec. (g). Pub. L. 86-507 inserted "or by certified mail" after "registered mail".

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112-144, title XI, §1134(b), July 9, 2012, 126 Stat. 1123, provided that: "The amendment made by subsection (a) [amending this section] shall apply to any petition that is submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), on or after the date of enactment of this Act [July 9, 2012]."

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110-85, title VII, §701(c), Sept. 27, 2007, 121 Stat. 904, provided that: "The amendments made by

this section [enacting section 379d-1 of this title and amending this section] shall take effect on October 1, 2007."

Amendment by sections 901(a), 903, and 905(a) of Pub. L. 110-85 effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110-85, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 2003 AMENDMENTS

Pub. L. 108-173, title XI, §1101(c), Dec. 8, 2003, 117 Stat. 2456, provided that:

"(1) IN GENERAL.—Except as provided in paragraphs (2) and (3), the amendments made by subsections (a) and (b) [amending this section] apply to any proceeding under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) that is pending on or after the date of the enactment of this Act [Dec. 8, 2003] regardless of the date on which the proceeding was commenced or is commenced.

"(2) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—The amendments made by subsections (a)(1) and (b)(1) apply with respect to any certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) submitted on or after August 18, 2003, in an application filed under subsection (b) or (j) of that section or in an amendment or supplement to an application filed under subsection (b) or (j) of that section.

"(3) EFFECTIVE DATE OF APPROVAL.—The amendments made by subsections (a)(2)(A)(ii)(I) and (b)(2)(B)(i) apply with respect to any patent information submitted under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) on or after August 18, 2003."

Pub. L. 108-173, title XI, §1102(b), Dec. 8, 2003, 117 Stat. 2460, provided that:

"(1) IN GENERAL.—Except as provided in paragraph (2), the amendment made by subsection (a) [amending this section] shall be effective only with respect to an application filed under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which no certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act.

"(2) COLLUSIVE AGREEMENTS.—If a forfeiture event described in section 505(j)(5)(D)(i)(V) of that Act occurs in the case of an applicant, the applicant shall forfeit the 180-day period under section 505(j)(5)(B)(iv) of that Act without regard to when the first certification under section 505(j)(2)(A)(vii)(IV) of that Act for the listed drug was made.

"(3) DECISION OF A COURT WHEN THE 180-DAY EXCLUSIVITY PERIOD HAS NOT BEEN TRIGGERED.—With respect to an application filed before, on, or after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which a certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act and for which neither of the events described in subclause (I) or (II) of section 505(j)(5)(B)(iv) of that Act (as in effect on the day before the date of the enactment of this Act) has occurred on or before the date of the enactment of this Act, the term 'decision of a court' as used in clause (iv) of section 505(j)(5)(B) of that Act means a final decision of a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken."

Amendment by Pub. L. 108-155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108-155, set out as an Effective Date note under section 355c of this title.

EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106-113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, §4731] of Pub. L. 106-113, set out as a note under section 1 of Title 35, Patents.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1984 AMENDMENT

Pub. L. 98-417, title I, §105, Sept. 24, 1984, 98 Stat. 1597, provided that:

“(a) The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 505 of the Federal Food, Drug, and Cosmetic Act [this section], as amended by sections 101, 102, and 103 of this Act, within one year of the date of enactment of this Act [Sept. 24, 1984].

“(b) During the period beginning sixty days after the date of the enactment of this Act [Sept. 24, 1984], and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new drug applications may be submitted in accordance with the provisions of section 314.2 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 505(c) of the Federal Food, Drug, and Cosmetic Act [subsec. (c) of this section] before the date of the enactment of this Act. If any such provision is inconsistent with the requirements of section 505(j) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall consider the application under the applicable requirements of such section. The Secretary of Health and Human Services may not approve such an abbreviated new drug application which is filed for a drug which is described in sections 505(c)(3)(D) and 505(j)(4)(D) of the Federal Food, Drug, and Cosmetic Act, except in accordance with such section.”

EFFECTIVE DATE OF 1972 AMENDMENT

Amendment by Pub. L. 92-387 effective on first day of sixth month beginning after Aug. 16, 1972, see section 5 of Pub. L. 92-387, set out as a note under section 360 of this title.

EFFECTIVE DATE OF 1962 AMENDMENT

Amendment by Pub. L. 87-781 effective on first day of seventh calendar month following October 1962, see section 107 of Pub. L. 87-781, set out as a note under section 321 of this title.

CONSTRUCTION OF AMENDMENT BY PUB. L. 110-85

Pub. L. 110-85, title IX, §905(b), Sept. 27, 2007, 121 Stat. 949, provided that: “Nothing in this section [amending this section] or the amendment made by this section shall be construed to prohibit the lawful disclosure or use of data or information by an entity other than as described in paragraph (4)(B) or (4)(G) of section 505(k) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(k)], as added by subsection (a).”

CONSTRUCTION OF AMENDMENTS BY PUB. L. 102-282

Amendment by Pub. L. 102-282 not to preclude any other civil, criminal, or administrative remedy provided under Federal or State law, including any private right of action against any person for the same action subject to any action or civil penalty under an amendment made by Pub. L. 102-282, see section 7 of Pub. L. 102-282, set out as a note under section 335a of this title.

TRANSFER OF FUNCTIONS

For transfer of functions of Federal Security Administrator to Secretary of Health, Education, and Welfare [now Health and Human Services], and of Food and Drug Administration in the Department of Agriculture to Federal Security Agency, see notes set out under section 321 of this title.

GUIDANCE ON PATHOGEN-FOCUSED ANTIBACTERIAL DRUG DEVELOPMENT

Pub. L. 112-144, title VIII, §806, July 9, 2012, 126 Stat. 1082, provided that:

“(a) DRAFT GUIDANCE.—Not later than June 30, 2013, in order to facilitate the development of antibacterial drugs for serious or life-threatening bacterial infections, particularly in areas of unmet need, the Secretary of Health and Human Services shall publish draft guidance that—

“(1) specifies how preclinical and clinical data can be utilized to inform an efficient and streamlined pathogen-focused antibacterial drug development program that meets the approval standards of the Food and Drug Administration; and

“(2) provides advice on approaches for the development of antibacterial drugs that target a more limited spectrum of pathogens.

“(b) FINAL GUIDANCE.—Not later than December 31, 2014, after notice and opportunity for public comment on the draft guidance under subsection (a), the Secretary of Health and Human Services shall publish final guidance consistent with this section.”

GUIDANCE ON ABUSE-DETERRENT PRODUCTS

Pub. L. 112-144, title XI, §1122(c), July 9, 2012, 126 Stat. 1113, provided that: “Not later than 6 months after the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall promulgate guidance on the development of abuse-deterrent drug products.”

EXTENSION OF PERIOD FOR FIRST APPLICANT TO OBTAIN TENTATIVE APPROVAL WITHOUT FORFEITING 180-DAY-EXCLUSIVITY PERIOD

Pub. L. 112-144, title XI, §1133, July 9, 2012, 126 Stat. 1122, provided that:

“(a) EXTENSION.—

“(1) IN GENERAL.—If a first applicant files an application during the 30-month period ending on the date of enactment of this Act [July 9, 2012] and such application initially contains a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), or if a first applicant files an application and the application is amended during such period to first contain such a certification, the phrase ‘30 months’ in paragraph (5)(D)(i)(IV) of such section shall, with respect to such application, be read as meaning—

“(A) during the period beginning on the date of enactment of this Act, and ending on September 30, 2015, ‘40 months’; and

“(B) during the period beginning on October 1, 2015, and ending on September 30, 2016, ‘36 months’.

“(2) CONFORMING AMENDMENT.—In the case of an application to which an extended period under paragraph (1) applies, the reference to the 30-month period under section 505(q)(1)(G) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(q)(1)(G)) shall be read to be the applicable period under paragraph (1).

“(b) PERIOD FOR OBTAINING TENTATIVE APPROVAL OF CERTAIN APPLICATIONS.—If an application is filed on or before the date of enactment of this Act [July 9, 2012] and such application is amended during the period beginning on the day after the date of enactment of this Act and ending on September 30, 2017, to first contain a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), the date of the filing of such amendment (rather than the date of the filing of such application) shall be treated as the beginning of the 30-month period described in paragraph (5)(D)(i)(IV) of such section 505(j).

“(c) DEFINITIONS.—For the purposes of this section, the terms ‘application’ and ‘first applicant’ mean application and first applicant, as such terms are used in section 505(j)(5)(D)(i)(IV) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(5)(D)(i)(IV)).”

EFFECT OF AMENDMENTS BY PUB. L. 110-85 ON
VETERINARY MEDICINE

Pub. L. 110-85, title IX, §907, Sept. 27, 2007, 121 Stat. 950, provided that: "This subtitle [subtitle A (§§901-909) of title IX of Pub. L. 110-85, enacting sections 353c and 355-1 of this title, amending this section and sections 331, 333, and 352 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under this section and sections 331, 352, and 355a of this title], and the amendments made by this subtitle, shall have no effect on the use of drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] by, or on the lawful written or oral order of, a licensed veterinarian within the context of a veterinarian-client-patient relationship, as provided for under section 512(a)(5) of such Act [21 U.S.C. 360b(a)(5)]."

EFFECT OF AMENDMENT BY PUB. L. 108-173 ON
ABBREVIATED NEW DRUG APPLICATIONS

Pub. L. 108-173, title XI, §1103(b), Dec. 8, 2003, 117 Stat. 2461, provided that: "The amendment made by subsection (a) [amending this section] does not alter the standards for approval of drugs under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j))."

FEDERAL TRADE COMMISSION REVIEW

Pub. L. 108-173, title XI, subtitle B, Dec. 8, 2003, 117 Stat. 2461, provided that:

"SEC. 1111. DEFINITIONS.

"In this subtitle:

"(1) ANDA.—The term 'ANDA' means an abbreviated drug application, as defined under section 201(aa) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(aa)].

"(2) ASSISTANT ATTORNEY GENERAL.—The term 'Assistant Attorney General' means the Assistant Attorney General in charge of the Antitrust Division of the Department of Justice.

"(3) BRAND NAME DRUG.—The term 'brand name drug' means a drug for which an application is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(c)], including an application referred to in section 505(b)(2) of such Act [21 U.S.C. 355(b)(2)].

"(4) BRAND NAME DRUG COMPANY.—The term 'brand name drug company' means the party that holds the approved application referred to in paragraph (3) for a brand name drug that is a listed drug in an ANDA, or a party that is the owner of a patent for which information is submitted for such drug under subsection (b) or (c) of section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(b), (c)].

"(5) COMMISSION.—The term 'Commission' means the Federal Trade Commission.

"(6) GENERIC DRUG.—The term 'generic drug' means a drug for which an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)] is approved.

"(7) GENERIC DRUG APPLICANT.—The term 'generic drug applicant' means a person who has filed or received approval for an ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)].

"(8) LISTED DRUG.—The term 'listed drug' means a brand name drug that is listed under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(7)].

"SEC. 1112. NOTIFICATION OF AGREEMENTS.

"(a) AGREEMENT WITH BRAND NAME DRUG COMPANY.—

"(1) REQUIREMENT.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] and a brand name drug company that enter into an agreement described in paragraph (2) shall each file the agreement in accordance with subsection (c). The

agreement shall be filed prior to the date of the first commercial marketing of the generic drug that is the subject of the ANDA.

"(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph between a generic drug applicant and a brand name drug company is an agreement regarding—

"(A) the manufacture, marketing or sale of the brand name drug that is the listed drug in the ANDA involved;

"(B) the manufacture, marketing, or sale of the generic drug for which the ANDA was submitted; or

"(C) the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to such ANDA or to any other ANDA based on the same brand name drug.

"(b) AGREEMENT WITH ANOTHER GENERIC DRUG APPLICANT.—

"(1) REQUIREMENT.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] with respect to a listed drug and another generic drug applicant that has submitted an ANDA containing such a certification for the same listed drug shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of either of the generic drugs for which such ANDAs were submitted.

"(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph between two generic drug applicants is an agreement regarding the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to the ANDAs with which the agreement is concerned.

"(c) FILING.—

"(1) AGREEMENT.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any such agreement, except that such parties are not required to file an agreement that solely concerns—

"(A) purchase orders for raw material supplies;

"(B) equipment and facility contracts;

"(C) employment or consulting contracts; or

"(D) packaging and labeling contracts.

"(2) OTHER AGREEMENTS.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any agreements between the parties that are not described in such subsections and are contingent upon, provide a contingent condition for, or are otherwise related to an agreement that is required in subsection (a) or (b) to be filed in accordance with this subsection.

"(3) DESCRIPTION.—In the event that any agreement required in subsection (a) or (b) to be filed in accordance with this subsection has not been reduced to text, each of the parties involved shall file written descriptions of such agreement that are sufficient to disclose all the terms and conditions of the agreement.

"SEC. 1113. FILING DEADLINES.

"Any filing required under section 1112 shall be filed with the Assistant Attorney General and the Commission not later than 10 business days after the date the agreements are executed.

"SEC. 1114. DISCLOSURE EXEMPTION.

"Any information or documentary material filed with the Assistant Attorney General or the Commission pursuant to this subtitle shall be exempt from disclosure under section 552 of title 5, United States Code, and no such information or documentary material may be made public, except as may be relevant to any administrative or judicial action or proceeding. Nothing

in this section is intended to prevent disclosure to either body of the Congress or to any duly authorized committee or subcommittee of the Congress.

“SEC. 1115. ENFORCEMENT.

“(a) CIVIL PENALTY.—Any brand name drug company or generic drug applicant which fails to comply with any provision of this subtitle shall be liable for a civil penalty of not more than \$11,000, for each day during which such entity is in violation of this subtitle. Such penalty may be recovered in a civil action brought by the United States, or brought by the Commission in accordance with the procedures established in section 16(a)(1) of the Federal Trade Commission Act (15 U.S.C. 56(a) [15 U.S.C. 56(a)(1)]).

“(b) COMPLIANCE AND EQUITABLE RELIEF.—If any brand name drug company or generic drug applicant fails to comply with any provision of this subtitle, the United States district court may order compliance, and may grant such other equitable relief as the court in its discretion determines necessary or appropriate, upon application of the Assistant Attorney General or the Commission.

“SEC. 1116. RULEMAKING.

“The Commission, with the concurrence of the Assistant Attorney General and by rule in accordance with section 553 of title 5, United States Code, consistent with the purposes of this subtitle—

“(1) may define the terms used in this subtitle;

“(2) may exempt classes of persons or agreements from the requirements of this subtitle; and

“(3) may prescribe such other rules as may be necessary and appropriate to carry out the purposes of this subtitle.

“SEC. 1117. SAVINGS CLAUSE.

“Any action taken by the Assistant Attorney General or the Commission, or any failure of the Assistant Attorney General or the Commission to take action, under this subtitle shall not at any time bar any proceeding or any action with respect to any agreement between a brand name drug company and a generic drug applicant, or any agreement between generic drug applicants, under any other provision of law, nor shall any filing under this subtitle constitute or create a presumption of any violation of any competition laws.

“SEC. 1118. EFFECTIVE DATE.

“This subtitle shall—

“(1) take effect 30 days after the date of the enactment of this Act [Dec. 8, 2003]; and

“(2) shall apply to agreements described in section 1112 that are entered into 30 days after the date of the enactment of this Act.”

REPORT ON PATIENT ACCESS TO NEW THERAPEUTIC AGENTS FOR PEDIATRIC CANCER

Pub. L. 107–109, §15(d), Jan. 4, 2002, 115 Stat. 1421, provided that: “Not later than January 31, 2003, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs and in consultation with the Director of the National Institutes of Health, shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents.”

DATA REQUIREMENTS FOR DRUGS AND BIOLOGICS

Pub. L. 105–115, title I, §118, Nov. 21, 1997, 111 Stat. 2316, provided that: “Within 12 months after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue guidance that describes when abbreviated study reports may be submitted, in lieu of full reports, with a new drug application under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) and with a biologics license application under section 351 of the Public Health

Service Act (42 U.S.C. 262) for certain types of studies. Such guidance shall describe the kinds of studies for which abbreviated reports are appropriate and the appropriate abbreviated report formats.”

REQUIREMENTS FOR REVIEW OF APPROVAL PROCEDURES AND CURRENT GOOD MANUFACTURING PRACTICES FOR POSITRON EMISSION TECHNOLOGY

Pub. L. 105–115, title I, §121(c), Nov. 21, 1997, 111 Stat. 2321, provided that:

“(1) PROCEDURES AND REQUIREMENTS.—

“(A) IN GENERAL.—In order to take account of the special characteristics of positron emission tomography drugs and the special techniques and processes required to produce these drugs, not later than 2 years after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall establish—

“(i) appropriate procedures for the approval of positron emission tomography drugs pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355); and

“(ii) appropriate current good manufacturing practice requirements for such drugs.

“(B) CONSIDERATIONS AND CONSULTATION.—In establishing the procedures and requirements required by subparagraph (A), the Secretary of Health and Human Services shall take due account of any relevant differences between not-for-profit institutions that compound the drugs for their patients and commercial manufacturers of the drugs. Prior to establishing the procedures and requirements, the Secretary of Health and Human Services shall consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists licensed to make or use positron emission tomography drugs.

“(2) SUBMISSION OF NEW DRUG APPLICATIONS AND ABBREVIATED NEW DRUG APPLICATIONS.—

“(A) IN GENERAL.—Except as provided in subparagraph (B), the Secretary of Health and Human Services shall not require the submission of new drug applications or abbreviated new drug applications under subsection (b) or (j) of section 505 (21 U.S.C. 355), for compounded positron emission tomography drugs that are not adulterated drugs described in section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) (as amended by subsection (b)), for a period of 4 years after the date of enactment of this Act [Nov. 21, 1997], or for 2 years after the date on which the Secretary establishes procedures and requirements under paragraph (1), whichever is longer.

“(B) EXCEPTION.—Nothing in this Act [see Short Title of 1997 Amendment note set out under section 301 of this title] shall prohibit the voluntary submission of such applications or the review of such applications by the Secretary of Health and Human Services. Nothing in this Act shall constitute an exemption for a positron emission tomography drug from the requirements of regulations issued under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)).”

“COMPOUNDED POSITRON EMISSION TOPOGRAPHY DRUG” DEFINED

Pub. L. 105–115, title I, §121(e), Nov. 21, 1997, 111 Stat. 2322, provided that: “As used in this section [amending sections 321 and 351 of this title and enacting provisions set out as notes under this section and section 351 of this title], the term ‘compounded positron emission tomography drug’ has the meaning given the term in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321).”

REQUIREMENTS FOR RADIOPHARMACEUTICALS

Pub. L. 105–115, title I, §122, Nov. 21, 1997, 111 Stat. 2322, provided that:

“(a) REQUIREMENTS.—

“(1) REGULATIONS.—

“(A) PROPOSED REGULATIONS.—Not later than 180 days after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, shall issue proposed regulations governing the approval of radiopharmaceuticals. The regulations shall provide that the determination of the safety and effectiveness of such a radiopharmaceutical under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) shall include consideration of the proposed use of the radiopharmaceutical in the practice of medicine, the pharmacological and toxicological activity of the radiopharmaceutical (including any carrier or ligand component of the radiopharmaceutical), and the estimated absorbed radiation dose of the radiopharmaceutical.

“(B) FINAL REGULATIONS.—Not later than 18 months after the date of enactment of this Act, the Secretary shall promulgate final regulations governing the approval of the radiopharmaceuticals.

“(2) SPECIAL RULE.—In the case of a radiopharmaceutical, the indications for which such radiopharmaceutical is approved for marketing may, in appropriate cases, refer to manifestations of disease (such as biochemical, physiological, anatomic, or pathological processes) common to, or present in, one or more disease states.

“(b) DEFINITION.—In this section, the term ‘radiopharmaceutical’ means—

“(1) an article—

“(A) that is intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans; and

“(B) that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

“(2) any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of any such article.”

SPECIAL RULE

Pub. L. 105–115, title I, §123(f), Nov. 21, 1997, 111 Stat. 2324, provided that: “The Secretary of Health and Human Services shall take measures to minimize differences in the review and approval of products required to have approved biologics license applications under section 351 of the Public Health Service Act (42 U.S.C. 262) and products required to have approved new drug applications under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)).”

TRANSITION

Pub. L. 110–379, §4(b), Oct. 8, 2008, 122 Stat. 4077, provided that:

“(1) With respect to a patent issued on or before the date of the enactment of this Act [Oct. 8, 2008], any patent information required to be filed with the Secretary of Health and Human Services under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) to be listed on a drug to which subsection (v)(1) of such section 505 (as added by this section) applies shall be filed with the Secretary not later than 60 days after the date of the enactment of this Act.

“(2) With respect to any patent information referred to in paragraph (1) of this subsection that is filed with the Secretary within the 60-day period after the date of the enactment of this Act [Oct. 8, 2008], the Secretary shall publish such information in the electronic version of the list referred to at section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) as soon as it is received, but in no event later than the date that is 90 days after the enactment of this Act.

“(3) With respect to any patent information referred to in paragraph (1) that is filed with the Secretary

within the 60-day period after the date of enactment of this Act [Oct. 8, 2008], each applicant that, not later than 120 days after the date of the enactment of this Act, amends an application that is, on or before the date of the enactment of this Act, a substantially complete application (as defined in paragraph (5)(B)(iv) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j))) to contain a certification described in paragraph (2)(A)(vii)(IV) of such section 505(j) with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j)).”

Pub. L. 105–115, title I, §125(d), Nov. 21, 1997, 111 Stat. 2326, provided that:

“(1) IN GENERAL.—An application that was approved by the Secretary of Health and Human Services before the date of the enactment of this Act [Nov. 21, 1997] for the marketing of an antibiotic drug under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as in effect on the day before the date of the enactment of this Act, shall, on and after such date of enactment, be considered to be an application that was submitted and filed under section 505(b) of such Act (21 U.S.C. 355(b)) and approved for safety and effectiveness under section 505(c) of such Act (21 U.S.C. 355(c)), except that if such application for marketing was in the form of an abbreviated application, the application shall be considered to have been filed and approved under section 505(j) of such Act (21 U.S.C. 355(j)).

“(2) EXCEPTION.—The following subsections of section 505 (21 U.S.C. 355) shall not apply to any application for marketing in which the drug that is the subject of the application contains an antibiotic drug and the antibiotic drug was the subject of any application for marketing received by the Secretary of Health and Human Services under section 507 of such Act (21 U.S.C. 357) before the date of the enactment of this Act [Nov. 21, 1997]:

“(A)(i) Subsections (c)(2), (d)(6), (e)(4), (j)(2)(A)(vii), (j)(2)(A)(viii), (j)(2)(B), (j)(4)(B), and (j)(4)(D); and

“(ii) The third and fourth sentences of subsection (b)(1) (regarding the filing and publication of patent information); and

“(B) Subsections (b)(2)(A), (b)(2)(B), (b)(3), and (c)(3) if the investigations relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

“(3) PUBLICATION.—For purposes of this section, the Secretary is authorized to make available to the public the established name of each antibiotic drug that was the subject of any application for marketing received by the Secretary for Health and Human Services under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357) before the date of enactment of this Act [Nov. 21, 1997].”

TERMINATION OF ADVISORY PANELS

Advisory panels established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless, in the case of a panel established by the President or an officer of the Federal Government, such panel is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a panel established by Congress, its duration is otherwise provided for by law. See sections 3(2) and 14 of Pub. L. 92–463, Oct. 6, 1972, 86 Stat. 770, 776, set out in the Appendix to Title 5, Government Organization and Employees.

APPEALS TAKEN PRIOR TO OCTOBER 10, 1962

Pub. L. 87–781, title I, §104(d)(3), Oct. 10, 1962, 76 Stat. 785, made amendments to subsec. (h) of this section inapplicable to any appeal taken prior to Oct. 10, 1962.

§ 355-1. Risk evaluation and mitigation strategies

(a) Submission of proposed strategy

(1) Initial approval

If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

(A) The estimated size of the population likely to use the drug involved.

(B) The seriousness of the disease or condition that is to be treated with the drug.

(C) The expected benefit of the drug with respect to such disease or condition.

(D) The expected or actual duration of treatment with the drug.

(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(F) Whether the drug is a new molecular entity.

(2) Postapproval requirement

(A) In general

If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices described in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

(B) Submission of proposed strategy

Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

(3) Abbreviated new drug applications

The applicability of this section to an application under section 355(j) of this title is subject to subsection (i).

(4) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individ-

uals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(b) Definitions

For purposes of this section:

(1) Adverse drug experience

The term “adverse drug experience” means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

(A) an adverse event occurring in the course of the use of the drug in professional practice;

(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

(C) an adverse event occurring from abuse of the drug;

(D) an adverse event occurring from withdrawal of the drug; and

(E) any failure of expected pharmacological action of the drug.

(2) Covered application

The term “covered application” means an application referred to in section 355(p)(1)(A) of this title.

(3) New safety information

The term “new safety information”, with respect to a drug, means information derived from a clinical trial, an adverse event report, a postapproval study (including a study under section 355(o)(3) of this title), or peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system under section 355(k) of this title; or other scientific data deemed appropriate by the Secretary about—

(A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of (that may be based on a new analysis of existing information) since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

(4) Serious adverse drug experience

The term “serious adverse drug experience” is an adverse drug experience that—

(A) results in—

(i) death;

(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);

(iii) inpatient hospitalization or prolongation of existing hospitalization;

(iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or

(v) a congenital anomaly or birth defect; or

(B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

(5) Serious risk

The term “serious risk” means a risk of a serious adverse drug experience.

(6) Signal of a serious risk

The term “signal of a serious risk” means information related to a serious adverse drug experience associated with use of a drug and derived from—

- (A) a clinical trial;
- (B) adverse event reports;
- (C) a postapproval study, including a study under section 355(o)(3) of this title;
- (D) peer-reviewed biomedical literature;
- (E) data derived from the postmarket risk identification and analysis system under section 355(k)(4) of this title; or
- (F) other scientific data deemed appropriate by the Secretary.

(7) Responsible person

The term “responsible person” means the person submitting a covered application or the holder of the approved such application.

(8) Unexpected serious risk

The term “unexpected serious risk” means a serious adverse drug experience that is not listed in the labeling of a drug, or that may be symptomatically and pathophysiologically related to an adverse drug experience identified in the labeling, but differs from such adverse drug experience because of greater severity, specificity, or prevalence.

(c) Contents

A proposed risk evaluation and mitigation strategy under subsection (a) shall—

- (1) include the timetable required under subsection (d); and
- (2) to the extent required by the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, include additional elements described in subsections (e) and (f).

(d) Minimal strategy

For purposes of subsection (c)(1), the risk evaluation and mitigation strategy for a drug shall require a timetable for submission of assessments of the strategy that—

- (1) includes an assessment, by the date that is 18 months after the strategy is initially approved;
- (2) includes an assessment by the date that is 3 years after the strategy is initially approved;
- (3) includes an assessment in the seventh year after the strategy is so approved; and
- (4) subject to paragraphs (1), (2), and (3)—
 - (A) is at a frequency specified in the strategy;
 - (B) is increased or reduced in frequency as necessary as provided for in subsection (g)(4)(A); and
 - (C) is eliminated after the 3-year period described in paragraph (1) if the Secretary de-

termines that serious risks of the drug have been adequately identified and assessed and are being adequately managed.

(e) Additional potential elements of strategy

(1) In general

The Secretary, in consultation with the offices described in subsection (c)(2), may under such subsection require that the risk evaluation and mitigation strategy for a drug include 1 or more of the additional elements described in this subsection if the Secretary makes the determination required with respect to each element involved.

(2) Medication Guide; patient package insert

The risk evaluation and mitigation strategy for a drug may require that, as applicable, the responsible person develop for distribution to each patient when the drug is dispensed—

(A) a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations); and

(B) a patient package insert, if the Secretary determines that such insert may help mitigate a serious risk of the drug.

(3) Communication plan

The risk evaluation and mitigation strategy for a drug may require that the responsible person conduct a communication plan to health care providers, if, with respect to such drug, the Secretary determines that such plan may support implementation of an element of the strategy (including under this paragraph). Such plan may include—

(A) sending letters to health care providers;

(B) disseminating information about the elements of the risk evaluation and mitigation strategy to encourage implementation by health care providers of components that apply to such health care providers, or to explain certain safety protocols (such as medical monitoring by periodic laboratory tests); or

(C) disseminating information to health care providers through professional societies about any serious risks of the drug and any protocol to assure safe use.

(f) Providing safe access for patients to drugs with known serious risks that would otherwise be unavailable

(1) Allowing safe access to drugs with known serious risks

The Secretary, in consultation with the offices described in subsection (c)(2), may require that the risk evaluation and mitigation strategy for a drug include such elements as are necessary to assure safe use of the drug, because of its inherent toxicity or potential harmfulness, if the Secretary determines that—

(A) the drug, which has been shown to be effective, but is associated with a serious adverse drug experience, can be approved only if, or would be withdrawn unless, such elements are required as part of such strategy to mitigate a specific serious risk listed in the labeling of the drug; and

(B) for a drug initially approved without elements to assure safe use, other elements under subsections (c), (d), and (e) are not sufficient to mitigate such serious risk.

(2) Assuring access and minimizing burden

Such elements to assure safe use under paragraph (1) shall—

(A) be commensurate with the specific serious risk listed in the labeling of the drug;

(B) within 30 days of the date on which any element under paragraph (1) is imposed, be posted publicly by the Secretary with an explanation of how such elements will mitigate the observed safety risk;

(C) considering such risk, not be unduly burdensome on patient access to the drug, considering in particular—

(i) patients with serious or life-threatening diseases or conditions; and

(ii) patients who have difficulty accessing health care (such as patients in rural or medically underserved areas); and

(D) to the extent practicable, so as to minimize the burden on the health care delivery system—

(i) conform with elements to assure safe use for other drugs with similar, serious risks; and

(ii) be designed to be compatible with established distribution, procurement, and dispensing systems for drugs.

(3) Elements to assure safe use

The elements to assure safe use under paragraph (1) shall include 1 or more goals to mitigate a specific serious risk listed in the labeling of the drug and, to mitigate such risk, may require that—

(A) health care providers who prescribe the drug have particular training or experience, or are specially certified (the opportunity to obtain such training or certification with respect to the drug shall be available to any willing provider from a frontier area in a widely available training or certification method (including an on-line course or via mail) as approved by the Secretary at reasonable cost to the provider);

(B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified (the opportunity to obtain such certification shall be available to any willing provider from a frontier area);

(C) the drug be dispensed to patients only in certain health care settings, such as hospitals;

(D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;

(E) each patient using the drug be subject to certain monitoring; or

(F) each patient using the drug be enrolled in a registry.

(4) Implementation system

The elements to assure safe use under paragraph (1) that are described in subparagraphs (B), (C), and (D) of paragraph (3) may include a system through which the applicant is able to take reasonable steps to—

(A) monitor and evaluate implementation of such elements by health care providers,

pharmacists, and other parties in the health care system who are responsible for implementing such elements; and

(B) work to improve implementation of such elements by such persons.

(5) Evaluation of elements to assure safe use

The Secretary, through the Drug Safety and Risk Management Advisory Committee (or successor committee) of the Food and Drug Administration, shall—

(A) seek input from patients, physicians, pharmacists, and other health care providers about how elements to assure safe use under this subsection for 1 or more drugs may be standardized so as not to be—

(i) unduly burdensome on patient access to the drug; and

(ii) to the extent practicable, minimize the burden on the health care delivery system;

(B) at least annually, evaluate, for 1 or more drugs, the elements to assure safe use of such drug to assess whether the elements—

(i) assure safe use of the drug;

(ii) are not unduly burdensome on patient access to the drug; and

(iii) to the extent practicable, minimize the burden on the health care delivery system; and

(C) considering such input and evaluations—

(i) issue or modify agency guidance about how to implement the requirements of this subsection; and

(ii) modify elements under this subsection for 1 or more drugs as appropriate.

(6) Additional mechanisms to assure access

The mechanisms under section 360bbb of this title to provide for expanded access for patients with serious or life-threatening diseases or conditions may be used to provide access for patients with a serious or life-threatening disease or condition, the treatment of which is not an approved use for the drug, to a drug that is subject to elements to assure safe use under this subsection. The Secretary shall promulgate regulations for how a physician may provide the drug under the mechanisms of section 360bbb of this title.

(7) Repealed. Pub. L. 113-5, title III, § 302(c)(1), Mar. 13, 2013, 127 Stat. 185

(8) Limitation

No holder of an approved covered application shall use any element to assure safe use required by the Secretary under this subsection to block or delay approval of an application under section 355(b)(2) or (j) of this title or to prevent application of such element under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application.

(g) Assessment and modification of approved strategy

(1) Voluntary assessments

After the approval of a risk evaluation and mitigation strategy under subsection (a), the

responsible person involved may, subject to paragraph (2), submit to the Secretary an assessment of the approved strategy for the drug involved at any time.

(2) Required assessments

A responsible person shall submit an assessment of the approved risk evaluation and mitigation strategy for a drug—

(A) when submitting a supplemental application for a new indication for use under section 355(b) of this title or under section 262 of title 42, unless the drug is not subject to section 353(b) of this title and the risk evaluation and mitigation strategy for the drug includes only the timetable under subsection (d);

(B) when required by the strategy, as provided for in such timetable under subsection (d);

(C) within a time period to be determined by the Secretary, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that an assessment is needed to evaluate whether the approved strategy should be modified to—

(i) ensure the benefits of the drug outweigh the risks of the drug; or

(ii) minimize the burden on the health care delivery system of complying with the strategy.

(3) Requirements for assessments

An assessment under paragraph (1) or (2) of an approved risk evaluation and mitigation strategy for a drug shall include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

(4) Modification

(A) On initiative of responsible person

After the approval of a risk evaluation and mitigation strategy by the Secretary, the responsible person may, at any time, submit to the Secretary a proposal to modify the approved strategy. Such proposal may propose the addition, modification, or removal of any goal or element of the approved strategy and shall include an adequate rationale to support such proposed addition, modification, or removal of any goal or element of the strategy.

(B) On initiative of Secretary

After the approval of a risk evaluation and mitigation strategy by the Secretary, the Secretary may, at any time, require a responsible person to submit a proposed modification to the strategy within 120 days or within such reasonable time as the Secretary specifies, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that 1 or more goals or elements should be added, modified, or removed from the approved strategy to—

(i) ensure the benefits of the drug outweigh the risks of the drug; or

(ii) minimize the burden on the health care delivery system of complying with the strategy.

(h) Review of proposed strategies; review of assessments and modifications of approved strategies

(1) In general

The Secretary, in consultation with the offices described in subsection (c)(2), shall promptly review each proposed risk evaluation and mitigation strategy for a drug submitted under subsection (a) and each assessment of and proposed modification to an approved risk evaluation and mitigation strategy for a drug submitted under subsection (g), and, if necessary, promptly initiate discussions with the responsible person about such proposed strategy, assessment, or modification.

(2) Action

(A) In general

(i) Timeframe

Unless the dispute resolution process described under paragraph (3) or (4) applies, and, except as provided in clause (ii) or clause (iii) below, the Secretary, in consultation with the offices described in subsection (c)(2), shall review and act on the proposed risk evaluation and mitigation strategy for a drug or any proposed modification to any required strategy within 180 days of receipt of the proposed strategy or modification.

(ii) Minor modifications

The Secretary shall review and act on a proposed minor modification, as defined by the Secretary in guidance, within 60 days of receipt of such modification.

(iii) REMS modification due to safety label changes

Not later than 60 days after the Secretary receives a proposed modification to an approved risk evaluation and mitigation strategy to conform the strategy to approved safety label changes, including safety labeling changes initiated by the sponsor in accordance with FDA regulatory requirements, or to a safety label change that the Secretary has directed the holder of the application to make pursuant to section 355(o)(4) of this title, the Secretary shall review and act on such proposed modification to the approved strategy.

(iv) Guidance

The Secretary shall establish, through guidance, that responsible persons may implement certain modifications to an approved risk evaluation and mitigation strategy following notification to the Secretary.

(B) Inaction

An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided under subparagraph (A).

(C) Public availability

Upon acting on a proposed risk evaluation and mitigation strategy or proposed modification to a risk evaluation and mitigation

strategy under subparagraph (A), the Secretary shall make publicly available an action letter describing the actions taken by the Secretary under such subparagraph (A).

(3) Dispute resolution at initial approval

If a proposed risk evaluation and mitigation strategy is submitted under subsection (a)(1) in an application for initial approval of a drug and there is a dispute about the strategy, the responsible person shall use the major dispute resolution procedures as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(4) Dispute resolution in all other cases

(A) Request for review

(i) In general

The responsible person may, after the sponsor is required to make a submission under subsection (a)(2) or (g), request in writing that a dispute about the strategy be reviewed by the Drug Safety Oversight Board under subsection (j), except that the determination of the Secretary to require a risk evaluation and mitigation strategy is not subject to review under this paragraph. The preceding sentence does not prohibit review under this paragraph of the particular elements of such a strategy.

(ii) Scheduling

Upon receipt of a request under clause (i), the Secretary shall schedule the dispute involved for review under subparagraph (B) and, not later than 5 business days of scheduling the dispute for review, shall publish by posting on the Internet or otherwise a notice that the dispute will be reviewed by the Drug Safety Oversight Board.

(B) Scheduling review

If a responsible person requests review under subparagraph (A), the Secretary—

(i) shall schedule the dispute for review at 1 of the next 2 regular meetings of the Drug Safety Oversight Board, whichever meeting date is more practicable; or

(ii) may convene a special meeting of the Drug Safety Oversight Board to review the matter more promptly, including to meet an action deadline on an application (including a supplemental application).

(C) Agreement after discussion or administrative appeals

(i) Further discussion or administrative appeals

A request for review under subparagraph (A) shall not preclude further discussions to reach agreement on the risk evaluation and mitigation strategy, and such a request shall not preclude the use of administrative appeals within the Food and Drug Administration to reach agreement on the strategy, including appeals as described in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007 for procedural or scientific matters involving the review of human drug applications and supplemental

applications that cannot be resolved at the divisional level. At the time a review has been scheduled under subparagraph (B) and notice of such review has been posted, the responsible person shall either withdraw the request under subparagraph (A) or terminate the use of such administrative appeals.

(ii) Agreement terminates dispute resolution

At any time before a decision and order is issued under subparagraph (G), the Secretary (in consultation with the offices described in subsection (c)(2)) and the responsible person may reach an agreement on the risk evaluation and mitigation strategy through further discussion or administrative appeals, terminating the dispute resolution process, and the Secretary shall issue an action letter or order, as appropriate, that describes the strategy.

(D) Meeting of the Board

At a meeting of the Drug Safety Oversight Board described in subparagraph (B), the Board shall—

(i) hear from both parties via written or oral presentation; and

(ii) review the dispute.

(E) Record of proceedings

The Secretary shall ensure that the proceedings of any such meeting are recorded, transcribed, and made public within 90 days of the meeting. The Secretary shall redact the transcript to protect any trade secrets and other information that is exempted from disclosure under section 552 of title 5 or section 552a of title 5.

(F) Recommendation of the Board

Not later than 5 days after any such meeting, the Drug Safety Oversight Board shall provide a written recommendation on resolving the dispute to the Secretary. Not later than 5 days after the Board provides such written recommendation to the Secretary, the Secretary shall make the recommendation available to the public.

(G) Action by the Secretary

(i) Action letter

With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall issue an action letter that resolves the dispute not later than the later of—

(I) the action deadline for the action letter on the application; or

(II) 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(ii) Order

With respect to an assessment of an approved risk evaluation and mitigation strategy under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2), the Secretary shall issue an order, which shall be made public, that resolves the dispute not later than 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(H) Inaction

An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided for under subparagraph (G).

(I) Effect on action deadline

With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall be considered to have met the action deadline for the action letter on the application if the responsible person requests the dispute resolution process described in this paragraph and if the Secretary has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.

(J) Disqualification

No individual who is an employee of the Food and Drug Administration and who reviews a drug or who participated in an administrative appeal under subparagraph (C)(i) with respect to such drug may serve on the Drug Safety Oversight Board at a meeting under subparagraph (D) to review a dispute about the risk evaluation and mitigation strategy for such drug.

(K) Additional expertise

The Drug Safety Oversight Board may add members with relevant expertise from the Food and Drug Administration, including the Office of Pediatrics, the Office of Women's Health, or the Office of Rare Diseases, or from other Federal public health or health care agencies, for a meeting under subparagraph (D) of the Drug Safety Oversight Board.

(5) Use of advisory committees

The Secretary may convene a meeting of 1 or more advisory committees of the Food and Drug Administration to—

(A) review a concern about the safety of a drug or class of drugs, including before an assessment of the risk evaluation and mitigation strategy or strategies of such drug or drugs is required to be submitted under subparagraph (B) or (C) of subsection (g)(2);

(B) review the risk evaluation and mitigation strategy or strategies of a drug or group of drugs; or

(C) review a dispute under paragraph (3) or (4).

(6) Process for addressing drug class effects**(A) In general**

When a concern about a serious risk of a drug may be related to the pharmacological class of the drug, the Secretary, in consultation with the offices described in subsection (c)(2), may defer assessments of the approved risk evaluation and mitigation strategies for such drugs until the Secretary has convened 1 or more public meetings to consider possible responses to such concern.

(B) Notice

If the Secretary defers an assessment under subparagraph (A), the Secretary shall—

(i) give notice of the deferral to the holder of the approved covered application not later than 5 days after the deferral;

(ii) publish the deferral in the Federal Register; and

(iii) give notice to the public of any public meetings to be convened under subparagraph (A), including a description of the deferral.

(C) Public meetings

Such public meetings may include—

(i) 1 or more meetings of the responsible person for such drugs;

(ii) 1 or more meetings of 1 or more advisory committees of the Food and Drug Administration, as provided for under paragraph (6); or

(iii) 1 or more workshops of scientific experts and other stakeholders.

(D) Action

After considering the discussions from any meetings under subparagraph (A), the Secretary may—

(i) announce in the Federal Register a planned regulatory action, including a modification to each risk evaluation and mitigation strategy, for drugs in the pharmacological class;

(ii) seek public comment about such action; and

(iii) after seeking such comment, issue an order addressing such regulatory action.

(7) International coordination

The Secretary, in consultation with the offices described in subsection (c)(2), may coordinate the timetable for submission of assessments under subsection (d), or a study or clinical trial under section 355(o)(3) of this title, with efforts to identify and assess the serious risks of such drug by the marketing authorities of other countries whose drug approval and risk management processes the Secretary deems comparable to the drug approval and risk management processes of the United States. If the Secretary takes action to coordinate such timetable, the Secretary shall give notice to the responsible person.

(8) Effect

Use of the processes described in paragraphs (6) and (7),¹ shall not be the sole source of delay of action on an application or a supplement to an application for a drug.

(i) Abbreviated new drug applications**(1) In general**

A drug that is the subject of an abbreviated new drug application under section 355(j) of this title is subject to only the following elements of the risk evaluation and mitigation strategy required under subsection (a) for the applicable listed drug:

(A) A Medication Guide or patient package insert, if required under subsection (e) for the applicable listed drug.

(B) Elements to assure safe use, if required under subsection (f) for the listed drug. A

¹ So in original. The period probably should not appear.

drug that is the subject of an abbreviated new drug application and the listed drug shall use a single, shared system under subsection (f). The Secretary may waive the requirement under the preceding sentence for a drug that is the subject of an abbreviated new drug application, and permit the applicant to use a different, comparable aspect of the elements to assure safe use, if the Secretary determines that—

(i) the burden of creating a single, shared system outweighs the benefit of a single, system,² taking into consideration the impact on health care providers, patients, the applicant for the abbreviated new drug application, and the holder of the reference drug product; or

(ii) an aspect of the elements to assure safe use for the applicable listed drug is claimed by a patent that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the abbreviated new drug application certifies that it has sought a license for use of an aspect of the elements to assure safe use for the applicable listed drug and that it was unable to obtain a license.

A certification under clause (ii) shall include a description of the efforts made by the applicant for the abbreviated new drug application to obtain a license. In a case described in clause (ii), the Secretary may seek to negotiate a voluntary agreement with the owner of the patent, method, or process for a license under which the applicant for such abbreviated new drug application may use an aspect of the elements to assure safe use, if required under subsection (f) for the applicable listed drug, that is claimed by a patent that has not expired or is a method or process that as a trade secret is entitled to protection.

(2) Action by Secretary

For an applicable listed drug for which a drug is approved under section 355(j) of this title, the Secretary—

(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug; and

(B) shall inform the responsible person for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

(j) Drug Safety Oversight Board

(1) In general

There is established a Drug Safety Oversight Board.

(2) Composition; meetings

The Drug Safety Oversight Board shall—

(A) be composed of scientists and health care practitioners appointed by the Secretary, each of whom is an employee of the Federal Government;

(B) include representatives from offices throughout the Food and Drug Administra-

tion, including the offices responsible for postapproval safety of drugs;

(C) include at least 1 representative each from the National Institutes of Health and the Department of Health and Human Services (other than the Food and Drug Administration);

(D) include such representatives as the Secretary shall designate from other appropriate agencies that wish to provide representatives; and

(E) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.

(k) Waiver in public health emergencies

The Secretary may waive any requirement of this section with respect to a qualified countermeasure (as defined in section 247d-6a(a)(2) of title 42) to which a requirement under this section has been applied, if the Secretary determines that such waiver is required to mitigate the effects of, or reduce the severity of, the circumstances under which—

(1) a determination described in subparagraph (A), (B), or (C) of section 360bbb-3(b)(1) of this title has been made by the Secretary of Homeland Security, the Secretary of Defense, or the Secretary, respectively; or

(2) the identification of a material threat described in subparagraph (D) of section 360bbb-3(b)(1) of this title has been made pursuant to section 247d-6b of title 42.

(June 25, 1938, ch. 675, §505-1, as added Pub. L. 110-85, title IX, §901(b), Sept. 27, 2007, 121 Stat. 926; amended Pub. L. 112-144, title XI, §1132(a), (b), July 9, 2012, 126 Stat. 1119, 1120; Pub. L. 113-5, title III, §302(c), Mar. 13, 2013, 127 Stat. 185.)

REFERENCES IN TEXT

For the effective date of this section, referred to in subsec. (a)(2)(A), see Effective Date note below.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (h)(3), (4)(C)(i), is section 101(c) of Pub. L. 110-85, which is set out as a note under section 379g of this title.

AMENDMENTS

2013—Subsec. (f)(7). Pub. L. 113-5, §302(c)(1), struck out par. (7) which related to waiver of subsec. (f) requirements in public health emergencies.

Subsec. (k). Pub. L. 113-5, §302(c)(2), added subsec. (k).

2012—Subsec. (g)(1). Pub. L. 112-144, §1132(a)(1), struck out “, and propose a modification to,” after “an assessment of”.

Subsec. (g)(2). Pub. L. 112-144, §1132(a)(2)(A), in introductory provisions, struck out “, subject to paragraph (5),” after “shall” and “, and may propose a modification to,” after “an assessment of”.

Subsec. (g)(2)(C). Pub. L. 112-144, §1132(a)(2)(B), substituted “an assessment is needed to evaluate whether the approved strategy should be modified to—” and cls. (i) and (ii) for “new safety or effectiveness information indicates that—

“(i) an element under subsection (d) or (e) should be modified or included in the strategy; or

“(ii) an element under subsection (f) should be modified or included in the strategy; or”.

Subsec. (g)(2)(D). Pub. L. 112-144, §1132(a)(2)(C), struck out subpar. (D) which read as follows: “within 15 days when ordered by the Secretary, in consultation with the offices described in subsection (c)(2), if the Secretary determines that there may be a cause for action by the Secretary under section 355(e) of this title.”

²So in original. Probably should be “single, shared system.”.

Subsec. (g)(3). Pub. L. 112-144, §1132(a)(3), substituted “for a drug shall include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.” for “for a drug shall include—” and struck out subpars. (A) to (C) which related to assessment of elements to assure safe use, postapproval studies, and postapproval clinical trials.

Subsec. (g)(4). Pub. L. 112-144, §1132(a)(4), amended par. (4) generally. Prior to amendment, text read as follows: “A modification (whether an enhancement or a reduction) to the approved risk evaluation and mitigation strategy for a drug may include the addition or modification of any element under subsection (d) or the addition, modification, or removal of any element under subsection (e) or (f), such as—

“(A) modifying the timetable for assessments of the strategy as provided in subsection (d)(3), including to eliminate assessments; or

“(B) adding, modifying, or removing an element to assure safe use under subsection (f).”

Subsec. (h). Pub. L. 112-144, §1132(b)(1), inserted “and modifications” after “review of assessments” in heading.

Subsec. (h)(1). Pub. L. 112-144, §1132(b)(2), inserted “and proposed modification to” after “under subsection (a) and each assessment of” and “, and, if necessary, promptly initiate discussions with the responsible person about such proposed strategy, assessment, or modification” after “subsection (g)”.

Subsec. (h)(2). Pub. L. 112-144, §1132(b)(3), (4), redesignated par. (3) as (2) and struck out former par. (2). Prior to amendment, text of par. (2) read as follows: “The Secretary, in consultation with the offices described in subsection (c)(2), shall initiate discussions with the responsible person for purposes of this subsection to determine a strategy not later than 60 days after any such assessment is submitted or, in the case of an assessment submitted under subsection (g)(2)(D), not later than 30 days after such assessment is submitted.”

Subsec. (h)(2)(A). Pub. L. 112-144, §1132(b)(5)(A), amended subpar. (A) generally. Prior to amendment, subpar. (A) related to Secretary’s description of any required risk evaluation and mitigation strategy for a drug as part of the action letter on the application or in an order.

Subsec. (h)(2)(C). Pub. L. 112-144, §1132(b)(5)(B), amended subpar. (C) generally. Prior to amendment, text read as follows: “Any action letter described in subparagraph (A)(i) or order described in subparagraph (A)(ii) shall be made publicly available.”

Subsec. (h)(3), (4). Pub. L. 112-144, §1132(b)(4), redesignated pars. (4) and (5) as (3) and (4), respectively. Former par. (3) redesignated (2).

Subsec. (h)(4)(A)(i). Pub. L. 112-144, §1132(b)(6)(A), substituted “The responsible” for “Not earlier than 15 days, and not later than 35 days, after discussions under paragraph (2) have begun, the responsible” and inserted “, after the sponsor is required to make a submission under subsection (a)(2) or (g),” before “request in writing”.

Subsec. (h)(4)(I). Pub. L. 112-144, §1132(b)(6)(B), substituted “if the Secretary has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.” for “if the Secretary—” and struck out cls. (i) and (ii) which read as follows:

“(i) has initiated the discussions described under paragraph (2) not less than 60 days before such action deadline; and

“(ii) has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.”

Subsec. (h)(5). Pub. L. 112-144, §1132(b)(4), (7), redesignated par. (6) as (5) and substituted “subparagraph (B)

or (C)” for “any of subparagraphs (B) through (D)” in subpar. (A) and “paragraph (3) or (4)” for “paragraph (4) or (5)” in subpar. (C). Former par. (5) redesignated (4).

Subsec. (h)(6), (7). Pub. L. 112-144, §1132(b)(4), redesignated pars. (7) and (8) as (6) and (7), respectively. Former par. (6) redesignated (5).

Subsec. (h)(8), (9). Pub. L. 112-144, §1132(b)(4), (8), redesignated par. (9) as (8) and substituted “paragraphs (6) and (7).” for “paragraphs (7) and (8)”. Former par. (8) redesignated (7).

EFFECTIVE DATE

Section effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110-85, set out as an Effective Date of 2007 Amendment note under section 331 of this title.

GUIDANCE

Pub. L. 112-144, title XI, §1132(c), July 9, 2012, 126 Stat. 1122, provided that: “Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services shall issue guidance that, for purposes of section 505-1(h)(2)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355-1(h)(2)(A)), describes the types of modifications to approved risk evaluation and mitigation strategies that shall be considered to be minor modifications of such strategies.”

§ 355a. Pediatric studies of drugs

(a) Definitions

As used in this section, the term “pediatric studies” or “studies” means at least one clinical investigation (that, at the Secretary’s discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used, and, at the discretion of the Secretary, may include preclinical studies.

(b) Market exclusivity for new drugs

(1) In general

Except as provided in paragraph (2), if, prior to approval of an application that is submitted under section 355(b)(1) of this title, the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(c) Market exclusivity for already-marketed drugs

(1) In general

Except as provided in paragraph (2), if the Secretary determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under section 355(b)(1) of this title for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-

half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B)(ii) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(d) Conduct of pediatric studies

(1) Request for studies

(A) In general

The Secretary may, after consultation with the sponsor of an application for an investigational new drug under section 355(i) of this title, the sponsor of an application for a new drug under section 355(b)(1) of this title, or the holder of an approved application for a drug under section 355(b)(1) of this title, issue to the sponsor or holder a written request for the conduct of pediatric studies for such drug. In issuing such request, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Such request to conduct pediatric studies shall be in writing and shall

include a timeframe for such studies and a request to the sponsor or holder to propose pediatric labeling resulting from such studies. If a request under this subparagraph does not request studies in neonates, such request shall include a statement describing the rationale for not requesting studies in neonates.

(B) Single written request

A single written request—

- (i) may relate to more than one use of a drug; and
- (ii) may include uses that are both approved and unapproved.

(2) Written request for pediatric studies

(A) Request and response

(i) In general

If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (b) or (c), the applicant or holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the applicant or holder to act on the request by—

(I) indicating when the pediatric studies will be initiated, if the applicant or holder agrees to the request; or

(II) indicating that the applicant or holder does not agree to the request and stating the reasons for declining the request.

(ii) Disagree with request

If, on or after September 27, 2007, the applicant or holder does not agree to the request on the grounds that it is not possible to develop the appropriate pediatric formulation, the applicant or holder shall submit to the Secretary the reasons such pediatric formulation cannot be developed.

(B) Adverse event reports

An applicant or holder that, on or after September 27, 2007, agrees to the request for such studies shall provide the Secretary, at the same time as the submission of the reports of such studies, with all postmarket adverse event reports regarding the drug that is the subject of such studies and are available prior to submission of such reports.

(3) Meeting the studies requirement

Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

(4) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(5) Consultation

With respect to a drug that is a qualified countermeasure (as defined in section 247d-6a of title 42), a security countermeasure (as defined in section 247d-6b of title 42), or a qualified pandemic or epidemic product (as defined in section 247d-6d of title 42), the Secretary shall solicit input from the Assistant Secretary for Preparedness and Response regarding the need for and, from the Director of the Biomedical Advanced Research and Development Authority regarding the conduct of, pediatric studies under this section.

(e) Notice of determinations on studies requirement

(1) In general

The Secretary shall publish a notice of any determination, made on or after September 27, 2007, that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 355 of this title for a drug will be subject to the provisions of this section. Such notice shall be published not later than 30 days after the date of the Secretary's determination regarding market exclusivity and shall include a copy of the written request made under subsection (b) or (c).

(2) Identification of certain drugs

The Secretary shall publish a notice identifying any drug for which, on or after September 27, 2007, a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population (or specified subpopulation) if the pediatric formulation for such drug is not introduced onto the market within one year after the date that the Secretary publishes the notice described in paragraph (1). Such notice identifying such drug shall be published not later than 30 days after the date of the expiration of such one year period.

(f) Internal review of written requests and pediatric studies

(1) Internal review

The Secretary shall utilize the internal review committee established under section 355d of this title to review all written requests issued on or after September 27, 2007, in accordance with paragraph (2).

(2) Review of written requests

The committee referred to in paragraph (1) shall review all written requests issued pursuant to this section prior to being issued.

(3) Review of pediatric studies

The committee referred to in paragraph (1) may review studies conducted pursuant to this section to make a recommendation to the Secretary whether to accept or reject such reports under subsection (d)(3).

(4) Activity by committee

The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(5) Documentation of committee action

For each drug, the committee referred to in paragraph (1) shall document, for each activ-

ity described in paragraph (2) or (3), which members of the committee participated in such activity.

(6) Tracking pediatric studies and labeling changes

The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public, in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of studies conducted under this section and under section 284m of title 42;

(B) the specific drugs and drug uses, including labeled and off-labeled indications, studied under such sections;

(C) the types of studies conducted under such sections, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons such formulations were not developed;

(E) the labeling changes made as a result of studies conducted under such sections;

(F) an annual summary of labeling changes made as a result of studies conducted under such sections for distribution pursuant to subsection (k)(2); and

(G) information regarding reports submitted on or after September 27, 2007.

(g) Limitations

Notwithstanding subsection (c)(2), a drug to which the six-month period under subsection (b) or (c) has already been applied—

(1) may receive an additional six-month period under subsection (c)(1)(A)(i)(II) for a supplemental application if all other requirements under this section are satisfied, except that such drug may not receive any additional such period under subsection (c)(1)(B); and

(2) may not receive any additional such period under subsection (c)(1)(A)(ii).

(h) Relationship to pediatric research requirements

Exclusivity under this section shall only be granted for the completion of a study or studies that are the subject of a written request and for which reports are submitted and accepted in accordance with subsection (d)(3). Written requests under this section may consist of a study or studies required under section 355c of this title.

(i) Labeling changes

(1) Priority status for pediatric applications and supplements

Any application or supplement to an application under section 355 of this title proposing a labeling change as a result of any pediatric study conducted pursuant to this section—

(A) shall be considered to be a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) Dispute resolution

(A) Request for labeling change and failure to agree

If, on or after September 27, 2007, the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor of the application does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) Action by the Pediatric Advisory Committee

Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) Consideration of recommendations

The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate.

(D) Misbranding

If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

(E) No effect on authority

Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(j) Other labeling changes

If, on or after September 27, 2007, the Secretary determines that a pediatric study conducted under this section does or does not demonstrate that the drug that is the subject of the study is safe and effective, including whether such study results are inconclusive, in pediatric populations or subpopulations, the Secretary shall order the labeling of such product to include information about the results of the study

and a statement of the Secretary's determination.

(k) Dissemination of pediatric information

(1) In general

Not later than 210 days after the date of submission of a report on a pediatric study under this section, the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of pediatric studies conducted under subsection (b) or (c).

(2) Dissemination of information regarding labeling changes

Beginning on September 27, 2007, the Secretary shall include as a requirement of a written request that the sponsors of the studies that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(F) distribute, at least annually (or more frequently if the Secretary determines that it would be beneficial to the public health), such information to physicians and other health care providers.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(l) Adverse event reporting

(1) Reporting in first 18-month period

Beginning on September 27, 2007, during the 18-month period beginning on the date a labeling change is approved pursuant to subsection (i), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics established under section 393a of this title. In considering the reports, the Director of such Office shall provide for the review of the reports by the Pediatric Advisory Committee, including obtaining any recommendations of such Committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) Reporting in subsequent periods

Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) Preservation of authority

Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) Effect

The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(m) Clarification of interaction of market exclusivity under this section and market exclusivity awarded to an applicant for approval of a drug under section 355(j) of this title

If a 180-day period under section 355(j)(5)(B)(iv) of this title overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 355(j) of this title entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

(n) Referral if pediatric studies not submitted

(1) In general

Beginning on September 27, 2007, if pediatric studies of a drug have not been submitted by the date specified in the written request issued or if the applicant or holder does not agree to the request under subsection (d) and if the Secretary, through the committee established under section 355d of this title, determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall carry out the following:

(A) For a drug for which a listed patent has not expired, or for which a period of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 has not ended, make a determination regarding whether an assessment shall be required to be submitted under section 355c(b) of this title.

(B) For a drug that has no unexpired listed patents and for which no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 apply, the Secretary shall refer the drug for inclusion on the list established under section 284m of title 42 for the conduct of studies.

(C) For a drug that is a qualified countermeasure (as defined in section 247d-6a of title 42), a security countermeasure (as defined in section 247d-6b of title 42), or a qualified pandemic or epidemic product (as defined in section 247d-6d of title 42), in addition to any action with respect to such drug under subparagraph (A) or (B), the Secretary shall notify the Assistant Secretary for Preparedness and Response and the Director of the Biomedical Advanced Research and Development Authority of all pediatric studies in the written request issued by the Commissioner of Food and Drugs.

(2) Public notice

The Secretary shall give the public notice of a decision under paragraph (1)(A) not to re-

quire an assessment under section 355c of this title and the basis for such decision.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(o) Prompt approval of drugs under section 355(j) when pediatric information is added to labeling

(1) General rule

A drug for which an application has been submitted or approved under section 355(j) of this title shall not be considered ineligible for approval under that section or misbranded under section 352 of this title on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title.

(2) Labeling

Notwithstanding clauses (iii) and (iv) of section 355(j)(5)(F) of this title, the Secretary may require that the labeling of a drug approved under section 355(j) of this title that omits a pediatric indication or other aspect of labeling as described in paragraph (1) include—

(A) a statement that, because of marketing exclusivity for a manufacturer—

(i) the drug is not labeled for pediatric use; or

(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

(B) a statement of any appropriate pediatric contraindications, warnings, precautions, or other information that the Secretary considers necessary to assure safe use.

(3) Preservation of pediatric exclusivity and other provisions

This subsection does not affect—

(A) the availability or scope of exclusivity under this section;

(B) the availability or scope of exclusivity under section 355 of this title for pediatric formulations;

(C) the question of the eligibility for approval of any application under section 355(j) of this title that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title; or

(D) except as expressly provided in paragraphs (1) and (2), the operation of section 355 of this title.

(p) Institute of Medicine study

Not later than 3 years after September 27, 2007, the Secretary shall enter into a contract with the Institute of Medicine to conduct a study and report to Congress regarding the written requests made and the studies conducted pursuant to this section. The Institute of Medicine may devise an appropriate mechanism to review a

representative sample of requests made and studies conducted pursuant to this section in order to conduct such study. Such study shall—

(1) review such representative written requests issued by the Secretary since 1997 under subsections (b) and (c);

(2) review and assess such representative pediatric studies conducted under subsections (b) and (c) since 1997 and labeling changes made as a result of such studies;

(3) review the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, and ethical issues in pediatric clinical trials;

(4) review and assess the number and importance of biological products for children that are being tested as a result of the amendments made by the Biologics Price Competition and Innovation Act of 2009 and the importance for children, health care providers, parents, and others of labeling changes made as a result of such testing;

(5) review and assess the number, importance, and prioritization of any biological products that are not being tested for pediatric use; and

(6) offer recommendations for ensuring pediatric testing of biological products, including consideration of any incentives, such as those provided under this section or section 262(m) of title 42.

(June 25, 1938, ch. 675, §505A, as added Pub. L. 105-115, title I, §111, Nov. 21, 1997, 111 Stat. 2305; amended Pub. L. 107-109, §§2, 4, 5(b)(2), 7-11(a), 18(a), 19, Jan. 4, 2002, 115 Stat. 1408, 1411, 1413-1415, 1423, 1424; Pub. L. 108-155, §§2(b)(2), 3(a), (b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108-173, title XI, §1104, Dec. 8, 2003, 117 Stat. 2461; Pub. L. 110-85, title V, §502(a)(1), Sept. 27, 2007, 121 Stat. 876; Pub. L. 111-148, title VII, §7002(g)(2)(B), Mar. 23, 2010, 124 Stat. 820; Pub. L. 112-144, title V, §§501(a), 502(a)(1), (b), 509(a), July 9, 2012, 126 Stat. 1039, 1040, 1047; Pub. L. 113-5, title III, §307(a), Mar. 13, 2013, 127 Stat. 191.)

REFERENCES IN TEXT

The Biologics Price Competition and Innovation Act of 2009, referred to in subsec. (p)(4), is subtitle A (§§7001-7003) of title VII of Pub. L. 111-148, Mar. 23, 2010, 124 Stat. 804, which amended sections 355, 355a, 355c, and 379g of this title, section 2201 of Title 28, Judiciary and Judicial Procedure, section 271 of Title 35, Patents, and sections 262 and 284m of Title 42, The Public Health and Welfare, and enacted provisions set out as notes under section 262 of Title 42. For complete classification of subtitle A to the Code, see Short Title of 2010 Amendment note set out under section 201 of Title 42 and Tables.

AMENDMENTS

2013—Subsec. (d)(5). Pub. L. 113-5, §307(a)(1), added par. (5).

Subsec. (n)(1)(C). Pub. L. 113-5, §307(a)(2), added subpar. (C).

2012—Subsec. (d)(1)(A). Pub. L. 112-144, §502(b), inserted at end “If a request under this subparagraph does not request studies in neonates, such request shall include a statement describing the rationale for not requesting studies in neonates.”

Subsec. (h). Pub. L. 112-144, §502(a)(1), amended subsec. (h) generally. Prior to amendment, text read as follows: “Notwithstanding any other provision of law, if

any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.”

Subsec. (k)(2). Pub. L. 112-144, §509(a)(1), substituted “subsection (f)(6)(F)” for “subsection (f)(3)(F)”.

Subsec. (l)(1). Pub. L. 112-144, §509(a)(2)(A), substituted “first 18-month period” for “year one” in heading and “18-month” for “one-year” in text.

Subsec. (l)(2). Pub. L. 112-144, §509(a)(2)(B), substituted “periods” for “years” in heading and “18-month period” for “one-year period” in text.

Subsec. (l)(3), (4). Pub. L. 112-144, §509(a)(2)(C), (D), added par. (3) and redesignated former par. (3) as (4).

Subsec. (n). Pub. L. 112-144, §509(a)(3)(A), substituted “submitted” for “completed” in heading.

Subsec. (n)(1). Pub. L. 112-144, §509(a)(3)(B)(i), substituted “have not been submitted by the date specified in the written request issued or if the applicant or holder does not agree to the request” for “have not been completed” in introductory provisions.

Subsec. (n)(1)(A). Pub. L. 112-144, §509(a)(3)(B)(ii), inserted “, or for which a period of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 has not ended” after “expired” and struck out at end “Prior to making such a determination, the Secretary may not take more than 30 days to certify whether the Foundation for the National Institutes of Health has sufficient funding at the time of such certification to initiate and fund all of the studies in the written request in their entirety within the timeframes specified within the written request. Only if the Secretary makes such certification in the affirmative, the Secretary shall refer all pediatric studies in the written request to the Foundation for the National Institutes of Health for the conduct of such studies, and such Foundation shall fund such studies. If no certification has been made at the end of the 30-day period, or if the Secretary certifies that funds are not sufficient to initiate and fund all the studies in their entirety, the Secretary shall consider whether assessments shall be required under section 355c(b) of this title for such drug.”

Subsec. (n)(1)(B). Pub. L. 112-144, §509(a)(3)(B)(iii), substituted “no unexpired listed patents and for which no unexpired periods of exclusivity eligible for extension under subsection (b)(1) or (c)(1) of this section or under subsection (m)(2) or (m)(3) of section 262 of title 42 apply,” for “no listed patents or has 1 or more listed patents that have expired,”.

Subsec. (o)(2)(B). Pub. L. 112-144, §509(a)(4), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: “a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary.”

Subsec. (q). Pub. L. 112-144, §501(a), struck out subsec. (q). Text read as follows: “A drug may not receive any 6-month period under subsection (b) or (c) unless—

“(1) on or before October 1, 2012, the Secretary makes a written request for pediatric studies of the drug;

“(2) on or before October 1, 2012, an application for the drug is accepted for filing under section 355(b) of this title; and

“(3) all requirements of this section are met.”

2010—Subsec. (p)(4) to (6). Pub. L. 111-148 added pars. (4) to (6) and struck out former pars. (4) and (5) which read as follows:

“(4) review and assess the pediatric studies of biological products as required under subsections (a) and (b) of section 355c of this title; and

“(5) make recommendations regarding appropriate incentives for encouraging pediatric studies of biologics.”

2007—Pub. L. 110-85 amended section generally. Prior to amendment, text consisted of subssecs. (a) to (n) relating to pediatric studies of drugs, including market

exclusivity, conduct of pediatric studies, delay of effective date for certain applications, notice of determinations on studies requirement, limitations, research requirements, labeling supplements, dissemination of information, prompt approval of drugs, report to Congress not later than Jan. 1, 2001, and sunset provisions. 2003—Subsec. (b)(1)(A)(i). Pub. L. 108-173, §1104(1), substituted “(j)(5)(F)(ii)” for “(j)(5)(D)(ii)” in two places.

Subsec. (b)(1)(A)(ii). Pub. L. 108-173, §1104(2), substituted “(j)(5)(F)” for “(j)(5)(D)”.

Subsec. (b)(2). Pub. L. 108-155, §3(a), substituted “355(j)(5)(B)” for “355(j)(4)(B)” in two places.

Subsec. (c)(1)(A)(i). Pub. L. 108-173, §1104(1), substituted “(j)(5)(F)(ii)” for “(j)(5)(D)(ii)” in two places.

Subsec. (c)(1)(A)(ii). Pub. L. 108-173, §1104(2), substituted “(j)(5)(F)” for “(j)(5)(D)”.

Subsec. (c)(2). Pub. L. 108-155, §3(a), substituted “355(j)(5)(B)” for “355(j)(4)(B)” in two places.

Subsec. (e). Pub. L. 108-173, §1104(3), substituted “355(j)(5)(F)” for “355(j)(5)(D)”.

Subsec. (h). Pub. L. 108-155, §2(b)(2), substituted “pediatric research requirements” for “regulations” in heading and “by a provision of law (including a regulation) other than this section” for “pursuant to regulations promulgated by the Secretary” in text.

Subsec. (i)(2). Pub. L. 108-155, §3(b)(1), struck out “Advisory Subcommittee of the Anti-Infective Drugs” before “Advisory Committee” wherever appearing.

Subsec. (l). Pub. L. 108-173, §1104(3), substituted “355(j)(5)(F)” for “355(j)(5)(D)” wherever appearing.

2002—Subsec. (a). Pub. L. 107-109, §19(2), (3), redesignated subsec. (g) as (a). Former subsec. (a) redesignated (b).

Subsec. (a)(1)(A). Pub. L. 107-109, §19(1)(A), (B), substituted “(j)(5)(D)(ii)” for “(j)(4)(D)(ii)” in two places in cl. (i) and “(j)(5)(D)” for “(j)(4)(D)” in cl. (ii).

Subsec. (b). Pub. L. 107-109, §19(2), (3), redesignated subsec. (a) as (b).

Pub. L. 107-109, §2(1), struck out heading and text of subsec. (b). Text read as follows: “Not later than 180 days after November 21, 1997, the Secretary, after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.”

Subsec. (c). Pub. L. 107-109, §2(2), in introductory provisions, inserted “determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and” after “the Secretary” and struck out “concerning a drug identified in the list described in subsection (b) of this section” after “such studies”.

Subsec. (c)(1)(A). Pub. L. 107-109, §19(1)(A), (B), substituted “(j)(5)(D)(ii)” for “(j)(4)(D)(ii)” in two places in cl. (i) and “(j)(5)(D)” for “(j)(4)(D)” in cl. (ii).

Subsec. (d)(1). Pub. L. 107-109, §19(4), substituted “subsection (b) or (c)” for “subsection (a) or (c)” in introductory provisions.

Subsec. (d)(2). Pub. L. 107-109, §§18(a), 19(4), substituted “subsection (b) or (c)” for “subsection (a) or (c)” and inserted “In reaching an agreement regarding written protocols, the Secretary shall take into account adequate representation of children of ethnic and racial minorities.” after first sentence.

Subsec. (d)(3). Pub. L. 107-109, §19(4), substituted “subsection (b) or (c)” for “subsection (a) or (c)”.

Subsec. (d)(4). Pub. L. 107-109, §4, added par. (4).

Subsec. (e). Pub. L. 107-109, §19(1)(C), (4), substituted “section 355(j)(5)(D)” for “section 355(j)(4)(D)” and “subsection (b) or (c)” for “subsection (a) or (c)”.

Subsec. (g). Pub. L. 107-109, §19(2), (3), (5), redesignated subsec. (h) as (g) and substituted “subsection (b) or (c)” for “subsection (a) or (b)” in introductory provisions. Former subsec. (g) redesignated (a).

Pub. L. 107-109, §7, inserted “(including neonates in appropriate cases)” after “pediatric age groups”.

Subsec. (h). Pub. L. 107-109, §19(2), (3), redesignated subsec. (i) as (h). Former subsec. (h) redesignated (g).

Subsec. (i). Pub. L. 107-109, §19(2), (3), redesignated subsec. (l) as (i). Former subsec. (i) redesignated (h).

Subsec. (j). Pub. L. 107–109, §19(2), (3), redesignated subsec. (m) as (j). Former subsec. (j) redesignated (n).

Pub. L. 107–109, §8, added subsec. (j) and struck out heading and text of former subsec. (j). Text read as follows: “A drug may not receive any six-month period under subsection (a) or (c) of this section unless the application for the drug under section 355(b)(1) of this title is submitted on or before January 1, 2002. After January 1, 2002, a drug shall receive a six-month period under subsection (c) of this section if—

“(1) the drug was in commercial distribution as of November 21, 1997;

“(2) the drug was included by the Secretary on the list under subsection (b) of this section as of January 1, 2002;

“(3) the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population and that the drug may provide health benefits in that population; and

“(4) all requirements of this section are met.”

Subsec. (k). Pub. L. 107–109, §19(2), (3), redesignated subsec. (n) as (k). Former subsec. (k) redesignated (m).

Subsec. (l). Pub. L. 107–109, §19(2), (3), redesignated subsec. (o) as (l). Former subsec. (l) redesignated (i).

Pub. L. 107–109, §5(b)(2), added subsec. (l).

Subsec. (m). Pub. L. 107–109, §19(2), (3), redesignated subsec. (k) as (m). Former subsec. (m) redesignated (j).

Pub. L. 107–109, §9, added subsec. (m).

Subsec. (n). Pub. L. 107–109, §19(4), which directed substitution of “subsection (b) or (c)” for “subsection (a) or (c)” in subsec. (m), was executed by making the substitution in introductory provisions of subsec. (n), to reflect the probable intent of Congress.

Pub. L. 107–109, §19(2), (3), redesignated subsec. (j) as (n). Former subsec. (n) redesignated (k).

Pub. L. 107–109, §10, added subsec. (n).

Subsec. (o). Pub. L. 107–109, §19(2), (3), redesignated subsec. (o) as (l).

Pub. L. 107–109, §11(a), added subsec. (o).

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112–144, title V, §509(g), July 9, 2012, 126 Stat. 1050, provided that:

“(1) APPLICATION.—Notwithstanding any provision of section 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) stating that a provision applies beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007 [Sept. 27, 2007] or the date of the enactment of the Pediatric Research Equity Act of 2007 [Sept. 27, 2007], any amendment made by this Act to such a provision applies beginning on the date of the enactment of this Act [July 9, 2012].

“(2) TRANSITIONAL RULE FOR ADVERSE EVENT REPORTING.—With respect to a drug for which a labeling change described under section 505A(l)(1) or 505B(i)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(l)(1); 355c(i)(1)) is approved or made, respectively, during the one-year period that ends on the day before the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall apply section 505A(l) and section 505B(i), as applicable, to such drug, as such sections were in effect on such day.”

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110–85, title V, §502(a)(2), Sept. 27, 2007, 121 Stat. 885, provided that:

“(A) IN GENERAL.—The amendment made by this subsection [amending this section] shall apply to written requests under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) issued on or after the date of the enactment of this Act [Sept. 27, 2007].

“(B) CERTAIN WRITTEN REQUESTS.—A written request issued under section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on the day before the date of the enactment of this Act, which has been accepted and for which no determination under subsection (d)(2) of such section has been made before such

date of enactment, shall be subject to such section 505A, except that such written requests shall be subject to subsections (d)(2)(A)(ii), (e)(1) and (2), (f), (i)(2)(A), (j), (k)(1), (l)(1), and (n) of section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on or after the date of the enactment of this Act.”

EFFECTIVE DATE OF 2003 AMENDMENT

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–109, §11(b), Jan. 4, 2002, 115 Stat. 1416, provided that: “The amendment made by subsection (a) [amending this section] takes effect on the date of enactment of this Act [Jan. 4, 2002], including with respect to applications under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) that are approved or pending on that date.”

CONSTRUCTION OF 2007 AMENDMENTS ON PEDIATRIC STUDIES

Pub. L. 110–85, title IX, §901(e), Sept. 27, 2007, 121 Stat. 942, provided that: “This title [enacting sections 353c, 355–1, 355e, 360a, and 360bbb–6 of this title, amending sections 331, 333, 334, 352, 355, and 381 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under sections 331, 352, and 355 of this title] and the amendments made by this title may not be construed as affecting the authority of the Secretary of Health and Human Services to request pediatric studies under section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a] or to require such studies under section 505B of such Act [21 U.S.C. 355c].”

COMMUNICATION WITH PEDIATRIC REVIEW COMMITTEE

Pub. L. 112–144, title V, §503, July 9, 2012, 126 Stat. 1040, provided that: “Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this title [see Tables for classification] as the ‘Secretary’) shall issue internal standard operating procedures that provide for the review by the internal review committee established under section 505C of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355d) of any significant modifications to initial pediatric study plans, agreed initial pediatric study plans, and written requests under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c). Such internal standard operating procedures shall be made publicly available on the Internet Web site of the Food and Drug Administration.”

ACCESS TO DATA

Pub. L. 112–144, title V, §504, July 9, 2012, 126 Stat. 1040, provided that: “Not later than 3 years after the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall make available to the public, including through posting on the Internet Web site of the Food and Drug Administration, the medical, statistical, and clinical pharmacology reviews of, and corresponding written requests issued to an applicant, sponsor, or holder for, pediatric studies submitted between January 4, 2002, and September 27, 2007, under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) for which 6 months of market exclusivity was granted and that resulted in a labeling change. The Secretary shall make public the information described in the preceding sentence in a manner consistent with how the Secretary releases information under section 505A(k) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(k)).”

REPORT ON PEDIATRIC EXCLUSIVITY PROGRAM

Pub. L. 107–109, §16, Jan. 4, 2002, 115 Stat. 1421, as amended by Pub. L. 108–155, §3(b)(4), Dec. 3, 2003, 117

Stat. 1942, required the Comptroller General, not later than Oct. 1, 2006, and in consultation with the Secretary of Health and Human Services, to submit to Congress a report on specified issues concerning the effectiveness of the pediatric exclusivity program.

STUDY BY GENERAL ACCOUNTING OFFICE

Pub. L. 107–109, §18(b), Jan. 4, 2002, 115 Stat. 1423, required the Comptroller General, not later than Jan. 10, 2003, to conduct a study relating to the representation of children of ethnic and racial minorities in studies under section 355a of this title and to submit a report to Congress describing the findings of the study.

§ 355b. Adverse-event reporting

(a) Toll-free number in labeling

Not later than one year after January 4, 2002, the Secretary of Health and Human Services shall promulgate a final rule requiring that the labeling of each drug for which an application is approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] (regardless of the date on which approved) include the toll-free number maintained by the Secretary for the purpose of receiving reports of adverse events regarding drugs and a statement that such number is to be used for reporting purposes only, not to receive medical advice. With respect to the final rule:

(1) The rule shall provide for the implementation of such labeling requirement in a manner that the Secretary considers to be most likely to reach the broadest consumer audience.

(2) In promulgating the rule, the Secretary shall seek to minimize the cost of the rule on the pharmacy profession.

(3) The rule shall take effect not later than 60 days after the date on which the rule is promulgated.

(b) Drugs with pediatric market exclusivity

(1) In general

During the one year beginning on the date on which a drug receives a period of market exclusivity under 505A¹ of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a], any report of an adverse event regarding the drug that the Secretary of Health and Human Services receives shall be referred to the Office of Pediatric Therapeutics established under section 393a of this title. In considering the report, the Director of such Office shall provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such subcommittee² regarding whether the Secretary should take action under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] in response to the report.

(2) Rule of construction

Paragraph (1) may not be construed as restricting the authority of the Secretary of Health and Human Services to continue carrying out the activities described in such paragraph regarding a drug after the one-year period described in such paragraph regarding the drug has expired.

¹ So in original. Probably should be preceded by “section”.

² So in original. Probably should be “Committee”.

(Pub. L. 107–109, §17, Jan. 4, 2002, 115 Stat. 1422; Pub. L. 108–155, §3(b)(5), Dec. 3, 2003, 117 Stat. 1942.)

REFERENCES IN TEXT

The Federal Food, Drug, and Cosmetic Act, referred to in subsec. (b)(1), is act June 25, 1938, ch. 675, 52 Stat. 1040, as amended, which is classified generally to this chapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

CODIFICATION

Section was enacted as part of the Best Pharmaceuticals for Children Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

AMENDMENTS

2003—Subsec. (b)(1). Pub. L. 108–155 struck out “Advisory Subcommittee of the Anti-Infective Drugs” before “Advisory Committee”.

EFFECTIVE DATE OF 2003 AMENDMENT

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

§ 355c. Research into pediatric uses for drugs and biological products

(a) New drugs and biological products

(1) In general

A person that submits, on or after September 27, 2007, an application (or supplement to an application) for a drug—

(A) under section 355 of this title for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration, or

(B) under section 262 of title 42 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration,

shall submit with the application the assessments described in paragraph (2).

(2) Assessments

(A) In general

The assessments referred to in paragraph (1) shall contain data, gathered using appropriate formulations for each age group for which the assessment is required, that are adequate—

(i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and

(ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

(B) Similar course of disease or similar effect of drug or biological product

(i) In general

If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in

adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

(ii) Extrapolation between age groups

A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.

(iii) Information on extrapolation

A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in any pertinent reviews for the application under section 355 of this title or section 262 of title 42.

(3) Deferral

(A) In general

On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1) until a specified date after approval of the drug or issuance of the license for a biological product if—

(i) the Secretary finds that—

(I) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;

(II) pediatric studies should be delayed until additional safety or effectiveness data have been collected; or

(III) there is another appropriate reason for deferral; and

(ii) the applicant submits to the Secretary—

(I) certification of the grounds for deferring the assessments;

(II) a pediatric study plan as described in subsection (e);

(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; and

(IV) a timeline for the completion of such studies.

(B) Deferral extension

(i) In general

On the initiative of the Secretary or at the request of the applicant, the Secretary may grant an extension of a deferral approved under subparagraph (A) for submission of some or all assessments required under paragraph (1) if—

(I) the Secretary determines that the conditions described in subclause (II) or (III) of subparagraph (A)(i) continue to be met; and

(II) the applicant submits a new timeline under subparagraph (A)(ii)(IV) and any significant updates to the information required under subparagraph (A)(ii).

(ii) Timing and information

If the deferral extension under this subparagraph is requested by the applicant, the applicant shall submit the deferral extension request containing the information described in this subparagraph not less than 90 days prior to the date that the

deferral would expire. The Secretary shall respond to such request not later than 45 days after the receipt of such letter. If the Secretary grants such an extension, the specified date shall be the extended date. The sponsor of the required assessment under paragraph (1) shall not be issued a letter described in subsection (d) unless the specified or extended date of submission for such required studies has passed or if the request for an extension is pending. For a deferral that has expired prior to July 9, 2012, or that will expire prior to 270 days after July 9, 2012, a deferral extension shall be requested by an applicant not later than 180 days after July 9, 2012. The Secretary shall respond to any such request as soon as practicable, but not later than 1 year after July 9, 2012. Nothing in this clause shall prevent the Secretary from updating the status of a study or studies publicly if components of such study or studies are late or delayed.

(C) Annual review

(i) In general

On an annual basis following the approval of a deferral under subparagraph (A), the applicant shall submit to the Secretary the following information:

(I) Information detailing the progress made in conducting pediatric studies.

(II) If no progress has been made in conducting such studies, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time.

(III) Projected completion date for pediatric studies.

(IV) The reason or reasons why a deferral or deferral extension continues to be necessary.

(ii) Public availability

Not later than 90 days after the submission to the Secretary of the information submitted through the annual review under clause (i), the Secretary shall make available to the public in an easily accessible manner, including through the Internet Web site of the Food and Drug Administration—

(I) such information;

(II) the name of the applicant for the product subject to the assessment;

(III) the date on which the product was approved; and

(IV) the date of each deferral or deferral extension under this paragraph for the product.

(4) Waivers

(A) Full waiver

On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for exam-

ple, the number of patients is so small or the patients are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups; or

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

(B) Partial waiver

On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) Pediatric formulation not possible

If a partial waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking such a partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) Labeling requirement

If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(b) Marketed drugs and biological products

(1) In general

The Secretary may (by order in the form of a letter) require the sponsor or holder of an approved application for a drug under section 355 of this title or the holder of a license for a

biological product under section 262 of title 42 to submit by a specified date the assessments described in subsection (a)(2), if the Secretary finds that—

(A)(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

(ii) adequate pediatric labeling could confer a benefit on pediatric patients;

(B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for 1 or more of the claimed indications; or

(C) the absence of adequate pediatric labeling could pose a risk to pediatric patients.

(2) Waivers

(A) Full waiver

At the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

(B) Partial waiver

At the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii)(I) the drug or biological product—

(aa) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) Pediatric formulation not possible

If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial

waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration.

(D) Labeling requirement

If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(c) Meaningful therapeutic benefit

For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary determines that—

(1) if approved, the drug or biological product could represent an improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

(d) Submission of assessments

If a person fails to submit a required assessment described in subsection (a)(2), fails to meet the applicable requirements in subsection (a)(3), or fails to submit a request for approval of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b), the following shall apply:

(1) Beginning 270 days after July 9, 2012, the Secretary shall issue a non-compliance letter to such person informing them of such failure to submit or meet the requirements of the applicable subsection. Such letter shall require the person to respond in writing within 45 calendar days of issuance of such letter. Such response may include the person's request for a deferral extension if applicable. Such letter and the person's written response to such letter shall be made publicly available on the Internet Web site of the Food and Drug Administration 60 calendar days after issuance, with redactions for any trade secrets and confidential commercial information. If the Secretary determines that the letter was issued in error, the requirements of this paragraph shall not apply.

(2) The drug or biological product that is the subject of an assessment described in subsection (a)(2), applicable requirements in subsection (a)(3), or request for approval of a pediatric formulation, may be considered mis-

branded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 333 of this title), but such failure shall not be the basis for a proceeding—

(A) to withdraw approval for a drug under section 355(e) of this title; or

(B) to revoke the license for a biological product under section 262 of title 42.

(e) Pediatric study plans

(1) In general

An applicant subject to subsection (a) shall submit to the Secretary an initial pediatric study plan prior to the submission of the assessments described under subsection (a)(2).

(2) Timing; content; meeting

(A) Timing

An applicant shall submit the initial pediatric plan under paragraph (1)—

(i) before the date on which the applicant submits the assessments under subsection (a)(2); and

(ii) not later than—

(I) 60 calendar days after the date of the end-of-Phase 2 meeting (as such term is used in section 312.47 of title 21, Code of Federal Regulations, or successor regulations); or

(II) such other time as may be agreed upon between the Secretary and the applicant.

Nothing in this section shall preclude the Secretary from accepting the submission of an initial pediatric plan earlier than the date otherwise applicable under this subparagraph.

(B) Content of initial plan

The initial pediatric study plan shall include—

(i) an outline of the pediatric study or studies that the applicant plans to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach);

(ii) any request for a deferral, partial waiver, or waiver under this section, if applicable, along with any supporting information; and

(iii) other information specified in the regulations promulgated under paragraph (7).

(C) Meeting

The Secretary—

(i) shall meet with the applicant to discuss the initial pediatric study plan as soon as practicable, but not later than 90 calendar days after the receipt of such plan under subparagraph (A);

(ii) may determine that a written response to the initial pediatric study plan is sufficient to communicate comments on the initial pediatric study plan, and that no meeting is necessary; and

(iii) if the Secretary determines that no meeting is necessary, shall so notify the applicant and provide written comments of

the Secretary as soon as practicable, but not later than 90 calendar days after the receipt of the initial pediatric study plan.

(3) Agreed initial pediatric study plan

Not later than 90 calendar days following the meeting under paragraph (2)(C)(i) or the receipt of a written response from the Secretary under paragraph (2)(C)(iii), the applicant shall document agreement on the initial pediatric study plan in a submission to the Secretary marked “Agreed Initial Pediatric Study Plan”, and the Secretary shall confirm such agreement to the applicant in writing not later than 30 calendar days of receipt of such agreed initial pediatric study plan.

(4) Deferral and waiver

If the agreed initial pediatric study plan contains a request from the applicant for a deferral, partial waiver, or waiver under this section, the written confirmation under paragraph (3) shall include a recommendation from the Secretary as to whether such request meets the standards under paragraphs (3) or (4) of subsection (a).

(5) Amendments to the plan

At the initiative of the Secretary or the applicant, the agreed initial pediatric study plan may be amended at any time. The requirements of paragraph (2)(C) shall apply to any such proposed amendment in the same manner and to the same extent as such requirements apply to an initial pediatric study plan under paragraph (1). The requirements of paragraphs (3) and (4) shall apply to any agreement resulting from such proposed amendment in the same manner and to the same extent as such requirements apply to an agreed initial pediatric study plan.

(6) Internal committee

The Secretary shall consult the internal committee under section 355d of this title on the review of the initial pediatric study plan, agreed initial pediatric plan, and any significant amendments to such plans.

(7) Required rulemaking

Not later than 1 year after July 9, 2012, the Secretary shall promulgate proposed regulations and issue guidance to implement the provisions of this subsection.

(f) Review of pediatric study plans, assessments, deferrals, deferral extensions, and waivers

(1) Review

Beginning not later than 30 days after September 27, 2007, the Secretary shall utilize the internal committee established under section 355d of this title to provide consultation to reviewing divisions on initial pediatric study plans, agreed initial pediatric study plans, and assessments prior to approval of an application or supplement for which a pediatric assessment is required under this section and all deferral, deferral extension, and waiver requests granted pursuant to this section.

(2) Activity by committee

The committee referred to in paragraph (1) may operate using appropriate members of

such committee and need not convene all members of the committee.

(3) Documentation of committee action

For each drug or biological product, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (4) or (5), which members of the committee participated in such activity.

(4) Review of pediatric study plans, assessments, deferrals, deferral extensions, and waivers

Consultation on initial pediatric study plans, agreed initial pediatric study plans, and assessments by the committee referred to in paragraph (1) pursuant to this section shall occur prior to approval of an application or supplement for which a pediatric assessment is required under this section. The committee shall review all requests for deferrals, deferral extensions, and waivers from the requirement to submit a pediatric assessment granted under this section and shall provide recommendations as needed to reviewing divisions, including with respect to whether such a supplement, when submitted, shall be considered for priority review.

(5) Retrospective review of pediatric assessments, deferrals, and waivers

Not later than 1 year after September 27, 2007, the committee referred to in paragraph (1) shall conduct a retrospective review and analysis of a representative sample of assessments submitted and deferrals and waivers approved under this section since December 3, 2003. Such review shall include an analysis of the quality and consistency of pediatric information in pediatric assessments and the appropriateness of waivers and deferrals granted. Based on such review, the Secretary shall issue recommendations to the review divisions for improvements and initiate guidance to industry related to the scope of pediatric studies required under this section.

(6) Tracking of assessments and labeling changes

The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of assessments conducted under this section;

(B) the specific drugs and biological products and their uses assessed under this section;

(C) the types of assessments conducted under this section, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) aggregated on an annual basis—

(i) the total number of deferrals and deferral extensions requested and granted under this section and, if granted, the reasons for each such deferral or deferral extension;

(ii) the timeline for completion of the assessments;

(iii) the number of assessments completed and pending; and

(iv) the number of postmarket non-compliance letters issued pursuant to subsection (d), and the recipients of such letters;

(E) the number of waivers requested and granted under this section and, if granted, the reasons for the waivers;

(F) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons any such formulation was not developed;

(G) the labeling changes made as a result of assessments conducted under this section;

(H) an annual summary of labeling changes made as a result of assessments conducted under this section for distribution pursuant to subsection (h)(2);

(I) an annual summary of information submitted pursuant to subsection (a)(3)(B); and

(J) the number of times the committee referred to in paragraph (1) made a recommendation to the Secretary under paragraph (4) regarding priority review, the number of times the Secretary followed or did not follow such a recommendation, and, if not followed, the reasons why such a recommendation was not followed.

(g) Labeling changes

(1) Dispute resolution

(A) Request for labeling change and failure to agree

If, on or after September 27, 2007, the Commissioner determines that a sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application or supplement, not later than 180 days after the date of the submission of the application or supplement that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) Action by the Pediatric Advisory Committee

Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) Consideration of recommendations

The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later

than 30 days after receiving the recommendation, make a request to the sponsor of the application or supplement to make any labeling changes that the Commissioner determines to be appropriate.

(D) Misbranding

If the sponsor of the application or supplement, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application or supplement to be misbranded.

(E) No effect on authority

Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(2) Other labeling changes

If, on or after September 27, 2007, the Secretary makes a determination that a pediatric assessment conducted under this section does or does not demonstrate that the drug that is the subject of such assessment is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary shall order the labeling of such product to include information about the results of the assessment and a statement of the Secretary's determination.

(h) Dissemination of pediatric information

(1) In general

Not later than 210 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a standard review, the Secretary shall make available to the public in an easily accessible manner the medical, statistical, and clinical pharmacology reviews of such pediatric assessments, and shall post such assessments on the Web site of the Food and Drug Administration.

(2) Dissemination of information regarding labeling changes

Beginning on September 27, 2007, the Secretary shall require that the sponsors of the assessments that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(H) distribute such information to physicians and other health care providers.

(3) Effect of subsection

Nothing in this subsection shall alter or amend section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(i) Adverse event reporting**(1) Reporting in first 18-month period**

Beginning on September 27, 2007, during the 18-month period beginning on the date a labeling change is made pursuant to subsection (g), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics. In considering such reports, the Director of such Office shall provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) Reporting in subsequent periods

Following the 18-month period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) Preservation of authority

Nothing in this subsection shall prohibit the Office of Pediatric Therapeutics from providing for the review of adverse event reports by the Pediatric Advisory Committee prior to the 18-month period referred to in paragraph (1), if such review is necessary to ensure safe use of a drug in a pediatric population.

(4) Effect

The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(j) Scope of authority

Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

(k) Orphan drugs

Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under section 360bb of this title.

(l) Institute of Medicine study**(1) In general**

Not later than three years after September 27, 2007, the Secretary shall contract with the Institute of Medicine to conduct a study and report to Congress regarding the pediatric studies conducted pursuant to this section or precursor regulations since 1997 and labeling changes made as a result of such studies.

(2) Content of study

The study under paragraph (1) shall review and assess the use of extrapolation for pedi-

atric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, the number and type of pediatric adverse events, and ethical issues in pediatric clinical trials.

(3) Representative sample

The Institute of Medicine may devise an appropriate mechanism to review a representative sample of studies conducted pursuant to this section from each review division within the Center for Drug Evaluation and Research in order to make the requested assessment.

(m) New active ingredient**(1) Non-interchangeable biosimilar biological product**

A biological product that is biosimilar to a reference product under section 262 of title 42, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.

(2) Interchangeable biosimilar biological product

A biological product that is interchangeable with a reference product under section 262 of title 42 shall not be considered to have a new active ingredient under this section.

(June 25, 1938, ch. 675, §505B, as added Pub. L. 108–155, §2(a), Dec. 3, 2003, 117 Stat. 1936; amended Pub. L. 110–85, title IV, §402(a), Sept. 27, 2007, 121 Stat. 866; Pub. L. 111–148, title VII, §7002(d)(2), Mar. 23, 2010, 124 Stat. 816; Pub. L. 112–144, title V, §§501(b), 505–506(b), 509(b), July 9, 2012, 126 Stat. 1040–1044, 1048.)

AMENDMENTS

2012—Subsec. (a)(1). Pub. L. 112–144, §509(b)(1)(A), inserted “for a drug” after “(or supplement to an application)” in introductory provisions.

Subsec. (a)(3)(A)(ii)(II). Pub. L. 112–144, §506(b)(1), amended subcl. (II) generally. Prior to amendment, subcl. (II) read as follows: “a description of the planned or ongoing studies;”.

Subsec. (a)(3)(B), (C). Pub. L. 112–144, §505(a)(1)(A), (B), added subpar. (B) and redesignated former subpar. (B) as (C).

Subsec. (a)(3)(C)(i)(III), (IV). Pub. L. 112–144, §505(a)(1)(C)(i), added subcls. (III) and (IV).

Subsec. (a)(3)(C)(ii). Pub. L. 112–144, §505(a)(1)(C)(ii), amended cl. (ii) generally. Prior to amendment, text read as follows: “The information submitted through the annual review under clause (i) shall promptly be made available to the public in an easily accessible manner, including through the Web site of the Food and Drug Administration.”

Subsec. (a)(4)(C). Pub. L. 112–144, §509(b)(1)(B), inserted “partial” after “If a” in first sentence and substituted “such a” for “either a full or” in second sentence.

Subsec. (b)(1). Pub. L. 112–144, §509(b)(2), substituted “The” for “After providing notice in the form of a letter (that, for a drug approved under section 355 of this title, references a declined written request under section 355a of this title for a labeled indication which written request is not referred under section 355a(n)(1)(A) of this title to the Foundation of the National Institutes of Health for the pediatric studies), the” in introductory provisions.

Subsec. (d). Pub. L. 112–144, §505(c)(1), amended subsec. (d) generally. Prior to amendment, subsec. (d) related to submission of assessments.

Subsec. (e). Pub. L. 112-144, § 506(a), amended subsec. (e) generally. Prior to amendment, text read as follows: "Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

"(1) information that the sponsor submits on plans and timelines for pediatric studies; or

"(2) any planned request by the sponsor for waiver or deferral of pediatric studies."

Subsec. (f). Pub. L. 112-144, § 506(b)(2)(A), substituted "pediatric study plans," for "pediatric plans," in heading.

Pub. L. 112-144, § 505(a)(2)(A), inserted "deferral extensions," after "deferrals," in heading.

Subsec. (f)(1). Pub. L. 112-144, § 506(b)(2)(B), substituted "initial pediatric study plans, agreed initial pediatric study plans," for "all pediatric plans".

Pub. L. 112-144, § 505(a)(2)(B), inserted ", deferral extension," after "deferral".

Subsec. (f)(4). Pub. L. 112-144, § 506(b)(2)(C), substituted "pediatric study plans," for "pediatric plans," in heading and "initial pediatric study plans, agreed initial pediatric study plans," for "pediatric plans" in text.

Pub. L. 112-144, § 505(a)(2)(C), inserted "deferral extensions," after "deferrals," in heading and ", deferral extensions," after "deferrals" in text.

Subsec. (f)(6)(D). Pub. L. 112-144, § 505(b), amended subpar. (D) generally. Prior to amendment, subpar. (D) read as follows: "the total number of deferrals requested and granted under this section and, if granted, the reasons for such deferrals, the timeline for completion, and the number completed and pending by the specified date, as outlined in subsection (a)(3);".

Subsec. (f)(6)(D)(iv). Pub. L. 112-144, § 505(c)(2), added cl. (iv).

Subsec. (g)(1)(A). Pub. L. 112-144, § 509(b)(3)(A), inserted "that receives a priority review or 330 days after the date of the submission of an application or supplement that receives a standard review" after "after the date of the submission of the application or supplement" in introductory provisions.

Subsec. (g)(2). Pub. L. 112-144, § 509(b)(3)(B), substituted "the labeling of such product" for "the label of such product".

Subsec. (h)(1). Pub. L. 112-144, § 509(b)(4), inserted "an application (or supplement to an application) that contains" after "date of submission of" and "if the application (or supplement) receives a priority review, or not later than 330 days after the date of submission of an application (or supplement to an application) that contains a pediatric assessment under this section, if the application (or supplement) receives a standard review," after "under this section,".

Subsec. (i)(1). Pub. L. 112-144, § 509(b)(5)(A), substituted "first 18-month period" for "year one" in heading and "18-month" for "one-year" in text.

Subsec. (i)(2). Pub. L. 112-144, § 509(b)(5)(B), substituted "periods" for "years" in heading and "18-month period" for "one-year period" in text.

Subsec. (i)(3), (4). Pub. L. 112-144, § 509(b)(5)(C), (D), added par. (3) and redesignated former par. (3) as (4).

Subsecs. (m), (n). Pub. L. 112-144, § 501(b), redesignated subsec. (n) as (m) and struck out former subsec. (m). Prior to amendment, text of subsec. (m) read as follows: "The authority under this section shall remain in effect so long as an application subject to this section may be accepted for filing by the Secretary on or before the date specified in section 355a(q) of this title."

2010—Subsec. (n). Pub. L. 111-148 added subsec. (n).

2007—Pub. L. 110-85 amended section generally. Prior to amendment, section related to required submission of assessments with an application for a new drug or new biological product and by order of the Secretary for certain marketed drugs and biological products used for pediatric patients, a definition of meaningful therapeutic benefit, consequences of failure to submit required assessments, meetings of the Secretary and

the sponsor of a new drug or biological product, a limitation of the scope of the Secretary's authority, application to orphan drugs, and integration with other pediatric studies.

EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112-144, title V, § 506(c), July 9, 2012, 126 Stat. 1045, provided that:

"(1) IN GENERAL.—Subject to paragraph (2), the amendments made by this section [amending this section] shall take effect 180 calendar days after the date of enactment of this Act [July 9, 2012], irrespective of whether the Secretary [of Health and Human Services] has promulgated final regulations to carry out such amendments.

"(2) RULE OF CONSTRUCTION.—Paragraph (1) shall not be construed to affect the deadline for promulgation of proposed regulations under section 505B(e)(7) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(e)(7)], as added by subsection (a) of this section."

Notwithstanding any provision of this section stating that a provision applies beginning on Sept. 27, 2007, any amendment made by Pub. L. 112-144 to such a provision applies beginning on July 9, 2012, subject to a transitional rule, see section 509(g) of Pub. L. 112-144, set out as a note under section 355a of this title.

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110-85, title IV, § 402(b), Sept. 27, 2007, 121 Stat. 875, provided that:

"(1) IN GENERAL.—Notwithstanding subsection (h) of section 505B of the Federal Food, Drug and Cosmetic Act [21 U.S.C. 355c(h)], as in effect on the day before the date of the enactment of this Act [Sept. 27, 2007], a pending assessment, including a deferred assessment, required under such section 505B shall be deemed to have been required under section 505B of the Federal Food, Drug and Cosmetic Act as in effect on or after the date of the enactment of this Act.

"(2) CERTAIN ASSESSMENTS AND WAIVER REQUESTS.—An assessment pending on or after the date that is 1 year prior to the date of the enactment of this Act shall be subject to the tracking and disclosure requirements established under such section 505B, as in effect on or after such date of enactment, except that any such assessments submitted or waivers of such assessments requested before such date of enactment shall not be subject to subsections (a)(4)(C), (b)(2)(C), (f)(6)(F), and (h) of such section 505B."

EFFECTIVE DATE

Pub. L. 108-155, § 4, Dec. 3, 2003, 117 Stat. 1942, provided that:

"(a) IN GENERAL.—Subject to subsection (b), this Act [enacting this section, amending sections 355, 355a, and 355b of this title and sections 262 and 284m of Title 42, The Public Health and Welfare, enacting provisions set out as a note under section 301 of this title, and amending provisions set out as notes under section 355a of this title and section 284m of Title 42] and the amendments made by this Act take effect on the date of enactment of this Act [Dec. 3, 2003].

"(b) APPLICABILITY TO NEW DRUGS AND BIOLOGICAL PRODUCTS.—

"(1) IN GENERAL.—Subsection (a) of section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)] (as added by section 2) shall apply to an application described in paragraph (1) of that subsection submitted to the Secretary of Health and Human Services on or after April 1, 1999.

"(2) WAIVERS AND DEFERRALS.—

"(A) WAIVER OR DEFERRAL GRANTED.—If, with respect to an application submitted to the Secretary of Health and Human Services between April 1, 1999, and the date of enactment of this Act [Dec. 3, 2003], a waiver or deferral of pediatric assessments was granted under regulations of the Secretary then in effect, the waiver or deferral shall be a waiver or deferral under subsection (a) of section 505B of the

Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)], except that any date specified in such a deferral shall be extended by the number of days that is equal to the number of days between October 17, 2002, and the date of enactment of this Act.

“(B) WAIVER AND DEFERRAL NOT GRANTED.—If, with respect to an application submitted to the Secretary of Health and Human Services between April 1, 1999, and the date of enactment of this Act [Dec. 3, 2003], neither a waiver nor deferral of pediatric assessments was granted under regulations of the Secretary then in effect, the person that submitted the application shall be required to submit assessments under subsection (a)(2) of section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(2)] on the date that is the later of—

“(i) the date that is 1 year after the date of enactment of this Act; or

“(ii) such date as the Secretary may specify under subsection (a)(3) of that section;

unless the Secretary grants a waiver under subsection (a)(4) of that section.

“(c) NO LIMITATION OF AUTHORITY.—Neither the lack of guidance or regulations to implement this Act or the amendments made by this Act nor the pendency of the process for issuing guidance or regulations shall limit the authority of the Secretary of Health and Human Services under, or defer any requirement under, this Act or those amendments.”

§ 355c-1. Report

(a) In general

Not later than four years after July 9, 2012, and every five years thereafter, the Secretary shall prepare and submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and make publicly available, including through posting on the Internet Web site of the Food and Drug Administration, a report on the implementation of sections 355a and 355c of this title.

(b) Contents

Each report under subsection (a) shall include—

(1) an assessment of the effectiveness of sections 355a and 355c of this title in improving information about pediatric uses for approved drugs and biological products, including the number and type of labeling changes made since July 9, 2012, and the importance of such uses in the improvement of the health of children;

(2) the number of required studies under such section 355c of this title that have not met the initial deadline provided under such section 355c of this title, including—

(A) the number of deferrals and deferral extensions granted and the reasons such extensions were granted;

(B) the number of waivers and partial waivers granted; and

(C) the number of letters issued under subsection (d) of such section 355c of this title;

(3) an assessment of the timeliness and effectiveness of pediatric study planning since July 9, 2012, including the number of initial pediatric study plans not submitted in accordance with the requirements of subsection (e) of such section 355c of this title and any resulting rulemaking;

(4) the number of written requests issued, accepted, and declined under such section 355a of

this title since July 9, 2012, and a listing of any important gaps in pediatric information as a result of such declined requests;

(5) a description and current status of referrals made under subsection (n) of such section 355a of this title;

(6) an assessment of the effectiveness of studying biological products in pediatric populations under such sections 355a and 355c of this title and section 284m of title 42;

(7)(A) the efforts made by the Secretary to increase the number of studies conducted in the neonatal population (including efforts made to encourage the conduct of appropriate studies in neonates by companies with products that have sufficient safety and other information to make the conduct of the studies ethical and safe); and

(B) the results of such efforts;

(8)(A) the number and importance of drugs and biological products for children with cancer that are being tested as a result of the programs under such sections 355a and 355c of this title and under section 284m of title 42; and

(B) any recommendations for modifications to such programs that would lead to new and better therapies for children with cancer, including a detailed rationale for each recommendation;

(9) any recommendations for modification to such programs that would improve pediatric drug research and increase pediatric labeling of drugs and biological products;

(10) an assessment of the successes of and limitations to studying drugs for rare diseases under such sections 355a and 355c of this title; and

(11) an assessment of the Secretary's efforts to address the suggestions and options described in any prior report issued by the Comptroller General, Institute of Medicine, or the Secretary, and any subsequent reports, including recommendations therein, regarding the topics addressed in the reports under this section, including with respect to—

(A) improving public access to information from pediatric studies conducted under such sections 355a and 355c of this title; and

(B) improving the timeliness of pediatric studies and pediatric study planning under such sections 355a and 355c of this title.

(c) Stakeholder comment

At least 180 days prior to the submission of each report under subsection (a), the Secretary shall consult with representatives of patient groups (including pediatric patient groups), consumer groups, regulated industry, academia, and other interested parties to obtain any recommendations or information relevant to the report including suggestions for modifications that would improve pediatric drug research and pediatric labeling of drugs and biological products.

(Pub. L. 112-144, title V, §508, July 9, 2012, 126 Stat. 1045.)

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

DEFINITION OF “SECRETARY”

The term “Secretary” as used in this section means the Secretary of Health and Human Services, see section 503 of Pub. L. 112-144, set out as a note under section 355a of this title.

§ 355d. Internal committee for review of pediatric plans, assessments, deferrals, deferral extensions, and waivers

The Secretary shall establish an internal committee within the Food and Drug Administration to carry out the activities as described in sections 355a(f) and 355c(f) of this title. Such internal committee shall include employees of the Food and Drug Administration, with expertise in pediatrics (including representation from the Office of Pediatric Therapeutics), biopharmacology, statistics, chemistry, legal issues, pediatric ethics, neonatology, and the appropriate expertise pertaining to the pediatric product under review, such as expertise in child and adolescent psychiatry, and other individuals designated by the Secretary.

(June 25, 1938, ch. 675, §505C, as added Pub. L. 110-85, title IV, §403, Sept. 27, 2007, 121 Stat. 875; amended Pub. L. 112-144, title V, §509(c), July 9, 2012, 126 Stat. 1049.)

AMENDMENTS

2012—Pub. L. 112-144 inserted “deferral extensions,” after “deferrals,” in section catchline and “neonatology,” after “pediatric ethics,” in text.

§ 355e. Pharmaceutical security

(a) In general

The Secretary shall develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

(b) Standards development

(1) In general

The Secretary shall, in consultation with the agencies specified in paragraph (4), manufacturers, distributors, pharmacies, and other supply chain stakeholders, prioritize and develop standards for the identification, validation, authentication, and tracking and tracing of prescription drugs.

(2) Standardized numeral identifier

Not later than 30 months after September 27, 2007, the Secretary shall develop a standardized numerical identifier (which, to the extent practicable, shall be harmonized with international consensus standards for such an identifier) to be applied to a prescription drug at the point of manufacturing and repackaging (in which case the numerical identifier shall be linked to the numerical identifier applied at the point of manufacturing) at the package or pallet level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the prescription drug.

(3) Promising technologies

The standards developed under this subsection shall address promising technologies, which may include—

- (A) radio frequency identification technology;
- (B) nanotechnology;
- (C) encryption technologies; and
- (D) other track-and-trace or authentication technologies.

(4) Interagency collaboration

In carrying out this subsection, the Secretary shall consult with Federal health and security agencies, including—

- (A) the Department of Justice;
- (B) the Department of Homeland Security;
- (C) the Department of Commerce; and
- (D) other appropriate Federal and State agencies.

(c) Inspection and enforcement

(1) In general

The Secretary shall expand and enhance the resources and facilities of agency components of the Food and Drug Administration involved with regulatory and criminal enforcement of this chapter to secure the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs including biological products and active pharmaceutical ingredients from domestic and foreign sources.

(2) Activities

The Secretary shall undertake enhanced and joint enforcement activities with other Federal and State agencies, and establish regional capacities for the validation of prescription drugs and the inspection of the prescription drug supply chain.

(d) Definition

In this section, the term “prescription drug” means a drug subject to section 353(b)(1) of this title.

(June 25, 1938, ch. 675, §505D, as added Pub. L. 110-85, title IX, §913, Sept. 27, 2007, 121 Stat. 952.)

§ 355f. Extension of exclusivity period for new qualified infectious disease products

(a) Extension

If the Secretary approves an application pursuant to section 355 of this title for a drug that has been designated as a qualified infectious disease product under subsection (d), the 4- and 5-year periods described in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of section 355 of this title, the 3-year periods described in clauses (iii) and (iv) of subsection (c)(3)(E) and clauses (iii) and (iv) of subsection (j)(5)(F) of section 355 of this title, or the 7-year period described in section 360cc of this title, as applicable, shall be extended by 5 years.

(b) Relation to pediatric exclusivity

Any extension under subsection (a) of a period shall be in addition to any extension of the period under section 355a of this title with respect to the drug.

(c) Limitations

Subsection (a) does not apply to the approval of—

- (1) a supplement to an application under section 355(b) of this title for any qualified infec-

tious disease product for which an extension described in subsection (a) is in effect or has expired;

(2) a subsequent application filed with respect to a product approved under section 355 of this title for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

(3) a product that does not meet the definition of a qualified infectious disease product under subsection (g) based upon its approved uses.

(d) Designation

(1) In general

The manufacturer or sponsor of a drug may request the Secretary to designate a drug as a qualified infectious disease product at any time before the submission of an application under section 355(b) of this title for such drug. The Secretary shall, not later than 60 days after the submission of such a request, determine whether the drug is a qualified infectious disease product.

(2) Limitation

Except as provided in paragraph (3), a designation under this subsection shall not be withdrawn for any reason, including modifications to the list of qualifying pathogens under subsection (f)(2)(C).

(3) Revocation of designation

The Secretary may revoke a designation of a drug as a qualified infectious disease product if the Secretary finds that the request for such designation contained an untrue statement of material fact.

(e) Regulations

(1) In general

Not later than 2 years after July 9, 2012, the Secretary shall adopt final regulations implementing this section, including developing the list of qualifying pathogens described in subsection (f).

(2) Procedure

In promulgating a regulation implementing this section, the Secretary shall—

(A) issue a notice of proposed rulemaking that includes the proposed regulation;

(B) provide a period of not less than 60 days for comments on the proposed regulation; and

(C) publish the final regulation not less than 30 days before the effective date of the regulation.

(3) Restrictions

Notwithstanding any other provision of law, the Secretary shall promulgate regulations implementing this section only as described in paragraph (2), except that the Secretary may issue interim guidance for sponsors seeking designation under subsection (d) prior to the promulgation of such regulations.

(4) Designation prior to regulations

The Secretary shall designate drugs as qualified infectious disease products under subsection (d) prior to the promulgation of

regulations under this subsection, if such drugs meet the definition of a qualified infectious disease product described in subsection (g).

(f) Qualifying pathogen

(1) Definition

In this section, the term “qualifying pathogen” means a pathogen identified and listed by the Secretary under paragraph (2) that has the potential to pose a serious threat to public health, such as—

(A) resistant gram positive pathogens, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Staphylococcus aureus*, and vancomycin-resistant enterococcus;

(B) multi-drug resistant gram negative bacteria, including *Acinetobacter*, *Klebsiella*, *Pseudomonas*, and *E. coli* species;

(C) multi-drug resistant tuberculosis; and

(D) *Clostridium difficile*.

(2) List of qualifying pathogens

(A) In general

The Secretary shall establish and maintain a list of qualifying pathogens, and shall make public the methodology for developing such list.

(B) Considerations

In establishing and maintaining the list of pathogens described under this section, the Secretary shall—

(i) consider—

(I) the impact on the public health due to drug-resistant organisms in humans;

(II) the rate of growth of drug-resistant organisms in humans;

(III) the increase in resistance rates in humans; and

(IV) the morbidity and mortality in humans; and

(ii) consult with experts in infectious diseases and antibiotic resistance, including the Centers for Disease Control and Prevention, the Food and Drug Administration, medical professionals, and the clinical research community.

(C) Review

Every 5 years, or more often as needed, the Secretary shall review, provide modifications to, and publish the list of qualifying pathogens under subparagraph (A) and shall by regulation revise the list as necessary, in accordance with subsection (e).

(g) Qualified infectious disease product

The term “qualified infectious disease product” means an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by—

(1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or

(2) qualifying pathogens listed by the Secretary under subsection (f).

(June 25, 1938, ch. 675, §505E, as added Pub. L. 112-144, title VIII, §801(a), July 9, 2012, 126 Stat. 1077.)

EFFECTIVE DATE

Pub. L. 112-144, title VIII, §801(b), July 9, 2012, 126 Stat. 1079, provided that: “Section 505E of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355f], as added by subsection (a), applies only with respect to a drug that is first approved under section 505(c) of such Act (21 U.S.C. 355(c)) on or after the date of the enactment of this Act [July 9, 2012].”

§ 356. Expedited approval of drugs for serious or life-threatening diseases or conditions

(a) Designation of a drug as a breakthrough therapy

(1) In general

The Secretary shall, at the request of the sponsor of a drug, expedite the development and review of such drug if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. (In this section, such a drug is referred to as a “breakthrough therapy”.)

(2) Request for designation

The sponsor of a drug may request the Secretary to designate the drug as a breakthrough therapy. A request for the designation may be made concurrently with, or at any time after, the submission of an application for the investigation of the drug under section 355(i) of this title or section 262(a)(3) of title 42.

(3) Designation

(A) In general

Not later than 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a breakthrough therapy and shall take such actions as are appropriate to expedite the development and review of the application for approval of such drug.

(B) Actions

The actions to expedite the development and review of an application under subparagraph (A) may include, as appropriate—

- (i) holding meetings with the sponsor and the review team throughout the development of the drug;
- (ii) providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable;
- (iii) involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review;
- (iv) assigning a cross-disciplinary project lead for the Food and Drug Administration

review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and

(v) taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment.

(b) Designation of drug as fast track product

(1) In general

The Secretary shall, at the request of the sponsor of a new drug, facilitate the development and expedite the review of such drug if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition, or if the Secretary designates the drug as a qualified infectious disease product under section 355f(d) of this title. (In this section, such a drug is referred to as a “fast track product”.)

(2) Request for designation

The sponsor of a new drug may request the Secretary to designate the drug as a fast track product. A request for the designation may be made concurrently with, or at any time after, submission of an application for the investigation of the drug under section 355(i) of this title or section 262(a)(3) of title 42.

(3) Designation

Within 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a fast track product and shall take such actions as are appropriate to expedite the development and review of the application for approval of such product.

(c) Accelerated approval of a drug for a serious or life-threatening disease or condition, including a fast track product

(1) In general

(A) Accelerated approval

The Secretary may approve an application for approval of a product for a serious or life-threatening disease or condition, including a fast track product, under section 355(c) of this title or section 262(a) of title 42 upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The approval described in the preceding sentence is referred to in this section as “accelerated approval”.

(B) Evidence

The evidence to support that an endpoint is reasonably likely to predict clinical benefit under subparagraph (A) may include epidemiological, pathophysiological, therapeutic, pharmacologic, or other evidence developed using biomarkers, for example, or other scientific methods or tools.

(2) Limitation

Approval of a product under this subsection may be subject to 1 or both of the following requirements:

(A) That the sponsor conduct appropriate postapproval studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit.

(B) That the sponsor submit copies of all promotional materials related to the product during the preapproval review period and, following approval and for such period thereafter as the Secretary determines to be appropriate, at least 30 days prior to dissemination of the materials.

(3) Expedited withdrawal of approval

The Secretary may withdraw approval of a product approved under accelerated approval using expedited procedures (as prescribed by the Secretary in regulations which shall include an opportunity for an informal hearing) if—

(A) the sponsor fails to conduct any required postapproval study of the drug with due diligence;

(B) a study required to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit of the product fails to verify and describe such effect or benefit;

(C) other evidence demonstrates that the product is not safe or effective under the conditions of use; or

(D) the sponsor disseminates false or misleading promotional materials with respect to the product.

(d) Review of incomplete applications for approval of a fast track product**(1) In general**

If the Secretary determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective, the Secretary shall evaluate for filing, and may commence review of portions of, an application for the approval of the product before the sponsor submits a complete application. The Secretary shall commence such review only if the applicant—

(A) provides a schedule for submission of information necessary to make the application complete; and

(B) pays any fee that may be required under section 379h of this title.

(2) Exception

Any time period for review of human drug applications that has been agreed to by the Secretary and that has been set forth in goals identified in letters of the Secretary (relating to the use of fees collected under section 379h of this title to expedite the drug development

process and the review of human drug applications) shall not apply to an application submitted under paragraph (1) until the date on which the application is complete.

(e) Construction**(1) Purpose**

The amendments made by the Food and Drug Administration Safety and Innovation Act to this section are intended to encourage the Secretary to utilize innovative and flexible approaches to the assessment of products under accelerated approval for treatments for patients with serious or life-threatening diseases or conditions and unmet medical needs.

(2) Construction

Nothing in this section shall be construed to alter the standards of evidence under subsection (c) or (d) of section 355 of this title (including the substantial evidence standard in section 355(d) of this title) or under section 262(a) of title 42. Such sections and standards of evidence apply to the review and approval of products under this section, including whether a product is safe and effective. Nothing in this section alters the ability of the Secretary to rely on evidence that does not come from adequate and well-controlled investigations for the purpose of determining whether an endpoint is reasonably likely to predict clinical benefit as described in subsection (b)(1)(B).

(f) Awareness efforts

The Secretary shall—

(1) develop and disseminate to physicians, patient organizations, pharmaceutical and biotechnology companies, and other appropriate persons a description of the provisions of this section applicable to breakthrough therapies, accelerated approval, and and¹ fast track products; and

(2) establish a program to encourage the development of surrogate and clinical endpoints, including biomarkers, and other scientific methods and tools that can assist the Secretary in determining whether the evidence submitted in an application is reasonably likely to predict clinical benefit for serious or life-threatening conditions for which significant unmet medical needs exist.

(June 25, 1938, ch. 675, §506, as added Pub. L. 105-115, title I, §112(a), Nov. 21, 1997, 111 Stat. 2309; amended Pub. L. 112-144, title VIII, §803, title IX, §§901(b), 902(a), July 9, 2012, 126 Stat. 1079, 1083, 1086.)

REFERENCES IN TEXT

The Food and Drug Administration Safety and Innovation Act, referred to in subsec. (e)(1), is Pub. L. 112-144. For the amendments made to this section by the Act, see 2012 Amendment notes below.

PRIOR PROVISIONS

A prior section 356, act June 25, 1938, ch. 675, §506, as added Dec. 22, 1941, ch. 613, §3, 55 Stat. 851; amended Pub. L. 102-300, §6(b)(2), June 16, 1992, 106 Stat. 240; Pub. L. 103-80, §3(o), Aug. 13, 1993, 107 Stat. 777, related to certification of drugs containing insulin, prior to re-

¹ So in original.

peal by Pub. L. 105–115, title I, §125(a)(1), Nov. 21, 1997, 111 Stat. 2325.

AMENDMENTS

2012—Pub. L. 112–144, §901(b), amended section generally. Prior to amendment, section consisted of subsecs. (a) to (d) relating to designation of drugs as fast track products, approval of applications for fast track products, review of incomplete applications for approval of fast track products, and awareness efforts, respectively.

Subsec. (a). Pub. L. 112–144, §902(a)(3), added subsec. (a). Former subsec. (a) redesignated (b).

Subsec. (a)(1). Pub. L. 112–144, §803, amended subsec. (a)(1), as amended by Pub. L. 112–144, §901(b), by inserting “, or if the Secretary designates the drug as a qualified infectious disease product under section 355f(d) of this title” after “such a disease or condition”.

Subsecs. (b) to (d). Pub. L. 112–144, §902(a)(1), redesignated subsecs. (a) to (c) as (b) to (d), respectively. Former subsec. (d) relating to awareness efforts redesignated (f).

Subsec. (f). Pub. L. 112–144, §902(a)(2), which directed the redesignation of subsec. (d) as (f), was executed by redesignating the subsec. (d) relating to awareness efforts as (f), to reflect the probable intent of Congress.

Subsec. (f)(1). Pub. L. 112–144, §902(a)(4), substituted “applicable to breakthrough therapies, accelerated approval, and” for “applicable to accelerated approval”.

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

FINDINGS AND SENSE OF CONGRESS ON ENHANCEMENT OF ACCELERATED PATIENT ACCESS TO NEW MEDICAL TREATMENTS

Pub. L. 112–144, title IX, §901(a), July 9, 2012, 126 Stat. 1082, provided that:

“(1) FINDINGS.—Congress finds as follows:

“(A) The Food and Drug Administration (referred to in this section as the ‘FDA’) serves a critical role in helping to assure that new medicines are safe and effective. Regulatory innovation is 1 element of the Nation’s strategy to address serious and life-threatening diseases or conditions by promoting investment in and development of innovative treatments for unmet medical needs.

“(B) During the 2 decades following the establishment of the accelerated approval mechanism, advances in medical sciences, including genomics, molecular biology, and bioinformatics, have provided an unprecedented understanding of the underlying biological mechanism and pathogenesis of disease. A new generation of modern, targeted medicines is under development to treat serious and life-threatening diseases, some applying drug development strategies based on biomarkers or pharmacogenomics, predictive toxicology, clinical trial enrichment techniques, and novel clinical trial designs, such as adaptive clinical trials.

“(C) As a result of these remarkable scientific and medical advances, the FDA should be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in fewer, smaller, or shorter clinical trials for the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for the approval of drugs.

“(D) Patients benefit from expedited access to safe and effective innovative therapies to treat unmet

medical needs for serious or life-threatening diseases or conditions.

“(E) For these reasons, the statutory authority in effect on the day before the date of enactment of this Act [July 9, 2012] governing expedited approval of drugs for serious or life-threatening diseases or conditions should be amended in order to enhance the authority of the FDA to consider appropriate scientific data, methods, and tools, and to expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions.

“(2) SENSE OF CONGRESS.—It is the sense of Congress that the Food and Drug Administration should apply the accelerated approval and fast track provisions set forth in section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356), as amended by this section, to help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards for such treatments.”

GUIDANCE; AMENDED REGULATIONS

Pub. L. 112–144, title IX, §901(c), July 9, 2012, 126 Stat. 1085, provided that:

“(1) DRAFT GUIDANCE.—Not later than 1 year after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this section as the ‘Secretary’) shall issue draft guidance to implement the amendments made by this section [amending this section]. In developing such guidance, the Secretary shall specifically consider issues arising under the accelerated approval and fast track processes under section 506 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356], as amended by subsection (b), for drugs designated for a rare disease or condition under section 526 of such Act (21 U.S.C. 360bb) and shall also consider any unique issues associated with very rare diseases.

“(2) FINAL GUIDANCE.—Not later than 1 year after the issuance of draft guidance under paragraph (1), and after an opportunity for public comment, the Secretary shall—

“(A) issue final guidance; and

“(B) amend the regulations governing accelerated approval in parts 314 and 601 of title 21, Code of Federal Regulations, as necessary to conform such regulations with the amendment made by subsection (b).

“(3) CONSIDERATION.—In developing the guidance under paragraphs (1) and (2)(A) and the amendments under paragraph (2)(B), the Secretary shall consider how to incorporate novel approaches to the review of surrogate endpoints based on pathophysiologic and pharmacologic evidence in such guidance, especially in instances where the low prevalence of a disease renders the existence or collection of other types of data unlikely or impractical.

“(4) CONFORMING CHANGES.—The Secretary shall issue, as necessary, conforming amendments to the applicable regulations under title 21, Code of Federal Regulations, governing accelerated approval.

“(5) NO EFFECT OF INACTION ON REQUESTS.—The issuance (or nonissuance) of guidance or conforming regulations implementing the amendment made by subsection (b) shall not preclude the review of, or action on, a request for designation or an application for approval submitted pursuant to section 506 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356], as amended by subsection (b).”

Pub. L. 112–144, title IX, §902(b), July 9, 2012, 126 Stat. 1087, provided that:

“(1) IN GENERAL.—

“(A) GUIDANCE.—Not later than 18 months after the date of enactment of this Act [July 9, 2012], the Secretary of Health and Human Services (referred to in this section as the ‘Secretary’) shall issue draft guidance on implementing the requirements with respect to breakthrough therapies, as set forth in section 506(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(a)), as amended by this section. The

Secretary shall issue final guidance not later than 1 year after the close of the comment period for the draft guidance.

“(B) AMENDED REGULATIONS.—

“(i) IN GENERAL.—If the Secretary determines that it is necessary to amend the regulations under title 21, Code of Federal Regulations in order to implement the amendments made by this section to section 506(a) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall amend such regulations not later than 2 years after the date of enactment of this Act.

“(ii) PROCEDURE.—In amending regulations under clause (i), the Secretary shall—

“(I) issue a notice of proposed rulemaking that includes the proposed regulation;

“(II) provide a period of not less than 60 days for comments on the proposed regulation; and

“(III) publish the final regulation not less than 30 days before the effective date of the regulation.

“(iii) RESTRICTIONS.—Notwithstanding any other provision of law, the Secretary shall promulgate regulations implementing the amendments made by this section only as described in clause (ii).

“(2) REQUIREMENTS.—Guidance issued under this section shall—

“(A) specify the process and criteria by which the Secretary makes a designation under section 506(a)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356(a)(3)]; and

“(B) specify the actions the Secretary shall take to expedite the development and review of a breakthrough therapy pursuant to such designation under such section 506(a)(3), including updating good review management practices to reflect breakthrough therapies.”

Pub. L. 105-115, title I, §112(b), Nov. 21, 1997, 111 Stat. 2310, provided that: “Within 1 year after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall issue guidance for fast track products (as defined in [former] section 506(a)(1) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356(a)(1)]) that describes the policies and procedures that pertain to section 506 of such Act.”

§ 356-1. Accelerated approval of priority countermeasures

(a) In general

The Secretary of Health and Human Services may designate a priority countermeasure as a fast-track product pursuant to section 356 of this title or as a device granted review priority pursuant to section 360e(d)(5) of this title. Such a designation may be made prior to the submission of—

(1) a request for designation by the sponsor or applicant; or

(2) an application for the investigation of the drug under section 355(i) of this title or section 262(a)(3) of title 42.

Nothing in this subsection shall be construed to prohibit a sponsor or applicant from declining such a designation.

(b) Use of animal trials

A drug for which approval is sought under section 355(b) of this title or section 262 of title 42 on the basis of evidence of effectiveness that is derived from animal studies pursuant to section 123¹ may be designated as a fast track product for purposes of this section.

(c) Priority review of drugs and biological products

A priority countermeasure that is a drug or biological product shall be considered a priority

drug or biological product for purposes of performance goals for priority drugs or biological products agreed to by the Commissioner of Food and Drugs.

(d) Definitions

For purposes of this title:¹

(1) The term “priority countermeasure” has the meaning given such term in section 247d-6(h)(4)¹ of title 42.

(2) The term “priority drugs or biological products” means a drug or biological product that is the subject of a drug or biologics application referred to in section 101(4) of the Food and Drug Administration Modernization Act of 1997.

(Pub. L. 107-188, title I, §122, June 12, 2002, 116 Stat. 613.)

REFERENCES IN TEXT

Section 123, referred to in subsec. (b), is section 123 of Pub. L. 107-188, title I, June 12, 2002, 116 Stat. 613, which is not classified to the Code.

This title, referred to in subsec. (d), is title I of Pub. L. 107-188, June 12, 2002, 116 Stat. 596, which enacted this section, section 669a of Title 29, Labor, and sections 244, 245, 247d-3a, 247d-3b, 247d-7a to 247d-7d, 300hh, 300hh-11 to 300hh-13, 1320b-5, and 7257d of Title 42, The Public Health and Welfare, amended sections 247d to 247d-6, 264, 266, 290hh-1, and 5196b of Title 42, and enacted provisions set out as notes preceding section 8101 of Title 38, Veterans' Benefits, and under sections 201, 244, 247d, 247d-6, 300hh, 300hh-12, and 1320b-5 of Title 42. For complete classification of this title to the Code, see Tables.

Section 247d-6(h)(4) of title 42, referred to in subsec. (d)(1), was redesignated section 247d-6(e)(4) by Pub. L. 109-417, title III, §304(3), Dec. 19, 2006, 120 Stat. 2861.

Section 101(4) of the Food and Drug Administration Modernization Act of 1997, referred to in subsec. (d)(2), is section 101(4) of Pub. L. 105-115, which is set out as a note under section 379g of this title.

CODIFICATION

Section was enacted as part of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 356a. Manufacturing changes

(a) In general

With respect to a drug for which there is in effect an approved application under section 355 or 360b of this title or a license under section 262 of title 42, a change from the manufacturing process approved pursuant to such application or license may be made, and the drug as made with the change may be distributed, if—

(1) the holder of the approved application or license (referred to in this section as a “holder”) has validated the effects of the change in accordance with subsection (b) of this section; and

(2)(A) in the case of a major manufacturing change, the holder has complied with the requirements of subsection (c) of this section; or

(B) in the case of a change that is not a major manufacturing change, the holder complies with the applicable requirements of subsection (d) of this section.

(b) Validation of effects of changes

For purposes of subsection (a)(1) of this section, a drug made with a manufacturing change

¹ See References in Text note below.

(whether a major manufacturing change or otherwise) may be distributed only if, before distribution of the drug as so made, the holder involved validates the effects of the change on the identity, strength, quality, purity, and potency of the drug as the identity, strength, quality, purity, and potency may relate to the safety or effectiveness of the drug.

(c) Major manufacturing changes

(1) Requirement of supplemental application

For purposes of subsection (a)(2)(A) of this section, a drug made with a major manufacturing change may be distributed only if, before the distribution of the drug as so made, the holder involved submits to the Secretary a supplemental application for such change and the Secretary approves the application. The application shall contain such information as the Secretary determines to be appropriate, and shall include the information developed under subsection (b) of this section by the holder in validating the effects of the change.

(2) Changes qualifying as major changes

For purposes of subsection (a)(2)(A) of this section, a major manufacturing change is a manufacturing change that is determined by the Secretary to have substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as they may relate to the safety or effectiveness of a drug. Such a change includes a change that—

(A) is made in the qualitative or quantitative formulation of the drug involved or in the specifications in the approved application or license referred to in subsection (a) of this section for the drug (unless exempted from the requirements by regulation or guidance from the Secretary by regulation or guidance);

(B) is determined by the Secretary by regulation or guidance to require completion of an appropriate clinical study demonstrating equivalence of the drug to the drug as manufactured without the change; or

(C) is another type of change determined by the Secretary by regulation or guidance to have a substantial potential to adversely affect the safety or effectiveness of the drug.

(d) Other manufacturing changes

(1) In general

For purposes of subsection (a)(2)(B) of this section, the Secretary may regulate drugs made with manufacturing changes that are not major manufacturing changes as follows:

(A) The Secretary may in accordance with paragraph (2) authorize holders to distribute such drugs without submitting a supplemental application for such changes.

(B) The Secretary may in accordance with paragraph (3) require that, prior to the distribution of such drugs, holders submit to the Secretary supplemental applications for such changes.

(C) The Secretary may establish categories of such changes and designate categories to which subparagraph (A) applies and categories to which subparagraph (B) applies.

(2) Changes not requiring supplemental application

(A) Submission of report

A holder making a manufacturing change to which paragraph (1)(A) applies shall submit to the Secretary a report on the change, which shall contain such information as the Secretary determines to be appropriate, and which shall include the information developed under subsection (b) of this section by the holder in validating the effects of the change. The report shall be submitted by such date as the Secretary may specify.

(B) Authority regarding annual reports

In the case of a holder that during a single year makes more than one manufacturing change to which paragraph (1)(A) applies, the Secretary may in carrying out subparagraph (A) authorize the holder to comply with such subparagraph by submitting a single report for the year that provides the information required in such subparagraph for all the changes made by the holder during the year.

(3) Changes requiring supplemental application

(A) Submission of supplemental application

The supplemental application required under paragraph (1)(B) for a manufacturing change shall contain such information as the Secretary determines to be appropriate, which shall include the information developed under subsection (b) of this section by the holder in validating the effects of the change.

(B) Authority for distribution

In the case of a manufacturing change to which paragraph (1)(B) applies:

(i) The holder involved may commence distribution of the drug involved 30 days after the Secretary receives the supplemental application under such paragraph, unless the Secretary notifies the holder within such 30-day period that prior approval of the application is required before distribution may be commenced.

(ii) The Secretary may designate a category of such changes for the purpose of providing that, in the case of a change that is in such category, the holder involved may commence distribution of the drug involved upon the receipt by the Secretary of a supplemental application for the change.

(iii) If the Secretary disapproves the supplemental application, the Secretary may order the manufacturer to cease the distribution of the drugs that have been made with the manufacturing change.

(June 25, 1938, ch. 675, §506A, as added Pub. L. 105-115, title I, §116(a), Nov. 21, 1997, 111 Stat. 2313.)

EFFECTIVE DATE

Pub. L. 105-115, title I, §116(b), Nov. 21, 1997, 111 Stat. 2315, provided that: “The amendment made by subsection (a) [enacting this section] takes effect upon the effective date of regulations promulgated by the Sec-

retary of Health and Human Services to implement such amendment, or upon the expiration of the 24-month period beginning on the date of the enactment of this Act [Nov. 21, 1997], whichever occurs first.”

§ 356b. Reports of postmarketing studies

(a) Submission

(1) In general

A sponsor of a drug that has entered into an agreement with the Secretary to conduct a postmarketing study of a drug shall submit to the Secretary, within 1 year after the approval of such drug and annually thereafter until the study is completed or terminated, a report of the progress of the study or the reasons for the failure of the sponsor to conduct the study. The report shall be submitted in such form as is prescribed by the Secretary in regulations issued by the Secretary.

(2) Agreements prior to effective date

Any agreement entered into between the Secretary and a sponsor of a drug, prior to November 21, 1997, to conduct a postmarketing study of a drug shall be subject to the requirements of paragraph (1). An initial report for such an agreement shall be submitted within 6 months after the date of the issuance of the regulations under paragraph (1).

(b) Consideration of information as public information

Any information pertaining to a report described in subsection (a) of this section shall be considered to be public information to the extent that the information is necessary—

- (1) to identify the sponsor; and
- (2) to establish the status of a study described in subsection (a) of this section and the reasons, if any, for any failure to carry out the study.

(c) Status of studies and reports

The Secretary shall annually develop and publish in the Federal Register a report that provides information on the status of the postmarketing studies—

- (1) that sponsors have entered into agreements to conduct; and
- (2) for which reports have been submitted under subsection (a)(1) of this section.

(d) Disclosure

If a sponsor fails to complete an agreed upon study required by this section by its original or otherwise negotiated deadline, the Secretary shall publish a statement on the Internet site of the Food and Drug Administration stating that the study was not completed and, if the reasons for such failure to complete the study were not satisfactory to the Secretary, a statement that such reasons were not satisfactory to the Secretary.

(e) Notification

With respect to studies of the type required under section 356(c)(2)(A) of this title or under section 314.510 or 601.41 of title 21, Code of Federal Regulations, as each of such sections was in effect on the day before the effective date of this subsection, the Secretary may require that a sponsor who, for reasons not satisfactory to the

Secretary, fails to complete by its deadline a study under any of such sections of such type for a drug or biological product (including such a study conducted after such effective date) notify practitioners who prescribe such drug or biological product of the failure to complete such study and the questions of clinical benefit, and, where appropriate, questions of safety, that remain unanswered as a result of the failure to complete such study. Nothing in this subsection shall be construed as altering the requirements of the types of studies required under section 356(c)(2)(A) of this title or under section 314.510 or 601.41 of title 21, Code of Federal Regulations, as so in effect, or as prohibiting the Secretary from modifying such sections of title 21 of such Code to provide for studies in addition to those of such type.

(June 25, 1938, ch. 675, §506B, as added Pub. L. 105-115, title I, §130(a), Nov. 21, 1997, 111 Stat. 2331; amended Pub. L. 107-188, title V, §506, June 12, 2002, 116 Stat. 693; Pub. L. 112-144, title IX, §902(c), July 9, 2012, 126 Stat. 1088.)

REFERENCES IN TEXT

The effective date of this subsection, referred to in subsec. (e), is Oct. 1, 2002, see Effective Date of 2002 Amendment note set out below.

AMENDMENTS

2012—Subsec. (e). Pub. L. 112-144 substituted “section 356(c)(2)(A) of this title” for “section 356(b)(2)(A) of this title” in two places.

2002—Subsecs. (d), (e). Pub. L. 107-188 added subsecs. (d) and (e).

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107-188, title V, §508, June 12, 2002, 116 Stat. 694, provided that: “The amendments made by this subtitle [subtitle A (§§501-509) of title V of Pub. L. 107-188, amending this section and sections 379g and 379h of this title] shall take effect October 1, 2002.”

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

REPORT TO CONGRESSIONAL COMMITTEES

Pub. L. 105-115, title I, §130(b), Nov. 21, 1997, 111 Stat. 2331, provided that not later than Oct. 1, 2001, the Secretary was to submit to Congress a report containing a summary of the reports submitted under section 356b of this title and an evaluation and legislative recommendations relating to postmarketing studies of drugs.

§ 356c. Discontinuance or interruption in the production of life-saving drugs

(a) In general

A manufacturer of a drug—

- (1) that is—
 - (A) life-supporting;
 - (B) life-sustaining; or
 - (C) intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug used in emergency medical care or during surgery; and
- (2) that is not a radio pharmaceutical drug product or any other product as designated by the Secretary,

shall notify the Secretary, in accordance with subsection (b), of a permanent discontinuance in

shall notify the Secretary, in accordance with subsection (b), of a permanent discontinuance in

the manufacture of the drug or an interruption of the manufacture of the drug that is likely to lead to a meaningful disruption in the supply of that drug in the United States, and the reasons for such discontinuance or interruption.

(b) Timing

A notice required under subsection (a) shall be submitted to the Secretary—

- (1) at least 6 months prior to the date of the discontinuance or interruption; or
- (2) if compliance with paragraph (1) is not possible, as soon as practicable.

(c) Distribution

To the maximum extent practicable, the Secretary shall distribute, through such means as the Secretary deems appropriate, information on the discontinuation or interruption of the manufacture of the drugs described in subsection (a) to appropriate organizations, including physician, health provider, and patient organizations, as described in section 356e of this title.

(d) Confidentiality

Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18.

(e) Coordination with Attorney General

Not later than 30 days after the receipt of a notification described in subsection (a), the Secretary shall—

- (1) determine whether the notification pertains to a controlled substance subject to a production quota under section 826 of this title; and
- (2) if necessary, as determined by the Secretary—
 - (A) notify the Attorney General that the Secretary has received such a notification;
 - (B) request that the Attorney General increase the aggregate and individual production quotas under section 826 of this title applicable to such controlled substance and any ingredient therein to a level the Secretary deems necessary to address a shortage of a controlled substance based on the best available market data; and
 - (C) if the Attorney General determines that the level requested is not necessary to address a shortage of a controlled substance, the Attorney General shall provide to the Secretary a written response detailing the basis for the Attorney General's determination.

The Secretary shall make the written response provided under subparagraph (C) available to the public on the Internet Web site of the Food and Drug Administration.

(f) Failure to meet requirements

If a person fails to submit information required under subsection (a) in accordance with subsection (b)—

- (1) the Secretary shall issue a letter to such person informing such person of such failure;
- (2) not later than 30 calendar days after the issuance of a letter under paragraph (1), the

person who receives such letter shall submit to the Secretary a written response to such letter setting forth the basis for noncompliance and providing information required under subsection (a); and

(3) not later than 45 calendar days after the issuance of a letter under paragraph (1), the Secretary shall make such letter and any response to such letter under paragraph (2) available to the public on the Internet Web site of the Food and Drug Administration, with appropriate redactions made to protect information described in subsection (d), except that, if the Secretary determines that the letter under paragraph (1) was issued in error or, after review of such response, the person had a reasonable basis for not notifying as required under subsection (a), the requirements of this paragraph shall not apply.

(g) Expedited inspections and reviews

If, based on notifications described in subsection (a) or any other relevant information, the Secretary concludes that there is, or is likely to be, a drug shortage of a drug described in subsection (a), the Secretary may—

- (1) expedite the review of a supplement to a new drug application submitted under section 355(b) of this title, an abbreviated new drug application submitted under section 355(j) of this title, or a supplement to such an application submitted under section 355(j) of this title that could help mitigate or prevent such shortage; or
- (2) expedite an inspection or reinspection of an establishment that could help mitigate or prevent such drug shortage.

(h) Definitions

For purposes of this section—

- (1) the term “drug”—
 - (A) means a drug (as defined in section 321(g) of this title) that is intended for human use and that is subject to section 353(b)(1) of this title; and
 - (B) does not include biological products (as defined in section 262 of title 42), unless otherwise provided by the Secretary in the regulations promulgated under subsection (i);
- (2) the term “drug shortage” or “shortage”, with respect to a drug, means a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug; and
- (3) the term “meaningful disruption”—
 - (A) means a change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product; and
 - (B) does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

(i) Regulations**(1) In general**

Not later than 18 months after July 9, 2012, the Secretary shall adopt a final regulation implementing this section.

(2) Contents

Such regulation shall define, for purposes of this section, the terms “life-supporting”, “life-sustaining”, and “intended for use in the prevention or treatment of a debilitating disease or condition”.

(3) Inclusion of biological products**(A) In general**

The Secretary may by regulation apply this section to biological products (as defined in section 262 of title 42), including plasma products derived from human plasma protein and their recombinant analogs, if the Secretary determines such inclusion would benefit the public health. Such regulation shall take into account any supply reporting programs and shall aim to reduce duplicative notification.

(B) Rule for vaccines

If the Secretary applies this section to vaccines pursuant to subparagraph (A), the Secretary shall—

(i) consider whether the notification requirement under subsection (a) may be satisfied by submitting a notification to the Centers for Disease Control and Prevention under the vaccine shortage notification program of such Centers; and

(ii) explain the determination made by the Secretary under clause (i) in the regulation.

(4) Procedure

In promulgating a regulation implementing this section, the Secretary shall—

(A) issue a notice of proposed rulemaking that includes the proposed regulation;

(B) provide a period of not less than 60 days for comments on the proposed regulation; and

(C) publish the final regulation not less than 30 days before the regulation’s effective date.

(5) Restrictions

Notwithstanding any other provision of Federal law, in implementing this section, the Secretary shall only promulgate regulations as described in paragraph (4).

(June 25, 1938, ch. 675, § 506C, as added Pub. L. 105–115, title I, § 131(a), Nov. 21, 1997, 111 Stat. 2332; amended Pub. L. 112–144, title X, § 1001(a), July 9, 2012, 126 Stat. 1099.)

AMENDMENTS

2012—Pub. L. 112–144 amended section generally. Prior to amendment, section related to discontinuance of life saving products.

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105–115, set out as an Effective Date of 1997 Amendment note under section 321 of this title.

EFFECT OF NOTIFICATION

Pub. L. 112–144, title X, § 1001(b), July 9, 2012, 126 Stat. 1101, provided that: “The submission of a notification to the Secretary of Health and Human Services (referred to in this title [see Tables for classification] as the ‘Secretary’) for purposes of complying with the requirement in section 506C(a) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 356c(a)] (as amended by subsection (a)) shall not be construed—

“(1) as an admission that any product that is the subject of such notification violates any provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.); or

“(2) as evidence of an intention to promote or market the product for an indication or use for which the product has not been approved by the Secretary.”

EX. ORD. NO. 13588. REDUCING PRESCRIPTION DRUG SHORTAGES

Ex. Ord. No. 13588, Oct. 31, 2011, 76 F.R. 68295, provided:

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

SECTION 1. *Policy.* Shortages of pharmaceutical drugs pose a serious and growing threat to public health. While a very small number of drugs in the United States experience a shortage in any given year, the number of prescription drug shortages in the United States nearly tripled between 2005 and 2010, and shortages are becoming more severe as well as more frequent. The affected medicines include cancer treatments, anesthesia drugs, and other drugs that are critical to the treatment and prevention of serious diseases and life-threatening conditions.

For example, over approximately the last 5 years, data indicates that the use of sterile injectable cancer treatments has increased by about 20 percent, without a corresponding increase in production capacity. While manufacturers are currently in the process of expanding capacity, it may be several years before production capacity has been significantly increased. Interruptions in the supplies of these drugs endanger patient safety and burden doctors, hospitals, pharmacists, and patients. They also increase health care costs, particularly because some participants in the market may use shortages as opportunities to hoard scarce drugs or charge exorbitant prices.

The Food and Drug Administration (FDA) in the Department of Health and Human Services has been working diligently to address this problem through its existing regulatory framework. While the root problems and many of their solutions are outside of the FDA’s control, the agency has worked cooperatively with manufacturers to prevent or mitigate shortages by expediting review of certain regulatory submissions and adopting a flexible approach to drug manufacturing and importation regulations where appropriate. As a result, the FDA prevented 137 drug shortages in 2010 and 2011. Despite these successes, however, the problem of drug shortages has continued to grow.

Many different factors contribute to drug shortages, and solving this critical public health problem will require a multifaceted approach. An important factor in many of the recent shortages appears to be an increase in demand that exceeds current manufacturing capacity. While manufacturers are in the process of expanding capacity, one important step is ensuring that the FDA and the public receive adequate advance notice of shortages whenever possible. The FDA cannot begin to work with manufacturers or use the other tools at its disposal until it knows there is a potential problem. Similarly, early disclosure of a shortage can help hospitals, doctors, and patients make alternative arrangements before a shortage becomes a crisis. However, drug manufacturers have not consistently provided the FDA with adequate notice of potential shortages.

As part of my Administration’s broader effort to work with manufacturers, health care providers, and

other stakeholders to prevent drug shortages, this order directs the FDA to take steps that will help to prevent and reduce current and future disruptions in the supply of lifesaving medicines.

SEC. 2. Broader Reporting of Manufacturing Discontinuances. To the extent permitted by law, the FDA shall use all appropriate administrative tools, including its authority to interpret and administer the reporting requirements in 21 U.S.C. 356c, to require drug manufacturers to provide adequate advance notice of manufacturing discontinuances that could lead to shortages of drugs that are life-supporting or life-sustaining, or that prevent debilitating disease.

SEC. 3. Expedited Regulatory Review. To the extent practicable, and consistent with its statutory responsibility to ensure the safety and effectiveness of the drug supply, the FDA shall take steps to expand its current efforts to expedite its regulatory reviews, including reviews of new drug suppliers, manufacturing sites, and manufacturing changes, whenever it determines that expedited review would help to avoid or mitigate existing or potential drug shortages. In prioritizing and allocating its limited resources, the FDA should consider both the severity of the shortage and the importance of the affected drug to public health.

SEC. 4. Review of Certain Behaviors by Market Participants. The FDA shall communicate to the Department of Justice (DOJ) any findings that shortages have led market participants to stockpile the affected drugs or sell them at exorbitant prices. The DOJ shall then determine whether these activities are consistent with applicable law. Based on its determination, DOJ, in coordination with other State and Federal regulatory agencies as appropriate, should undertake whatever enforcement actions, if any, it deems appropriate.

SEC. 5. General Provisions. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) authority granted by law to an agency, or the head thereof; or

(ii) functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

BARACK OBAMA.

§ 356c-1. Annual reporting on drug shortages

(a) Annual reports to Congress

Not later than the end of calendar year 2013, and not later than the end of each calendar year thereafter, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report on drug shortages that—

(1) specifies the number of manufacturers that submitted a notification to the Secretary under section 356c(a) of this title during such calendar year;

(2) describes the communication between the field investigators of the Food and Drug Administration and the staff of the Center for Drug Evaluation and Research's Office of Compliance and Drug Shortage Program, including the Food and Drug Administration's procedures for enabling and ensuring such communication;

(3)(A) lists the major actions taken by the Secretary to prevent or mitigate the drug shortages described in paragraph (7);

(B) in the list under subparagraph (A), includes—

(i) the number of applications and supplements for which the Secretary expedited review under section 356c(g)(1) of this title during such calendar year; and

(ii) the number of establishment inspections or reinspections that the Secretary expedited under section 356c(g)(2) of this title during such calendar year;

(4) describes the coordination between the Food and Drug Administration and the Drug Enforcement Administration on efforts to prevent or alleviate drug shortages;

(5) identifies the number of and describes the instances in which the Food and Drug Administration exercised regulatory flexibility and discretion to prevent or alleviate a drug shortage;

(6) lists the names of manufacturers that were issued letters under section 356c(f) of this title; and

(7) specifies the number of drug shortages occurring during such calendar year, as identified by the Secretary.

(b) Trend analysis

The Secretary is authorized to retain a third party to conduct a study, if the Secretary believes such a study would help clarify the causes, trends, or solutions related to drug shortages.

(c) Definition

In this section, the term “drug shortage” or “shortage” has the meaning given such term in section 356c of this title.

(June 25, 1938, ch. 675, §506C-1, as added Pub. L. 112-144, title X, §1002, July 9, 2012, 126 Stat. 1102.)

§ 356d. Coordination; task force and strategic plan

(a) Task force and strategic plan

(1) In general

(A) Task force

As soon as practicable after July 9, 2012, the Secretary shall establish a task force to develop and implement a strategic plan for enhancing the Secretary's response to preventing and mitigating drug shortages.

(B) Strategic plan

The strategic plan described in subparagraph (A) shall include—

(i) plans for enhanced interagency and intra-agency coordination, communication, and decisionmaking;

(ii) plans for ensuring that drug shortages are considered when the Secretary initiates a regulatory action that could precipitate a drug shortage or exacerbate an existing drug shortage;

(iii) plans for effective communication with outside stakeholders, including who the Secretary should alert about potential or actual drug shortages, how the communication should occur, and what types of information should be shared;

(iv) plans for considering the impact of drug shortages on research and clinical trials; and

(v) an examination of whether to establish a “qualified manufacturing partner program”, as described in subparagraph (C).

(C) Description of program

In conducting the examination of a “qualified manufacturing partner program” under subparagraph (B)(v), the Secretary—

(i) shall take into account that—

(I) a “qualified manufacturer”, for purposes of such program, would need to have the capability and capacity to supply products determined or anticipated to be in shortage; and

(II) in examining the capability and capacity to supply products in shortage, the “qualified manufacturer” could have a site that manufactures a drug listed under section 356e of this title or have the capacity to produce drugs in response to a shortage within a rapid time-frame; and

(ii) shall examine whether incentives are necessary to encourage the participation of “qualified manufacturers” in such a program.

(D) Consultation

In carrying out this paragraph, the task force shall ensure consultation with the appropriate offices within the Food and Drug Administration, including the Office of the Commissioner, the Center for Drug Evaluation and Research, the Office of Regulatory Affairs, and employees within the Department of Health and Human Services with expertise regarding drug shortages. The Secretary shall engage external stakeholders and experts as appropriate.

(2) Timing

Not later than 1 year after July 9, 2012, the task force shall—

(A) publish the strategic plan described in paragraph (1); and

(B) submit such plan to Congress.

(b) Communication

The Secretary shall ensure that, prior to any enforcement action or issuance of a warning letter that the Secretary determines could reasonably be anticipated to lead to a meaningful disruption in the supply in the United States of a drug described under section 356c(a) of this title, there is communication with the appropriate office of the Food and Drug Administration with expertise regarding drug shortages regarding whether the action or letter could cause, or exacerbate, a shortage of the drug.

(c) Action

If the Secretary determines, after the communication described in subsection (b), that an enforcement action or a warning letter could reasonably cause or exacerbate a shortage of a drug described under section 356c(a) of this title, then the Secretary shall evaluate the risks associated with the impact of such shortage upon patients and those risks associated with the violation involved before taking such action or issuing such letter, unless there is imminent risk of serious

adverse health consequences or death to humans.

(d) Reporting by other entities

The Secretary shall identify or establish a mechanism by which health care providers and other third-party organizations may report to the Secretary evidence of a drug shortage.

(e) Review and construction

No determination, finding, action, or omission of the Secretary under this section shall—

(1) be subject to judicial review; or

(2) be construed to establish a defense to an enforcement action by the Secretary.

(f) Sunset

Subsections (a), (b), (c), and (e) shall cease to be effective on the date that is 5 years after July 9, 2012.

(June 25, 1938, ch. 675, §506D, as added Pub. L. 112-144, title X, §1003, July 9, 2012, 126 Stat. 1103.)

§ 356e. Drug shortage list

(a) Establishment

The Secretary shall maintain an up-to-date list of drugs that are determined by the Secretary to be in shortage in the United States.

(b) Contents

For each drug on such list, the Secretary shall include the following information:

(1) The name of the drug in shortage, including the National Drug Code number for such drug.

(2) The name of each manufacturer of such drug.

(3) The reason for the shortage, as determined by the Secretary, selecting from the following categories:

(A) Requirements related to complying with good manufacturing practices.

(B) Regulatory delay.

(C) Shortage of an active ingredient.

(D) Shortage of an inactive ingredient component.

(E) Discontinuation of the manufacture of the drug.

(F) Delay in shipping of the drug.

(G) Demand increase for the drug.

(4) The estimated duration of the shortage as determined by the Secretary.

(c) Public availability

(1) In general

Subject to paragraphs (2) and (3), the Secretary shall make the information in such list publicly available.

(2) Trade secrets and confidential information

Nothing in this section alters or amends section 1905 of title 18 or section 552(b)(4) of title 5.

(3) Public health exception

The Secretary may choose not to make information collected under this section publicly available under paragraph (1) or section 356c(c) of this title if the Secretary determines that disclosure of such information would adversely affect the public health (such as by in-

creasing the possibility of hoarding or other disruption of the availability of drug products to patients).

(June 25, 1938, ch. 675, §506E, as added Pub. L. 112-144, title X, §1004, July 9, 2012, 126 Stat. 1104.)

§ 356f. Hospital repackaging of drugs in shortage

(a) Definitions

In this section:

(1) Drug

The term “drug” excludes any controlled substance (as such term is defined in section 802 of this title).

(2) Health system

The term “health system” means a collection of hospitals that are owned and operated by the same entity and that share access to databases with drug order information for their patients.

(3) Repackage

For the purposes of this section only, the term “repackage”, with respect to a drug, means to divide the volume of a drug into smaller amounts in order to—

(A) extend the supply of a drug in response to the placement of the drug on a drug shortage list under section 356e of this title; and

(B) facilitate access to the drug by hospitals within the same health system.

(b) Exclusion from registration

Notwithstanding any other provision of this chapter, a hospital shall not be considered an establishment for which registration is required under section 360 of this title solely because it repackages a drug and transfers it to another hospital within the same health system in accordance with the conditions in subsection (c)—

(1) during any period in which the drug is listed on the drug shortage list under section 356e of this title; or

(2) during the 60-day period following any period described in paragraph (1).

(c) Conditions

Subsection (b) shall only apply to a hospital, with respect to the repackaging of a drug for transfer to another hospital within the same health system, if the following conditions are met:

(1) Drug for intrasystem use only

In no case may a drug that has been repackaged in accordance with this section be sold or otherwise distributed by the health system or a hospital within the system to an entity or individual that is not a hospital within such health system.

(2) Compliance with State rules

Repackaging of a drug under this section shall be done in compliance with applicable State requirements of each State in which the drug is repackaged and received.

(d) Termination

This section shall not apply on or after the date on which the Secretary issues final guidance that clarifies the policy of the Food and

Drug Administration regarding hospital pharmacies repackaging and safely transferring repackaged drugs to other hospitals within the same health system during a drug shortage.

(June 25, 1938, ch. 675, §506F, as added Pub. L. 112-144, title X, §1007, July 9, 2012, 126 Stat. 1106.)

§ 357. Repealed. Pub. L. 105-115, title I, § 125(b)(1), Nov. 21, 1997, 111 Stat. 2325

Section, act June 25, 1938, ch. 675, §507, as added July 6, 1945, ch. 281, §3, 59 Stat. 463; amended Mar. 10, 1947, ch. 16, §3, 61 Stat. 12; July 13, 1949, ch. 305, §2, 63 Stat. 409; Aug. 5, 1953, ch. 334, §2, 67 Stat. 389; Pub. L. 87-781, title I, §§105(a), (b), (d)-(f), 106(a), (b), Oct. 10, 1962, 76 Stat. 785, 786, 787; Pub. L. 90-399, §105(b), July 13, 1968, 82 Stat. 352; Pub. L. 102-300, §6(b)(2), June 16, 1992, 106 Stat. 240; Pub. L. 103-80, §3(p), Aug. 13, 1993, 107 Stat. 777, related to certification of drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug.

§ 358. Authority to designate official names

(a) Necessity or desirability; use in official compendiums; infringement of trademarks

The Secretary may designate an official name for any drug or device if he determines that such action is necessary or desirable in the interest of usefulness and simplicity. Any official name designated under this section for any drug or device shall be the only official name of that drug or device used in any official compendium published after such name has been prescribed or for any other purpose of this chapter. In no event, however, shall the Secretary establish an official name so as to infringe a valid trademark.

(b) Review of names in official compendiums

Within a reasonable time after October 10, 1962, and at such other times as he may deem necessary, the Secretary shall cause a review to be made of the official names by which drugs are identified in the official United States Pharmacopoeia, the official Homoeopathic Pharmacopoeia of the United States, and the official National Formulary, and all supplements thereto, and at such times as he may deem necessary shall cause a review to be made of the official names by which devices are identified in any official compendium (and all supplements thereto) to determine whether revision of any of those names is necessary or desirable in the interest of usefulness and simplicity.

(c) Determinations of complexity, usefulness, multiplicity, or lack of name; designation by Secretary

Whenever he determines after any such review that (1) any such official name is unduly complex or is not useful for any other reason, (2) two or more official names have been applied to a single drug or device, or to two or more drugs which are identical in chemical structure and pharmacological action and which are substantially identical in strength, quality, and purity, or to two or more devices which are substantially equivalent in design and purpose or (3) no official name has been applied to a medically useful drug or device, he shall transmit in writing to the compiler of each official compendium in which that drug or drugs or device are identified and recognized his request for the recom-

mentation of a single official name for such drug or drugs or device which will have usefulness and simplicity. Whenever such a single official name has not been recommended within one hundred and eighty days after such request, or the Secretary determines that any name so recommended is not useful for any reason, he shall designate a single official name for such drug or drugs or device. Whenever he determines that the name so recommended is useful, he shall designate that name as the official name of such drug or drugs or device. Such designation shall be made as a regulation upon public notice and in accordance with the procedure set forth in section 553 of title 5.

(d) Revised official names; compilation, publication, and public distribution of listings

After each such review, and at such other times as the Secretary may determine to be necessary or desirable, the Secretary shall cause to be compiled, published, and publicly distributed a list which shall list all revised official names of drugs or devices designated under this section and shall contain such descriptive and explanatory matter as the Secretary may determine to be required for the effective use of those names.

(e) Request by compiler of official compendium for designation of name

Upon a request in writing by any compiler of an official compendium that the Secretary exercise the authority granted to him under subsection (a) of this section, he shall upon public notice and in accordance with the procedure set forth in section 553 of title 5 designate the official name of the drug or device for which the request is made.

(June 25, 1938, ch. 675, §508, as added Pub. L. 87-781, title I, §111(a), Oct. 10, 1962, 76 Stat. 789; amended Pub. L. 94-295, §5(b), May 28, 1976, 90 Stat. 581; Pub. L. 103-80, §3(q), Aug. 13, 1993, 107 Stat. 777.)

AMENDMENTS

1993—Subsecs. (c), (e). Pub. L. 103-80 substituted reference to section 553 of title 5 for “section 4 of the Administrative Procedure Act (5 U.S.C. 1003)”.

1976—Subsec. (a). Pub. L. 94-295 substituted “drug or device” for “drug” wherever appearing.

Subsec. (b). Pub. L. 94-295 substituted “National Formulary, and all supplements thereto, and at such times as he may deem necessary shall cause a review to be made of the official names by which devices are identified in any official compendium (and all supplements thereto)” for “National Formulary, and all supplements thereto.”

Subsec. (c)(2). Pub. L. 94-295 inserted “or device” after “single drug”, and “or to two or more devices which are substantially equivalent in design and purpose” after “purity.”

Subsec. (c)(3). Pub. L. 94-295 inserted “or device” after “useful drug” and after “drug or drugs” wherever appearing.

Subsec. (d). Pub. L. 94-295 inserted “or devices” after “drugs”.

Subsec. (e). Pub. L. 94-295 substituted “drug or device” for “drug”.

EFFECTIVE DATE

Pub. L. 87-781, title I, §111(b), Oct. 10, 1962, 76 Stat. 790, provided that: “This section [enacting this section] shall take effect on the date of its enactment [Oct. 10, 1962].”

§ 359. Nonapplicability of subchapter to cosmetics

This subchapter, as amended by the Drug Amendments of 1962, shall not apply to any cosmetic unless such cosmetic is also a drug or device or component thereof.

(June 25, 1938, ch. 675, §509, as added Pub. L. 87-781, title I, §113, Oct. 10, 1962, 76 Stat. 791.)

REFERENCES IN TEXT

This subchapter, as amended by the Drug Amendments of 1962, referred to in text, means the amendment of this subchapter by Pub. L. 87-781 which enacted sections 358 to 360 of this title, amended sections 351 to 353, 355, and 357 of this title, and enacted provisions set out as notes under sections 352, 355, 358, and 360 of this title.

The Drug Amendments of 1962, referred to in text, is Pub. L. 87-781, Oct. 10, 1962, 76 Stat. 780, as amended. For complete classification of this Act to the Code, see Short Title of 1962 Amendment note set out under section 301 of this title and Tables.

§ 360. Registration of producers of drugs or devices

(a) Definitions

As used in this section—

(1) the term “manufacture, preparation, propagation, compounding, or processing” shall include repackaging or otherwise changing the container, wrapper, or labeling of any drug package or device package in furtherance of the distribution of the drug or device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user; and

(2) the term “name” shall include in the case of a partnership the name of each partner and, in the case of a corporation, the name of each corporate officer and director, and the State of incorporation.

(b) Annual registration

(1) During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary the name of such person, places of business of such person, all such establishments, the unique facility identifier of each such establishment, and a point of contact e-mail address.

(2) During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a device or devices shall register with the Secretary his name, places of business, and all such establishments.

(3) The Secretary shall specify the unique facility identifier system that shall be used by registrants under paragraph (1). The requirement to include a unique facility identifier in a registration under paragraph (1) shall not apply until the date that the identifier system is specified by the Secretary under the preceding sentence.

(c) New producers

Every person upon first engaging in the manufacture, preparation, propagation, compounding,

or processing of a drug or drugs or a device or devices in any establishment which he owns or operates in any State shall immediately register with the Secretary—

(1) with respect to drugs, the information described under subsection (b)(1); and

(2) with respect to devices, the information described under subsection (b)(2).¹

(d) Additional establishments

Every person duly registered in accordance with the foregoing subsections of this section shall immediately register with the Secretary any additional establishment which he owns or operates in any State and in which he begins the manufacture, preparation, propagation, compounding, or processing of a drug or drugs or a device or devices.

(e) Registration number; uniform system for identification of devices intended for human use

The Secretary may assign a registration number to any person or any establishment registered in accordance with this section. The Secretary may also assign a listing number to each drug or class of drugs listed under subsection (j) of this section. Any number assigned pursuant to the preceding sentence shall be the same as that assigned pursuant to the National Drug Code. The Secretary may by regulation prescribe a uniform system for the identification of devices intended for human use and may require that persons who are required to list such devices pursuant to subsection (j) of this section shall list such devices in accordance with such system.

(f) Availability of registrations for inspection

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this section; except that any list submitted pursuant to paragraph (3) of subsection (j) of this section and the information accompanying any list or notice filed under paragraph (1) or (2) of that subsection shall be exempt from such inspection unless the Secretary finds that such an exemption would be inconsistent with protection of the public health.

(g) Exclusions from application of section

The foregoing subsections of this section shall not apply to—

(1) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail;

(2) practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, compound, or

process drugs or devices solely for use in the course of their professional practice;

(3) persons who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in research, teaching, or chemical analysis and not for sale;

(4) any distributor who acts as a wholesale distributor of devices, and who does not manufacture, repackage, process, or relabel a device; or

(5) such other classes of persons as the Secretary may by regulation exempt from the application of this section upon a finding that registration by such classes of persons in accordance with this section is not necessary for the protection of the public health.

In this subsection, the term “wholesale distributor” means any person (other than the manufacturer or the initial importer) who distributes a device from the original place of manufacture to the person who makes the final delivery or sale of the device to the ultimate consumer or user.

(h) Inspections

(1) In general

Every establishment that is required to be registered with the Secretary under this section shall be subject to inspection pursuant to section 374 of this title.

(2) Biennial inspections for devices

Every establishment described in paragraph (1), in any State, that is engaged in the manufacture, propagation, compounding, or processing of a device or devices classified in class II or III shall be so inspected by one or more officers or employees duly designated by the Secretary, or by persons accredited to conduct inspections under section 374(g) of this title, at least once in the 2-year period beginning with the date of registration of such establishment pursuant to this section and at least once in every successive 2-year period thereafter.

(3) Risk-based schedule for drugs

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect establishments described in paragraph (1) that are engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs (referred to in this subsection as “drug establishments”) in accordance with a risk-based schedule established by the Secretary.

(4) Risk factors

In establishing the risk-based schedule² under paragraph (3), the Secretary shall inspect establishments according to the known safety risks of such establishments, which shall be based on the following factors:

(A) The compliance history of the establishment.

(B) The record, history, and nature of recalls linked to the establishment.

(C) The inherent risk of the drug manufactured, prepared, propagated, compounded, or processed at the establishment.

¹ So in original.

² So in original. Probably should be “schedule”.

(D) The inspection frequency and history of the establishment, including whether the establishment has been inspected pursuant to section 374 of this title within the last 4 years.

(E) Whether the establishment has been inspected by a foreign government or an agency of a foreign government recognized under section 384e of this title.

(F) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

(5) Effect of status

In determining the risk associated with an establishment for purposes of establishing a risk-based schedule under paragraph (3), the Secretary shall not consider whether the drugs manufactured, prepared, propagated, compounded, or processed by such establishment are drugs described in section 353(b) of this title.

(6) Annual report on inspections of establishments

Beginning in 2014, not later than February 1 of each year, the Secretary shall make available on the Internet Web site of the Food and Drug Administration a report regarding—

(A)(i) the number of domestic and foreign establishments registered pursuant to this section in the previous fiscal year; and

(ii) the number of such domestic establishments and the number of such foreign establishments that the Secretary inspected in the previous fiscal year;

(B) with respect to establishments that manufacture, prepare, propagate, compound, or process an active ingredient of a drug, a finished drug product, or an excipient of a drug, the number of each such type of establishment; and

(C) the percentage of the budget of the Food and Drug Administration used to fund the inspections described under subparagraph (A).

(i) Registration of foreign establishments

(1) Every person who owns or operates any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary—

(A) upon first engaging in any such activity, immediately submit a registration to the Secretary that includes—

(i) with respect to drugs, the name and place of business of such person, all such establishments, the unique facility identifier of each such establishment, a point of contact e-mail address, the name of the United States agent of each such establishment, the name of each importer of such drug in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug to the United States for purposes of importation; and

(ii) with respect to devices, the name and place of business of the establishment, the

name of the United States agent for the establishment, the name of each importer of such device in the United States that is known to the establishment, and the name of each person who imports or offers for import such device to the United States for purposes of importation; and

(B) each establishment subject to the requirements of subparagraph (A) shall thereafter register with the Secretary during the period beginning on October 1 and ending on December 31 of each year.

(2) The establishment shall also provide the information required by subsection (j) of this section.

(3) The Secretary is authorized to enter into cooperative arrangements with officials of foreign countries to ensure that adequate and effective means are available for purposes of determining, from time to time, whether drugs or devices manufactured, prepared, propagated, compounded, or processed by an establishment described in paragraph (1), if imported or offered for import into the United States, shall be refused admission on any of the grounds set forth in section 381(a) of this title.

(4) The Secretary shall specify the unique facility identifier system that shall be used by registrants under paragraph (1) with respect to drugs. The requirement to include a unique facility identifier in a registration under paragraph (1) with respect to drugs shall not apply until the date that the identifier system is specified by the Secretary under the preceding sentence.

(j) Filing of lists of drugs and devices manufactured, prepared, propagated and compounded by registrants; statements; accompanying disclosures

(1) Every person who registers with the Secretary under subsection (b), (c), (d), or (i) of this section shall, at the time of registration under any such subsection, file with the Secretary a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name (as defined in section 352(e) of this title) and by any proprietary name) which are being manufactured, prepared, propagated, compounded, or processed by him for commercial distribution and which he has not included in any list of drugs or devices filed by him with the Secretary under this paragraph or paragraph (2) before such time of registration. Such list shall be prepared in such form and manner as the Secretary may prescribe and shall be accompanied by—

(A) in the case of a drug contained in the applicable list and subject to section 355 or 360b of this title, or a device intended for human use contained in the applicable list with respect to which a performance standard has been established under section 360d of this title or which is subject to section 360e of this title, a reference to the authority for the marketing of such drug or device and a copy of all labeling for such drug or device;

(B) in the case of any other drug or device contained in an applicable list—

(i) which drug is subject to section 353(b)(1) of this title, or which device is a restricted device, a copy of all labeling for such drug or device, a representative sampling of advertisements for such drug or device, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or

(ii) which drug is not subject to section 353(b)(1) of this title or which device is not a restricted device, the label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device;

(C) in the case of any drug contained in an applicable list which is described in subparagraph (B), a quantitative listing of its active ingredient or ingredients, except that with respect to a particular drug product the Secretary may require the submission of a quantitative listing of all ingredients if he finds that such submission is necessary to carry out the purposes of this chapter;

(D) if the registrant filing a list has determined that a particular drug product or device contained in such list is not subject to section 355 or 360b of this title, or the particular device contained in such list is not subject to a performance standard established under section 360d of this title or to section 360e of this title or is not a restricted device a brief statement of the basis upon which the registrant made such determination if the Secretary requests such a statement with respect to that particular drug product or device; and

(E) in the case of a drug contained in the applicable list, the name and place of business of each manufacturer of an excipient of the listed drug with which the person listing the drug conducts business, including all establishments used in the production of such excipient, the unique facility identifier of each such establishment, and a point of contact e-mail address for each such excipient manufacturer.

(2) Each person who registers with the Secretary under this section shall report to the Secretary, with regard to drugs once during the month of June of each year and once during the month of December of each year, and with regard to devices once each year during the period beginning on October 1 and ending on December 31, the following information:

(A) A list of each drug or device introduced by the registrant for commercial distribution which has not been included in any list previously filed by him with the Secretary under this subparagraph or paragraph (1) of this subsection. A list under this subparagraph shall list a drug or device by its established name (as defined in section 352(e) of this title), and by any proprietary name it may have and shall be accompanied by the other information required by paragraph (1).

(B) If since the date the registrant last made a report under this paragraph (or if he has not made a report under this paragraph, since February 1, 1973) he has discontinued the manufacture, preparation, propagation, compounding, or processing for commercial distribution of a drug or device included in a list filed by

him under subparagraph (A) or paragraph (1); notice of such discontinuance, the date of such discontinuance, and the identity (by established name (as defined in section 352(e) of this title) and by any proprietary name) of such drug or device.

(C) If since the date the registrant reported pursuant to subparagraph (B) a notice of discontinuance he has resumed the manufacture, preparation, propagation, compounding, or processing for commercial distribution of the drug or device with respect to which such notice of discontinuance was reported; notice of such resumption, the date of such resumption, the identity of such drug or device (each by established name (as defined in section 352(e) of this title) and by any proprietary name), and the other information required by paragraph (1), unless the registrant has previously reported such resumption to the Secretary pursuant to this subparagraph.

(D) Any material change in any information previously submitted pursuant to this paragraph or paragraph (1).

(3) The Secretary may also require each registrant under this section to submit a list of each drug product which (A) the registrant is manufacturing, preparing, propagating, compounding, or processing for commercial distribution, and (B) contains a particular ingredient. The Secretary may not require the submission of such a list unless he has made a finding that the submission of such a list is necessary to carry out the purposes of this chapter.

(4) The Secretary shall require persons subject to this subsection to use, for purposes of this subsection, the unique facility identifier systems specified under subsections (b)(3) and (i)(4) with respect to drugs. Such requirement shall not apply until the date that the identifier system under subsection (b)(3) or (i)(4), as applicable, is specified by the Secretary.

(k) Report preceding introduction of devices into interstate commerce

Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least ninety days before making such introduction or delivery, report to the Secretary or person who is accredited under section 360m(a) of this title (in such form and manner as the Secretary shall by regulation prescribe)—

(1) the class in which the device is classified under section 360c of this title or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified, and

(2) action taken by such person to comply with requirements under section 360d or 360e of this title which are applicable to the device.

A notification submitted under this subsection that contains clinical trial data for an applicable device clinical trial (as defined in section 282(j)(1) of title 42) shall be accompanied by the certification required under section 282(j)(5)(B)

of such title. Such certification shall not be considered an element of such notification.

(l) Exemption from reporting requirements

A report under subsection (k) of this section is not required for a device intended for human use that is exempted from the requirements of this subsection under subsection (m) of this section or is within a type that has been classified into class I under section 360c of this title. The exception established in the preceding sentence does not apply to any class I device that is intended for a use which is of substantial importance in preventing impairment of human health, or to any class I device that presents a potential unreasonable risk of illness or injury.

(m) List of exempt class II devices; determination by Secretary; publication in Federal Register

(1) Not later than 60 days after November 21, 1997, the Secretary shall publish in the Federal Register a list of each type of class II device that does not require a report under subsection (k) of this section to provide reasonable assurance of safety and effectiveness. Each type of class II device identified by the Secretary as not requiring the report shall be exempt from the requirement to provide a report under subsection (k) of this section as of the date of the publication of the list in the Federal Register. The Secretary shall publish such list on the Internet site of the Food and Drug Administration. The list so published shall be updated not later than 30 days after each revision of the list by the Secretary.

(2) Beginning on the date that is 1 day after the date of the publication of a list under this subsection, the Secretary may exempt a class II device from the requirement to submit a report under subsection (k) of this section, upon the Secretary's own initiative or a petition of an interested person, if the Secretary determines that such report is not necessary to assure the safety and effectiveness of the device. The Secretary shall publish in the Federal Register notice of the intent of the Secretary to exempt the device, or of the petition, and provide a 30-day period for public comment. Within 120 days after the issuance of the notice in the Federal Register, the Secretary shall publish an order in the Federal Register that sets forth the final determination of the Secretary regarding the exemption of the device that was the subject of the notice. If the Secretary fails to respond to a petition within 180 days of receiving it, the petition shall be deemed to be granted.

(n) Review of report; time for determination by Secretary

(1) The Secretary shall review the report required in subsection (k) of this section and make a determination under section 360c(f)(1) of this title not later than 90 days after receiving the report.

(2)(A) Not later than 18 months after July 9, 2012, the Secretary shall submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report regarding when a premarket notification under subsection (k) should be submitted for a

modification or change to a legally marketed device. The report shall include the Secretary's interpretation of the following terms: "could significantly affect the safety or effectiveness of the device", "a significant change or modification in design, material, chemical composition, energy source, or manufacturing process", and "major change or modification in the intended use of the device". The report also shall discuss possible processes for industry to use to determine whether a new submission under subsection (k) is required and shall analyze how to leverage existing quality system requirements to reduce premarket burden, facilitate continual device improvement, and provide reasonable assurance of safety and effectiveness of modified devices. In developing such report, the Secretary shall consider the input of interested stakeholders.

(B) The Secretary shall withdraw the Food and Drug Administration draft guidance entitled "Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device", dated July 27, 2011, and shall not use this draft guidance as part of, or for the basis of, any premarket review or any compliance or enforcement decisions or actions. The Secretary shall not issue—

(i) any draft guidance or proposed regulation that addresses when to submit a premarket notification submission for changes and modifications made to a manufacturer's previously cleared device before the receipt by the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate of the report required in subparagraph (A); and

(ii) any final guidance or regulation on that topic for one year after date of receipt of such report by the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate.

(C) The Food and Drug Administration guidance entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device", dated January 10, 1997, shall be in effect until the subsequent issuance of guidance or promulgation, if appropriate, of a regulation described in subparagraph (B), and the Secretary shall interpret such guidance in a manner that is consistent with the manner in which the Secretary has interpreted such guidance since 1997.

(o) Reprocessed single-use devices

(1) With respect to reprocessed single-use devices for which reports are required under subsection (k) of this section:

(A) The Secretary shall identify such devices or types of devices for which reports under such subsection must, in order to ensure that the device is substantially equivalent to a predicate device, include validation data, the types of which shall be specified by the Secretary, regarding cleaning and sterilization, and functional performance demonstrating that the single-use device will remain substantially equivalent to its predicate device after the maximum number of times the device is

reprocessed as intended by the person submitting the premarket notification. Within six months after October 26, 2002, the Secretary shall publish in the Federal Register a list of the types so identified, and shall revise the list as appropriate. Reports under subsection (k) of this section for devices or types of devices within a type included on the list are, upon publication of the list, required to include such validation data.

(B) In the case of each report under subsection (k) of this section that was submitted to the Secretary before the publication of the initial list under subparagraph (A), or any revision thereof, and was for a device or type of device included on such list, the person who submitted the report under subsection (k) of this section shall submit validation data as described in subparagraph (A) to the Secretary not later than nine months after the publication of the list. During such nine-month period, the Secretary may not take any action under this chapter against such device solely on the basis that the validation data for the device have not been submitted to the Secretary. After the submission of the validation data to the Secretary, the Secretary may not determine that the device is misbranded under section 352(o) of this title or adulterated under section 351(f)(1)(B) of this title, or take action against the device under section 331(p) of this title for failure to provide any information required by subsection (k) of this section until (i) the review is terminated by withdrawal of the submission of the report under subsection (k) of this section; (ii) the Secretary finds the data to be acceptable and issues a letter; or (iii) the Secretary determines that the device is not substantially equivalent to a predicate device. Upon a determination that a device is not substantially equivalent to a predicate device, or if such submission is withdrawn, the device can no longer be legally marketed.

(C) In the case of a report under subsection (k) of this section for a device identified under subparagraph (A) that is of a type for which the Secretary has not previously received a report under such subsection, the Secretary may, in advance of revising the list under subparagraph (A) to include such type, require that the report include the validation data specified in subparagraph (A).

(D) Section 352(o) of this title applies with respect to the failure of a report under subsection (k) of this section to include validation data required under subparagraph (A).

(2) With respect to critical or semi-critical reprocessed single-use devices that, under subsection (l) or (m) of this section, are exempt from the requirement of submitting reports under subsection (k) of this section:

(A) The Secretary shall identify such devices or types of devices for which such exemptions should be terminated in order to provide a reasonable assurance of the safety and effectiveness of the devices. The Secretary shall publish in the Federal Register a list of the devices or types of devices so identified, and shall revise the list as appropriate. The exemption for each device or type included on the list is terminated upon the publication of

the list. For each report under subsection (k) of this section submitted pursuant to this subparagraph the Secretary shall require the validation data described in paragraph (1)(A).

(B) For each device or type of device included on the list under subparagraph (A), a report under subsection (k) of this section shall be submitted to the Secretary not later than 15 months after the publication of the initial list, or a revision of the list, whichever terminates the exemption for the device. During such 15-month period, the Secretary may not take any action under this chapter against such device solely on the basis that such report has not been submitted to the Secretary. After the submission of the report to the Secretary the Secretary may not determine that the device is misbranded under section 352(o) of this title or adulterated under section 351(f)(1)(B) of this title, or take action against the device under section 331(p) of this title for failure to provide any information required by subsection (k) of this section until (i) the review is terminated by withdrawal of the submission; (ii) the Secretary determines by order that the device is substantially equivalent to a predicate device; or (iii) the Secretary determines by order that the device is not substantially equivalent to a predicate device. Upon a determination that a device is not substantially equivalent to a predicate device, the device can no longer be legally marketed.

(C) In the case of semi-critical devices, the initial list under subparagraph (A) shall be published not later than 18 months after the effective date of this subsection. In the case of critical devices, the initial list under such subparagraph shall be published not later than six months after such effective date.

(D) Section 352(o) of this title applies with respect to the failure to submit a report under subsection (k) of this section that is required pursuant to subparagraph (A), including a failure of the report to include validation data required in such subparagraph.

(E) The termination under subparagraph (A) of an exemption under subsection (l) or (m) of this section for a critical or semi-critical reprocessed single-use device does not terminate the exemption under subsection (l) or (m) of this section for the original device.

(p) Electronic registration and listing

(1) In general

Registrations and listings under this section (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver.

(2) Electronic database

Not later than 2 years after the Secretary specifies a unique facility identifier system under subsections (b) and (i), the Secretary shall maintain an electronic database, which shall not be subject to inspection under subsection (f), populated with the information submitted as described under paragraph (1) that—

(A) enables personnel of the Food and Drug Administration to search the database by any field of information submitted in a registration described under paragraph (1), or combination of such fields; and

(B) uses the unique facility identifier system to link with other relevant databases within the Food and Drug Administration, including the database for submission of information under section 381(r) of this title.

(3) Risk-based information and coordination

The Secretary shall ensure the accuracy and coordination of relevant Food and Drug Administration databases in order to identify and inform risk-based inspections under subsection (h).

(June 25, 1938, ch. 675, §510, as added Pub. L. 87-781, title III, §302, Oct. 10, 1962, 76 Stat. 794; amended Pub. L. 89-74, §4, July 15, 1965, 79 Stat. 231; Pub. L. 91-513, title II, §701(e), Oct. 27, 1970, 84 Stat. 1282; Pub. L. 92-387, §§3, 4(a)-(c), Aug. 16, 1972, 86 Stat. 560-562; Pub. L. 94-295, §4(a), May 28, 1976, 90 Stat. 579; Pub. L. 105-115, title I, §125(a)(2)(C), title II, §§206(a), 209(a), 213(b), title IV, §417, Nov. 21, 1997, 111 Stat. 2325, 2338, 2341, 2347, 2379; Pub. L. 107-188, title III, §321(a), June 12, 2002, 116 Stat. 675; Pub. L. 107-250, title II, §§201(e), 207, 211, title III, §302(b), Oct. 26, 2002, 116 Stat. 1609, 1613, 1614, 1616; Pub. L. 108-214, §2(c)(2), Apr. 1, 2004, 118 Stat. 576; Pub. L. 110-85, title II, §§222-224, title VIII, §801(b)(3)(C), Sept. 27, 2007, 121 Stat. 853, 921; Pub. L. 112-144, title VI, §604, title VII, §§701, 702(b)-705, July 9, 2012, 126 Stat. 1052, 1064-1066.)

REFERENCES IN TEXT

The effective date of this subsection, referred to in subsec. (o)(2)(C), probably means the date of the enactment of Pub. L. 107-250, which enacted subsec. (o) of this section and was approved Oct. 26, 2002.

AMENDMENTS

2012—Subsec. (b)(1). Pub. L. 112-144, §701(1)(A), which directed amendment of par. (1) by “striking ‘On or before’ and all that follows through the period at the end and inserting the following: ‘During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary the name of such person, places of business of such person, all such establishments, the unique facility identifier of each such establishment, and a point of contact e-mail address; and’”, was executed as if an end quotation mark for the inserted material followed “address.”, to reflect the probable intent of Congress. Prior to amendment, stricken text read as follows: “On or before December 31 of each year every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register with the Secretary his name, places of business, and all such establishments.”

Subsec. (b)(3). Pub. L. 112-144, §701(1)(B), added par. (3).

Subsec. (c). Pub. L. 112-144, §701(2), substituted “with the Secretary—” and pars. (1) and (2) for “with the Secretary his name, place of business, and such establishment”.

Subsec. (h). Pub. L. 112-144, §705, amended subsec. (h) generally. Prior to amendment, text read as follows: “Every establishment in any State registered with the Secretary pursuant to this section shall be subject to

inspection pursuant to section 374 of this title and every such establishment engaged in the manufacture, propagation, compounding, or processing of a drug or drugs or of a device or devices classified in class II or III shall be so inspected by one or more officers or employees duly designated by the Secretary, or by persons accredited to conduct inspections under section 374(g) of this title, at least once in the two-year period beginning with the date of registration of such establishment pursuant to this section and at least once in every successive two-year period thereafter.”

Subsec. (i)(1). Pub. L. 112-144, §702(b)(1)(A), amended introductory provisions generally. Prior to amendment, text read as follows: “Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary—”.

Subsec. (i)(1)(A). Pub. L. 112-144, §702(b)(1)(B), amended subpar. (A) generally. Prior to amendment, subpar. (A) read as follows: “upon first engaging in any such activity, immediately register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation; and”.

Subsec. (i)(1)(B). Pub. L. 112-144, §702(b)(1)(C), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: “each establishment subject to the requirements of subparagraph (A) shall thereafter—

“(i) with respect to drugs, register with the Secretary on or before December 31 of each year; and

“(ii) with respect to devices, register with the Secretary during the period beginning on October 1 and ending on December 31 of each year.”

Subsec. (i)(4). Pub. L. 112-144, §702(b)(2), added par. (4).

Subsec. (j)(1)(E). Pub. L. 112-144, §703(1), added subpar. (E).

Subsec. (j)(4). Pub. L. 112-144, §703(2), added par. (4).

Subsec. (n). Pub. L. 112-144, §604, designated existing provisions as par. (1) and added par. (2).

Subsec. (p). Pub. L. 112-144, §704, inserted subsec. heading, designated existing provisions as par. (1) and inserted par. heading, and added pars. (2) and (3).

2007—Subsec. (b). Pub. L. 110-85, §222(a), designated existing provisions as par. (1), struck out “or a device or devices” after “drug or drugs”, and added par. (2).

Subsec. (i)(1). Pub. L. 110-85, §222(b), inserted text of par. (1) and struck out former text of par. (1) which related to registration requirement for foreign establishments engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device to be imported or offered for import into the United States.

Subsec. (j)(2). Pub. L. 110-85, §223, in introductory provisions, substituted “Each person who registers with the Secretary under this section shall report to the Secretary, with regard to drugs once during the month of June of each year and once during the month of December of each year, and with regard to devices once each year during the period beginning on October 1 and ending on December 31, the following information:” for “Each person who registers with the Secretary under this section shall report to the Secretary once during the month of June of each year and once during the month of December of each year the following information:”.

Subsec. (k). Pub. L. 110-85, §801(b)(3)(C), inserted concluding provisions.

Subsec. (p). Pub. L. 110-85, §224, amended subsec. (p) generally. Prior to amendment, subsec. (p) read as follows: “Registrations under subsections (b), (c), (d), and (i) of this section (including the submission of updated information) shall be submitted to the Secretary by electronic means, upon a finding by the Secretary that

the electronic receipt of such registrations is feasible, unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver."

2004—Subsec. (o)(1)(B), (2)(B). Pub. L. 108-214, §2(c)(2)(A), (B)(i), substituted "or adulterated" for "adulterated".

Subsec. (o)(2)(E). Pub. L. 108-214, §2(c)(2)(B)(ii), substituted "semi-critical" for "semicritical".

2002—Subsec. (h). Pub. L. 107-250, §201(e), inserted "or by persons accredited to conduct inspections under section 374(g) of this title," after "duly designated by the Secretary".

Subsec. (i)(1). Pub. L. 107-188, §321(a)(1), substituted "On or before December 31 of each year, any establishment" for "Any establishment" and "shall, through electronic means in accordance with the criteria of the Secretary, register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation" for "shall register with the Secretary the name and place of business of the establishment and the name of the United States agent for the establishment".

Subsec. (j)(1). Pub. L. 107-188, §321(a)(2), substituted "subsection (b), (c), (d), or (i)" for "subsection (b), (c), or (d)" in first sentence.

Subsec. (m)(1). Pub. L. 107-250, §211, inserted at end "The Secretary shall publish such list on the Internet site of the Food and Drug Administration. The list so published shall be updated not later than 30 days after each revision of the list by the Secretary."

Subsec. (o). Pub. L. 107-250, §302(b), added subsec. (o).

Subsec. (p). Pub. L. 107-250, §207, added subsec. (p).

1997—Subsec. (g). Pub. L. 105-115, §213(b)(3), inserted at end "In this subsection, the term 'wholesale distributor' means any person (other than the manufacturer or the initial importer) who distributes a device from the original place of manufacture to the person who makes the final delivery or sale of the device to the ultimate consumer or user."

Subsec. (g)(4), (5). Pub. L. 105-115, §213(b)(1), (2), added par. (4) and redesignated former par. (4) as (5).

Subsec. (i). Pub. L. 105-115, §417, amended subsec. (i) generally. Prior to amendment, subsec. (i) read as follows: "Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs, or a device or devices, shall be permitted to register under this section pursuant to regulations promulgated by the Secretary. Such regulations shall require such establishment to provide the information required by subsection (j) of this section and shall require such establishment to provide the information required by subsection (j) of this section in the case of a device or devices and shall include provisions for registration of any such establishment upon condition that adequate and effective means are available, by arrangement with the government of such foreign country or otherwise, to enable the Secretary to determine from time to time whether drugs or devices manufactured, prepared, propagated, compounded, or processed in such establishment, if imported or offered for import into the United States, shall be refused admission on any of the grounds set forth in section 381(a) of this title."

Subsec. (j)(1)(A), (D). Pub. L. 105-115, §125(a)(2)(C), struck out "356, 357," before "or 360b of this title".

Subsec. (k). Pub. L. 105-115, §206(a)(1), inserted "or person who is accredited under section 360m(a) of this title" after "report to the Secretary".

Subsecs. (l), (m). Pub. L. 105-115, §206(a)(2), added subsecs. (l) and (m).

Subsec. (n). Pub. L. 105-115, §209(a), added subsec. (n). 1976—Subsec. (a)(1). Pub. L. 94-295, §4(a)(2), substituted "drug package or device package" for "drug package", "distribution of the drug or device" for "dis-

tribution of the drug", and "ultimate consumer or user" for "ultimate consumer".

Subsecs. (b) to (d). Pub. L. 94-295, §4(a)(3), inserted "or a device or devices" after "drug or drugs".

Subsec. (e). Pub. L. 94-295, §4(a)(4), authorized the Secretary to prescribe by regulation a uniform system for the identification of devices intended for human use and authorized him, in addition, to require that persons who are required to list devices pursuant to subsec. (j) also list such devices in accordance with the system.

Subsec. (g)(1) to (3). Pub. L. 94-295, §4(a)(5), substituted "drugs or devices" for "drugs".

Subsec. (h). Pub. L. 94-295, §4(a)(6), inserted reference to establishments engaged in the manufacture, propagation, compounding, or processing of a drug or drugs or of a device or devices classified in class II or III.

Subsec. (i). Pub. L. 94-295, §4(a)(7), inserted reference to devices and inserted requirement that regulations require establishments to provide the information required by subsection (j) of this section in the case of a device or devices.

Subsec. (j)(1). Pub. L. 94-295, §4(a)(8)(A), in introductory provisions substituted "a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name" for "a list of all drugs (by established name" and "drugs or devices filed" for "drugs filed".

Subsec. (j)(1)(A). Pub. L. 94-295, §4(a)(8)(B), substituted "the applicable list" for "such list", inserted "or a device intended for human use contained in the applicable list with respect to which a performance standard has been established under section 360d of this title or which is subject to section 360e of this title," after "360b of this title," and substituted "such drug or device" for "such drug" wherever appearing.

Subsec. (j)(1)(B). Pub. L. 94-295, §4(a)(8)(C), in introductory provisions substituted "drug or device contained in an applicable list" for "drug contained in such list".

Subsec. (j)(1)(B)(i). Pub. L. 94-295, §4(a)(8)(D), substituted "which drug is subject to section 353(b)(1) of this title, or which device is a restricted device, a copy of all labeling for such drug or device, a representative sampling of advertisements for such drug or device, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or" for "which is subject to section 353(b)(1) of this title, a copy of all labeling for such drug, a representative sampling of advertisements for such drug, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product, or".

Subsec. (j)(1)(B)(ii). Pub. L. 94-295, §4(a)(8)(E), substituted "which drug is not subject to section 353(b)(1) of this title or which device is not a restricted device, the label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device" for "which is not subject to section 353(b)(1) of this title, the label and package insert for such drug and a representative sampling of any other labeling for such drug".

Subsec. (j)(1)(C). Pub. L. 94-295, §4(a)(8)(F), substituted "an applicable list" for "such list".

Subsec. (j)(1)(D). Pub. L. 94-295, §4(a)(8)(G), substituted "a list" for "the list", inserted "or the particular device contained in such list is not subject to a performance standard established under section 360d of this title or to section 360e of this title or is not a restricted device" after "or 360b of this title," and substituted "particular drug product or device" for "particular drug product" wherever appearing.

Subsec. (j)(2). Pub. L. 94-295, §4(a)(8)(H), substituted "drug or device" for "drug" in subpars. (A), (B), and (C), and substituted "(each by established name" for "(by established name" in subpar. (C).

Subsec. (k). Pub. L. 94-295, §4(a)(9), added subsec. (k). 1972—Subsec. (e). Pub. L. 92-387, §4(a), inserted provision that the Secretary may assign a listing number to each drug or class of drugs listed under subsec. (j).

Subsec. (f). Pub. L. 92-387, §4(b), inserted exception that the list submitted under subsec. (j)(3) and information submitted under subsec. (j)(1), (2) shall be exempt from inspection unless the Secretary determines otherwise.

Subsec. (i). Pub. L. 92-387, §4(c), inserted provision that the regulations shall require such establishment to provide the information required by subsec. (j).

Subsec. (j). Pub. L. 92-387, §3, added subsec. (j).

1970—Subsec. (a). Pub. L. 91-513 struck out provisions defining the wholesaling, jobbing, or distributing of depressant or stimulant drugs.

Subsec. (b). Pub. L. 91-513 struck out provisions covering establishments engaged in the wholesaling, jobbing, or distributing of depressant or stimulant drugs and the inclusion of the fact of such activity in the annual registration.

Subsec. (c). Pub. L. 91-513 struck out provisions covering new registrations of persons first engaging in the wholesaling, jobbing, or distributing of depressant or stimulant drugs and the inclusion of the fact of such activity in the registration.

Subsec. (d). Pub. L. 91-513 struck out number designation “(1)” preceding first sentence, struck out portion of such redesignated provisions covering the wholesaling, jobbing, or distributing of depressant or stimulant drugs, and struck out par. (2) covering the filing of supplemental registration whenever a person not previously engaged or involved with depressant or stimulant drugs goes into the manufacturing, preparation, or processing thereof.

1965—Pub. L. 89-74, §4(e), included certain wholesalers in section catchline.

Subsec. (a)(2), (3). Pub. L. 89-74, §4(a), added par. (2) and redesignated former par. (2) as (3).

Subsecs. (b), (c). Pub. L. 89-74, §4(b), (c), inserted “or in the wholesaling, jobbing, or distributing of any depressant or stimulant drug” after “drug or drugs” and inserted requirement that establishment indicate activity in depressant or stimulant drugs at time of registration.

Subsec. (d). Pub. L. 89-74 §4(d), designated existing provisions as par. (1), inserted “or the wholesaling, jobbing, or distributing of any depressant or stimulant drug” and the requirement that the additional establishment indicate activity in depressant or stimulant drugs at time of registration, and added par. (2).

EFFECTIVE DATE OF 2002 AMENDMENT

Amendment by Pub. L. 107-188 effective upon the expiration of the 180-day period beginning June 12, 2002, see section 321(c) of Pub. L. 107-188, set out as a note under section 331 of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 206(a), 209(a), 213(b), and 417 of Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1972 AMENDMENT

Pub. L. 92-387, §5, Aug. 16, 1972, 86 Stat. 562, provided that: “The amendments made by this Act [amending this section and sections 331 and 335 of this title and enacting provisions set out below] shall take effect on the first day of the sixth month beginning after the date of enactment of this Act [Aug. 16, 1972].”

EFFECTIVE DATE OF 1970 AMENDMENT

Amendment by Pub. L. 91-513 effective on first day of seventh calendar month that begins after Oct. 26, 1970, see section 704 of Pub. L. 91-513, set out as an Effective Date note under section 801 of this title.

EFFECTIVE DATE OF 1965 AMENDMENT

Amendment by Pub. L. 89-74 effective Feb. 1, 1966, subject to registration with Secretary of names, places of business, establishments, and other prescribed information prior to Feb. 1, 1966, see section 11 of Pub. L. 89-74, set out as a note under section 321 of this title.

SAVINGS PROVISION

Amendment by Pub. L. 91-513 not to affect or abate any prosecutions for any violation of law or any civil seizures or forfeitures and injunctive proceedings commenced prior to the effective date of such amendment, and all administrative proceedings pending before the Bureau of Narcotics and Dangerous Drugs [now the Drug Enforcement Administration] on Oct. 27, 1970, to be continued and brought to final determination in accord with laws and regulations in effect prior to Oct. 27, 1970, see section 702 of Pub. L. 91-513, set out as a note under section 321 of this title.

CONGRESSIONAL DECLARATION OF NEED FOR REGISTRATION AND INSPECTION OF DRUG ESTABLISHMENTS

Pub. L. 87-781, title III, §301, Oct. 10, 1962, 76 Stat. 793, provided that: “The Congress hereby finds and declares that in order to make regulation of interstate commerce in drugs effective, it is necessary to provide for registration and inspection of all establishments in which drugs are manufactured, prepared, propagated, compounded, or processed; that the products of all such establishments are likely to enter the channels of interstate commerce and directly affect such commerce; and that the regulation of interstate commerce in drugs without provision for registration and inspection of establishments that may be engaged only in intrastate commerce in such drugs would discriminate against and depress interstate commerce in such drugs, and adversely burden, obstruct, and affect such interstate commerce.”

DECLARATION OF POLICY OF DRUG LISTING ACT OF 1972

Pub. L. 92-387, §2, Aug. 16, 1972, 86 Stat. 559, provided that: “The Federal Government which is responsible for regulating drugs has no ready means of determining what drugs are actually being manufactured or packed by establishments registered under the Federal Food, Drug, and Cosmetic Act [this chapter] except by periodic inspection of such registered establishments. Knowledge of which particular drugs are being manufactured or packed by each registered establishment would substantially assist in the enforcement of Federal laws requiring that such drugs be pure, safe, effective, and properly labeled. Information on the discontinuance of a particular drug could serve to alleviate the burden of reviewing and implementing enforcement actions against drugs which, although commercially discontinued, remain active for regulatory purposes. Information on the type and number of different drugs being manufactured or packed by drug establishments could permit more effective and timely regulation by the agencies of the Federal Government responsible for regulating drugs, including identification of which drugs in interstate commerce are subject to section 505 or 507 [section 355 or 357 of this title], or to other provisions of the Federal Food, Drug, and Cosmetic Act.”

REGISTRATION OF CERTAIN PERSONS OWNING OR OPERATING DRUG ESTABLISHMENTS PRIOR TO OCT. 10, 1962

Pub. L. 87-781, title III, §303, Oct. 10, 1962, 76 Stat. 795, provided that any person who, on the day immediately preceding Oct. 10, 1962, owned or operated an establishment which manufactured or processed drugs, registered before the first day of the seventh month following October, 1962, would be deemed to be registered in accordance with subsec. (b) of this section for the calendar year 1962 and if registered within this period and effected in 1963, be deemed in compliance for that calendar year.

§360a. Clinical trial guidance for antibiotic drugs

(a) In general

Not later than 1 year after September 27, 2007, the Secretary shall issue guidance for the con-

duct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat acute bacterial sinusitis, acute bacterial otitis media, and acute bacterial exacerbation of chronic bronchitis. Such guidance shall indicate the appropriate models and valid surrogate markers.

(b) Review

Not later than 5 years after September 27, 2007, the Secretary shall review and update the guidance described under subsection (a) to reflect developments in scientific and medical information and technology.

(June 25, 1938, ch. 675, §511, as added Pub. L. 110-85, title IX, §911, Sept. 27, 2007, 121 Stat. 951.)

PRIOR PROVISIONS

A prior section 360a, act June 25, 1938, ch. 675, §511, as added July 15, 1965, Pub. L. 89-74, §3(b), 79 Stat. 227; amended Oct. 24, 1968, Pub. L. 90-639, §2(a), 82 Stat. 1361, regulated the manufacture, compounding, and processing of depressant and stimulant drugs and their sale, delivery, disposal, possession, and recordkeeping activities connected therewith, prior to repeal by Pub. L. 91-513, title II, §§701(a), 704, Oct. 27, 1970, 84 Stat. 1281, 1284, effective on the first day of the seventh calendar month that began after Oct. 26, 1970.

§ 360a-1. Clinical trials

(a) Review and revision of guidance documents

(1) In general

The Secretary of Health and Human Services (referred to in this section as the “Secretary”) shall review and, as appropriate, revise not fewer than 3 guidance documents per year, which shall include—

(A) reviewing the guidance documents of the Food and Drug Administration for the conduct of clinical trials with respect to antibacterial and antifungal drugs; and

(B) as appropriate, revising such guidance documents to reflect developments in scientific and medical information and technology and to ensure clarity regarding the procedures and requirements for approval of antibacterial and antifungal drugs under chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.).

(2) Issues for review

At a minimum, the review under paragraph (1) shall address the appropriate animal models of infection, in vitro techniques, valid microbiological surrogate markers, the use of noninferiority versus superiority trials, trial enrollment, data requirements, and appropriate delta values for noninferiority trials.

(3) Rule of construction

Except to the extent to which the Secretary makes revisions under paragraph (1)(B), nothing in this section shall be construed to repeal or otherwise effect the guidance documents of the Food and Drug Administration.

(b) Recommendations for investigations

(1) Request

The sponsor of a drug intended to be designated as a qualified infectious disease product may request that the Secretary provide written recommendations for nonclinical and clinical investigations which the Secretary be-

lieves may be necessary to be conducted with the drug before such drug may be approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) for use in treating, detecting, preventing, or identifying a qualifying pathogen, as defined in section 505E of such Act [21 U.S.C. 355f].

(2) Recommendations

If the Secretary has reason to believe that a drug for which a request is made under this subsection is a qualified infectious disease product, the Secretary shall provide the person making the request written recommendations for the nonclinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request, would be necessary for approval under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) of such drug for the use described in paragraph (1).

(c) Qualified infectious disease product

For purposes of this section, the term “qualified infectious disease product” has the meaning given such term in section 505E(g) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355f(g)], as added by section 801 of this Act.

(Pub. L. 112-144, title VIII, §804, July 9, 2012, 126 Stat. 1080.)

REFERENCES IN TEXT

The Federal Food, Drug, and Cosmetic Act, referred to in subsec. (a)(1)(B), is act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter. Chapter V of the Act is classified generally to this subchapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

This Act, referred to in subsec. (c), is Pub. L. 112-144, July 9, 2012, 126 Stat. 993, known as the Food and Drug Administration Safety and Innovation Act. For complete classification of this Act to the Code, see Tables.

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 360b. New animal drugs

(a) Unsafe new animal drugs and animal feed containing such drugs; conditions of safety; exemption of drugs for research; import tolerances

(1) A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for purposes of section 351(a)(5) of this title and section 342(a)(2)(C)(ii) of this title unless—

(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such approved application;

(B) there is in effect a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such conditionally approved application; or

(C) there is in effect an index listing pursuant to section 360ccc-1 of this title with respect to such use or intended use of such drug in a minor species, and such drug, its labeling, and such use conform to such index listing.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee (i) holds a license issued under subsection (m) of this section and has in its possession current approved labeling for such drug in animal feed; or (ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of a license issued under subsection (m) of this section.

(2) An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed be deemed unsafe for purposes of section 351(a)(6) of this title unless—

(A) there is in effect—

(i) an approval of an application filed pursuant to subsection (b) of this section with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such approved application;

(ii) a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such conditionally approved application; or

(iii) an index listing pursuant to section 360ccc-1 of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such index listing; and

(B) such animal feed is manufactured at a site for which there is in effect a license issued pursuant to subsection (m)(1) of this section to manufacture such animal feed.

(3) A new animal drug or an animal feed bearing or containing a new animal drug shall not be deemed unsafe for the purposes of section 351(a)(5) or (6) of this title if such article is for investigational use and conforms to the terms of an exemption in effect with respect thereto under subsection (j) of this section.

(4)(A) Except as provided in subparagraph (B), if an approval of an application filed under subsection (b) of this section is in effect with respect to a particular use or intended use of a new animal drug, the drug shall not be deemed unsafe for the purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a different use or intended use of the drug, other than a use in or on animal feed, if such use or intended use—

(i) is by or on the lawful written or oral order of a licensed veterinarian within the

context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(ii) is in compliance with regulations promulgated by the Secretary that establish the conditions for such different use or intended use.

The regulations promulgated by the Secretary under clause (ii) may prohibit particular uses of an animal drug and shall not permit such different use of an animal drug if the labeling of another animal drug that contains the same active ingredient and which is in the same dosage form and concentration provides for such different use.

(B) If the Secretary finds that there is a reasonable probability that a use of an animal drug authorized under subparagraph (A) may present a risk to the public health, the Secretary may—

(i) establish a safe level for a residue of an animal drug when it is used for such different use authorized by subparagraph (A); and

(ii) require the development of a practical, analytical method for the detection of residues of such drug above the safe level established under clause (i).

The use of an animal drug that results in residues exceeding a safe level established under clause (i) shall be considered an unsafe use of such drug under paragraph (1). Safe levels may be established under clause (i) either by regulation or order.

(C) The Secretary may by general regulation provide access to the records of veterinarians to ascertain any use or intended use authorized under subparagraph (A) that the Secretary has determined may present a risk to the public health.

(D) If the Secretary finds, after affording an opportunity for public comment, that a use of an animal drug authorized under subparagraph (A) presents a risk to the public health or that an analytical method required under subparagraph (B) has not been developed and submitted to the Secretary, the Secretary may, by order, prohibit any such use.

(5) If the approval of an application filed under section 355 of this title is in effect, the drug under such application shall not be deemed unsafe for purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a use or intended use of the drug in animals if such use or intended use—

(A) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(B) is in compliance with regulations promulgated by the Secretary that establish the conditions for the use or intended use of the drug in animals.

(6) For purposes of section 342(a)(2)(D)¹ of this title, a use or intended use of a new animal drug shall not be deemed unsafe under this section if the Secretary establishes a tolerance for such drug and any edible portion of any animal imported into the United States does not contain residues exceeding such tolerance. In establish-

¹ See References in Text note below.

ing such tolerance, the Secretary shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used by the Secretary to establish tolerances for applications for new animal drugs filed under subsection (b)(1) of this section. The Secretary may consider and rely on data submitted by the drug manufacturer, including data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used or data available from a relevant international organization, to the extent such data are not inconsistent with the criteria used by the Secretary to establish a tolerance for applications for new animal drugs filed under subsection (b)(1) of this section. For purposes of this paragraph, "relevant international organization" means the Codex Alimentarius² Commission or other international organization deemed appropriate by the Secretary. The Secretary may, under procedures specified by regulation, revoke a tolerance established under this paragraph if information demonstrates that the use of the new animal drug under actual use conditions results in food being imported into the United States with residues exceeding the tolerance or if scientific evidence shows the tolerance to be unsafe.

(b) Filing application for uses of new animal drug; contents; patent information; abbreviated application; presubmission conference

(1) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe. The applicant shall file with the application the patent number and the expiration date of any patent which claims the new animal drug for which the applicant filed the application or

which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) Any person may file with the Secretary an abbreviated application for the approval of a new animal drug. An abbreviated application shall contain the information required by subsection (n) of this section.

(3) Any person intending to file an application under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j) of this section shall be entitled to one or more conferences prior to such submission to reach an agreement acceptable to the Secretary establishing a submission or an investigational requirement, which may include a requirement for a field investigation. A decision establishing a submission or an investigational requirement shall bind the Secretary and the applicant or requestor unless (A) the Secretary and the applicant or requestor mutually agree to modify the requirement, or (B) the Secretary by written order determines that a substantiated scientific requirement essential to the determination of safety or effectiveness of the animal drug involved has appeared after the conference. No later than 25 calendar days after each such conference, the Secretary shall provide a written order setting forth a scientific justification specific to the animal drug and intended uses under consideration if the agreement referred to in the first sentence requires more than one field investigation as being essential to provide substantial evidence of effectiveness for the intended uses of the drug. Nothing in this paragraph shall be construed as compelling the Secretary to require a field investigation.

(c) Period for submission and approval of application; period for notice and expedition of hearing; period for issuance of order; abbreviated applications; withdrawal periods; effective date of approval; relationship to other applications; withdrawal or suspension of approval; bioequivalence; filing of additional patent information

(1) Within one hundred and eighty days after the filing of an application pursuant to subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either (A) issue an order approving the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity

²So in original. Probably should be "Alimentarius".

for a hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2)(A) Subject to subparagraph (C), the Secretary shall approve an abbreviated application for a drug unless the Secretary finds—

(i) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(ii) the conditions of use prescribed, recommended, or suggested in the proposed labeling are not reasonably certain to be followed in practice or, except as provided in subparagraph (B), information submitted with the application is insufficient to show that each of the proposed conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i) of this section) have been previously approved for the approved new animal drug referred to in the application;

(iii) information submitted with the application is insufficient to show that the active ingredients are the same as those of the approved new animal drug referred to in the application;

(iv)(I) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug referred to in the application, information submitted in the application is insufficient to show that the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as that of the approved new animal drug, or

(II) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is different from that of the approved new animal drug referred to in the application, no petition to file an application for the drug with the different active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed was approved under subsection (n)(3) of this section;

(v) if the application was filed pursuant to the approval of a petition under subsection (n)(3) of this section, the application did not contain the information required by the Secretary respecting the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which is not the same;

(vi) information submitted in the application is insufficient to show that the drug is bioequivalent to the approved new animal drug referred to in the application, or if the application is filed under a petition approved

pursuant to subsection (n)(3) of this section, information submitted in the application is insufficient to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(vii) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the approved new animal drug referred to in the application except for changes required because of differences approved under a petition filed under subsection (n)(3) of this section, because of a different withdrawal period, or because the drug and the approved new animal drug are produced or distributed by different manufacturers;

(viii) information submitted in the application or any other information available to the Secretary shows that (I) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, (II) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included, or (III) in the case of a drug for food producing animals, the inactive ingredients of the drug or its composition may be unsafe with respect to human food safety;

(ix) the approval under subsection (b)(1) of this section of the approved new animal drug referred to in the application filed under subsection (b)(2) of this section has been withdrawn or suspended for grounds described in paragraph (1) of subsection (e) of this section, the Secretary has published a notice of a hearing to withdraw approval of the approved new animal drug for such grounds, the approval under this paragraph of the new animal drug for which the application under subsection (b)(2) of this section was filed has been withdrawn or suspended under subparagraph (G) for such grounds, or the Secretary has determined that the approved new animal drug has been withdrawn from sale for safety or effectiveness reasons;

(x) the application does not meet any other requirement of subsection (n) of this section; or

(xi) the application contains an untrue statement of material fact.

(B) If the Secretary finds that a new animal drug for which an application is submitted under subsection (b)(2) of this section is bioequivalent to the approved new animal drug referred to in such application and that residues of the new animal drug are consistent with the tolerances established for such approved new animal drug but at a withdrawal period which is different than the withdrawal period approved for such approved new animal drug, the Secretary may establish, on the basis of information submitted, such different withdrawal period as the withdrawal period for the new animal

drug for purposes of the approval of such application for such drug.

(C) Within 180 days of the initial receipt of an application under subsection (b)(2) of this section or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(D) The approval of an application filed under subsection (b)(2) of this section shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in clause (i) or (ii) of subsection (n)(1)(G) of this section or in both such clauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in clause (iii) of subsection (n)(1)(G) of this section, the approval may be made effective on the date certified under clause (iii).

(iii) If the applicant made a certification described in clause (iv) of subsection (n)(1)(G) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of 45 days from the date the notice provided under subsection (n)(2)(B)(i) of this section is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the 30 month period beginning on the date of the receipt of the notice provided under subsection (n)(2)(B) of this section or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that if before the expiration of such period—

(I) the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or

(III) the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of 45 days from the date the notice made under subsection (n)(2)(B) of this section is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under section 2201 of title 28 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in clause (iv) of subsection (n)(1)(G) of this section and is for a drug for which a previous application has been filed

under this subsection containing such a certification, the application shall be made effective not earlier than 180 days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in subclause (III)³ holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within 30 days after such notice, such hearing shall commence not more than 90 days after the expiration of such 30 days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within 90 days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application submitted under subsection (b)(1) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b)(1) of this section, is approved after November 16, 1988, no application may be submitted under subsection (b)(2) of this section which refers to the drug for which the subsection (b)(1) application was submitted before the expiration of 5 years from the date of the approval of the application under subsection (b)(1) of this section, except that such an application may be submitted under subsection (b)(2) of this section after the expiration of 4 years from the date of the approval of the subsection (b)(1) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (n)(1)(G) of this section. The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning 48 months after the date of the approval of the subsection (b) application, the 30 month period referred to in subparagraph (D)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(ii) If an application submitted under subsection (b)(1) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under such subsection, is approved after November 16, 1988, and if such application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue

³ So in original. Probably should be "clause (iii)(III)".

depletion studies for minor uses or minor species) required for the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b)(2) of this section for the conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of 3 years from the date of the approval of the application under subsection (b)(1) of this section for such drug.

(iii) If a supplement to an application approved under subsection (b)(1) of this section is approved after November 16, 1988, and the supplement contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b)(2) of this section for a change approved in the supplement effective before the expiration of 3 years from the date of the approval of the supplement.

(iv) An applicant under subsection (b)(1) of this section who comes within the provisions of clause (i) of this subparagraph as a result of an application which seeks approval for a use solely in non-food producing animals, may elect, within 10 days of receiving such approval, to waive clause (i) of this subparagraph, in which event the limitation on approval of applications submitted under subsection (b)(2) of this section set forth in clause (ii) of this subparagraph shall be applicable to the subsection (b)(1) application.

(v) If an application (including any supplement to a new animal drug application) submitted under subsection (b)(1) of this section for a new animal drug for a food-producing animal use, which includes an active ingredient (including any ester or salt of the active ingredient) which has been the subject of a waiver under clause (iv) is approved after November 16, 1988, and if the application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the new approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application (including any supplement to such application) submitted under subsection (b)(2) of this section for the new conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of five years from the date of approval of the application under subsection (b)(1) of this section for such drug. The provisions of this paragraph shall apply only to the first approval for a food-producing animal use for the same applicant after the waiver under clause (iv).

(G) If an approved application submitted under subsection (b)(2) of this section for a new animal drug refers to a drug the approval of which was withdrawn or suspended for grounds described in paragraph (1) or (2) of subsection (e) of this sec-

tion or was withdrawn or suspended under this subparagraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this paragraph shall be withdrawn or suspended—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or this subparagraph, or

(ii) if the approved new animal drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(H) For purposes of this paragraph:

(i) The term “bioequivalence” means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a new animal drug and becomes available at the site of drug action.

(ii) A new animal drug shall be considered to be bioequivalent to the approved new animal drug referred to in its application under subsection (n) of this section if—

(I) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses;

(II) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the approved new animal drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective drug concentrations in use, and is considered scientifically insignificant for the drug in attaining the intended purposes of its use and preserving human food safety; or

(III) in any case in which the Secretary determines that the measurement of the rate and extent of absorption or excretion of the new animal drug in biological fluids is inappropriate or impractical, an appropriate acute pharmacological effects test or other test of the new animal drug and, when deemed scientifically necessary, of the approved new animal drug referred to in the application in the species to be tested or in an appropriate animal model does not show a significant difference between the new animal drug and such approved new animal drug when administered at the same dose under similar experimental conditions.

If the approved new animal drug referred to in the application for a new animal drug under subsection (n) of this section is approved for use in more than one animal species, the bioequivalency information described in subclauses (I), (II), and (III) shall be obtained for

one species, or if the Secretary deems appropriate based on scientific principles, shall be obtained for more than one species. The Secretary may prescribe the dose to be used in determining bioequivalency under subclause (I), (II), or (III). To assure that the residues of the new animal drug will be consistent with the established tolerances for the approved new animal drug referred to in the application under subsection (b)(2) of this section upon the expiration of the withdrawal period contained in the application for the new animal drug, the Secretary shall require bioequivalency data or residue depletion studies of the new animal drug or such other data or studies as the Secretary considers appropriate based on scientific principles. If the Secretary requires one or more residue studies under the preceding sentence, the Secretary may not require that the assay methodology used to determine the withdrawal period of the new animal drug be more rigorous than the methodology used to determine the withdrawal period for the approved new animal drug referred to in the application. If such studies are required and if the approved new animal drug, referred to in the application for the new animal drug for which such studies are required, is approved for use in more than one animal species, such studies shall be conducted for one species, or if the Secretary deems appropriate based on scientific principles, shall be conducted for more than one species.

(3) If the patent information described in subsection (b)(1) of this section could not be filed with the submission of an application under subsection (b)(1) of this section because the application was filed before the patent information was required under subsection (b)(1) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the new animal drug for which the application was filed or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b)(1) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than 30 days after November 16, 1988, and if the holder of an approved application could not file patent information under subsection (b)(1) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than 30 days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale

production facility is necessary to ensure the safety or effectiveness of the drug.

(d) Grounds for refusing application; approval of application; factors; "substantial evidence" defined; combination drugs

(1) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that—

(A) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;

(B) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions;

(C) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity;

(D) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions;

(E) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(F) upon the basis of information submitted to the Secretary as part of the application or any other information before the Secretary with respect to such drug, any use prescribed, recommended, or suggested in labeling proposed for such drug will result in a residue of such drug in excess of a tolerance found by the Secretary to be safe for such drug;

(G) the application failed to contain the patent information prescribed by subsection (b)(1) of this section;

(H) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; or

(I) such drug induces cancer when ingested by man or animal or, after tests which are appropriate for the evaluation of the safety of such drug, induces cancer in man or animal, except that the foregoing provisions of this subparagraph shall not apply with respect to such drug if the Secretary finds that, under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice (i) such drug will not adversely affect the animals for which it is intended, and (ii) no residue of such drug will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (c),

(d), and (h) of this section), in any edible portion of such animals after slaughter or in any food yielded by or derived from the living animals;

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearings, the Secretary finds that subparagraphs (A) through (I) do not apply, he shall issue an order approving the application.

(2) In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) the probable consumption of such drug and of any substance formed in or on food because of the use of such drug, (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substance, (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice. Any order issued under this subsection refusing to approve an application shall state the findings upon which it is based.

(3) As used in this section, the term "substantial evidence" means evidence consisting of one or more adequate and well controlled investigations, such as—

- (A) a study in a target species;
- (B) a study in laboratory animals;
- (C) any field investigation that may be required under this section and that meets the requirements of subsection (b)(3) of this section if a presubmission conference is requested by the applicant;
- (D) a bioequivalence study; or
- (E) an in vitro study;

by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(4) In a case in which an animal drug contains more than one active ingredient, or the labeling of the drug prescribes, recommends, or suggests use of the drug in combination with one or more other animal drugs, and the active ingredients or drugs intended for use in the combination have previously been separately approved pursuant to an application submitted under subsection (b)(1) of this section for particular uses and conditions of use for which they are intended for use in the combination—

(A) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on human food safety grounds unless the Secretary finds that the application fails to establish that—

- (i) none of the active ingredients or drugs intended for use in the combination, respec-

tively, at the longest withdrawal time of any of the active ingredients or drugs in the combination, respectively, exceeds its established tolerance; or

(ii) none of the active ingredients or drugs in the combination interferes with the methods of analysis for another of the active ingredients or drugs in the combination, respectively;

(B) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on target animal safety grounds unless the Secretary finds that—

(i)(I) there is a substantiated scientific issue, specific to one or more of the active ingredients or animal drugs in the combination, that cannot adequately be evaluated based on information contained in the application for the combination (including any investigations, studies, or tests for which the applicant has a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted); or

(II) there is a scientific issue raised by target animal observations contained in studies submitted to the Secretary as part of the application; and

(ii) based on the Secretary's evaluation of the information contained in the application with respect to the issues identified in clauses (i)(I) and (II), paragraph (1)(A), (B), or (D) apply;

(C) except in the case of a combination that contains a nontopical antibacterial ingredient or animal drug, the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use other than in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

(i) there is substantial evidence that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to labeled effectiveness;

(ii) each active ingredient or animal drug intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population; or

(iii) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs may be physically incompatible or have disparate dosing regimens, such active ingredients or animal drugs are physically compatible or do not have disparate dosing regimens; and

(D) the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

- (i) there is substantial evidence that any active ingredient or animal drug intended

only for the same use as another active ingredient or animal drug in the combination makes a contribution to the labeled effectiveness;

(ii) each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population;

(iii) where a combination contains more than one nontopical antibacterial ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial ingredients or animal drugs makes a contribution to the labeled effectiveness, except that for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs; or

(iv) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs intended for use in drinking water may be physically incompatible, such active ingredients or animal drugs intended for use in drinking water are physically compatible.

(5) In reviewing an application that proposes a change to add an intended use for a minor use or a minor species to an approved new animal drug application, the Secretary shall reevaluate only the relevant information in the approved application to determine whether the application for the minor use or minor species can be approved. A decision to approve the application for the minor use or minor species is not, implicitly or explicitly, a reaffirmation of the approval of the original application.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to health of man or animals

(1) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application filed pursuant to subsection (b) of this section with respect to any new animal drug if the Secretary finds—

(A) that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved or the condition of use authorized under subsection (a)(4)(A) of this section;

(B) that new evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved or that subparagraph (I) of paragraph (1) of subsection (d) of this section applies to such drug;

(C) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there

is a lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(D) the patent information prescribed by subsection (c)(3) of this section was not filed within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information;

(E) that the application contains any untrue statement of a material fact; or

(F) that the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application. The supplemental application shall be treated in the same manner as the original application.

If the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the health of man or of the animals for which such drug is intended, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence to suspend the approval of an application shall not be delegated.

(2) The Secretary may also, after due notice and opportunity for hearing to the applicant, issue an order withdrawing the approval of an application with respect to any new animal drug under this section if the Secretary finds—

(A) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under subsection (1) of this section, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection;

(B) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(C) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(3) Any order under this subsection shall state the findings upon which it is based.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d), (e), or (m) of this section, or section 360ccc(c), (d), or (e) of this title refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section, or section 360ccc of this title (other than orders issuing, amending, or repealing regulations) shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application filed under subsection (b) or (m) of this section. The provisions of subsection (h) of section 355 of this title shall govern any such appeal.

(i) Publication in Federal Register; effective date and revocation or suspension of regulation

When a new animal drug application filed pursuant to subsection (b) of this section or section 360ccc of this title is approved, the Secretary shall by notice, which upon publication shall be effective as a regulation, publish in the Federal Register the name and address of the applicant and the conditions and indications of use of the new animal drug covered by such application, including any tolerance and withdrawal period or other use restrictions and, if such new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian) applicable to any animal feed for use in which such drug is approved, and such other information, upon the basis of which such application was approved, as the Secretary deems necessary to assure the safe and effective use of such drug. Upon withdrawal of approval of such new animal drug application or upon its suspension or upon failure to renew a conditional approval under section 360ccc of this title, the Secretary shall forthwith revoke or suspend, as the case may be, the regulation published pursuant to this subsection (i) insofar as it is based on the approval of such application.

(j) Exemption of drugs for research; discretionary and mandatory conditions

To the extent consistent with the public health, the Secretary shall promulgate regulations for exempting from the operation of this section new animal drugs, and animal feeds bearing or containing new animal drugs, intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of ani-

mal drugs. Such regulations may, in the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such article, of data (including but not limited to analytical reports by investigators) obtained as a result of such investigational use of such article, as the Secretary finds will enable him to evaluate the safety and effectiveness of such article in the event of the filing of an application pursuant to this section. Such regulations, among other things, shall set forth the conditions (if any) upon which animals treated with such articles, and any products of such animals (before or after slaughter), may be marketed for food use.

(k) Food containing new animal drug considered unadulterated while approval of application for such drug is effective

While approval of an application for a new animal drug is effective, a food shall not, by reason of bearing or containing such drug or any substance formed in or on the food because of its use in accordance with such application (including the conditions and indications of use prescribed pursuant to subsection (i) of this section), be considered adulterated within the meaning of clause (1) of section 342(a) of this title.

(l) Records and reports; required information; regulations and orders; examination of data; access to records

(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) of this section or section 360ccc of this title is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A) of this section, and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3)(A) In the case of each new animal drug described in paragraph (1) that contains an antimicrobial active ingredient, the sponsor of the

drug shall submit an annual report to the Secretary on the amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals, including information on any distributor-labeled product.

(B) Each report under this paragraph shall specify the amount of each antimicrobial active ingredient—

- (i) by container size, strength, and dosage form;
- (ii) by quantities distributed domestically and quantities exported; and
- (iii) by dosage form, including, for each such dosage form, a listing of the target animals, indications, and production classes that are specified on the approved label of the product.

(C) Each report under this paragraph shall—

- (i) be submitted not later than March 31 each year;
- (ii) cover the period of the preceding calendar year; and
- (iii) include separate information for each month of such calendar year.

(D) The Secretary may share information reported under this paragraph with the Antimicrobial Resistance Task Force established under section 247d-5 of title 42.

(E) The Secretary shall make summaries of the information reported under this paragraph publicly available, except that—

- (i) the summary data shall be reported by antimicrobial class, and no class with fewer than 3 distinct sponsors of approved applications shall be independently reported; and
- (ii) the data shall be reported in a manner consistent with protecting both national security and confidential business information.

(m) Feed mill licenses

(1) Any person may file with the Secretary an application for a license to manufacture animal feeds bearing or containing new animal drugs. Such person shall submit to the Secretary as part of the application (A) a full statement of the business name and address of the specific facility at which the manufacturing is to take place and the facility's registration number, (B) the name and signature of the responsible individual or individuals for that facility, (C) a certification that the animal feeds bearing or containing new animal drugs are manufactured and labeled in accordance with the applicable regulations published pursuant to subsection (i) of this section or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc-1(e)(2) of this title and the labeling requirements set forth in section 360ccc-1(h) of this title, and (D) a certification that the methods used in, and the facilities and controls used for, manufacturing, processing, packaging, and holding such animal feeds are in conformity with current good manufacturing practice as described in section 351(a)(2)(B) of this title.

(2) Within 90 days after the filing of an application pursuant to paragraph (1), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall (A) issue an order approving the application if the

Secretary then finds that none of the grounds for denying approval specified in paragraph (3) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under paragraph (3) on the question whether such application is approvable. The procedure governing such a hearing shall be the procedure set forth in the last two sentences of subsection (c)(1) of this section.

(3) If the Secretary, after due notice to the applicant in accordance with paragraph (2) and giving the applicant an opportunity for a hearing in accordance with such paragraph, finds, on the basis of information submitted to the Secretary as part of the application, on the basis of a preapproval inspection, or on the basis of any other information before the Secretary—

- (A) that the application is incomplete, false, or misleading in any particular;
- (B) that the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed are inadequate to preserve the identity, strength, quality, and purity of the new animal drug therein; or
- (C) that the facility manufactures animal feeds bearing or containing new animal drugs in a manner that does not accord with the specifications for manufacture or labels animal feeds bearing or containing new animal drugs in a manner that does not accord with the conditions or indications of use that are published pursuant to subsection (i) of this section or an index listing pursuant to section 360ccc-1(e) of this title,

the Secretary shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (C) do not apply, the Secretary shall issue an order approving the application. An order under this subsection approving an application for a license to manufacture animal feeds bearing or containing new animal drugs shall permit a facility to manufacture only those animal feeds bearing or containing new animal drugs for which there are in effect regulations pursuant to subsection (i) of this section or an index listing pursuant to section 360ccc-1(e) of this title relating to the use of such drugs in or on such animal feed.

(4)(A) The Secretary shall, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feeds bearing or containing new animal drugs under this subsection if the Secretary finds—

- (i) that the application for such license contains any untrue statement of a material fact; or
- (ii) that the applicant has made changes that would cause the application to contain any untrue statements of material fact or that would affect the safety or effectiveness of the animal feeds manufactured at the facility unless the applicant has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application.

If the Secretary (or in the Secretary's absence the officer acting as the Secretary) finds that

there is an imminent hazard to the health of humans or of the animals for which such animal feed is intended, the Secretary may suspend the license immediately, and give the applicant prompt notice of the action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence shall not be delegated.

(B) The Secretary may also, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feed under this subsection if the Secretary finds—

(i) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under paragraph (5)(A) of this subsection or section 354(a)(3)(A) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by subparagraph (B) of such paragraph or section 354(a)(3)(B) of this title;

(ii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the methods used in, or the facilities and controls used for, the manufacture, processing, packing, and holding of such animal feed are inadequate to assure and preserve the identity, strength, quality, and purity of the new animal drug therein, and were not made adequate within a reasonable time after receipt of written notice from the Secretary, specifying the matter complained of;

(iii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the labeling of any animal feeds, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(iv) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the facility has manufactured, processed, packed, or held animal feed bearing or containing a new animal drug adulterated under section 351(a)(6) of this title and the facility did not discontinue the manufacture, processing, packing, or holding of such animal feed within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(C) The Secretary may also revoke a license to manufacture animal feeds under this subsection if an applicant gives notice to the Secretary of intention to discontinue the manufacture of all animal feed covered under this subsection and waives an opportunity for a hearing on the matter.

(D) Any order under this paragraph shall state the findings upon which it is based.

(5) When a license to manufacture animal feeds bearing or containing new animal drugs has been issued—

(A) the applicant shall establish and maintain such records, and make such reports to

the Secretary, or (at the option of the Secretary) to the appropriate person or persons holding an approved application filed under subsection (b) of this section, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section or paragraph (4); and

(B) every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(6) To the extent consistent with the public health, the Secretary may promulgate regulations for exempting from the operation of this subsection facilities that manufacture, process, pack, or hold animal feeds bearing or containing new animal drugs.

(n) Abbreviated applications for new animal drugs; contents, filing, etc.; lists of approved drugs

(1) An abbreviated application for a new animal drug shall contain—

(A)(i) except as provided in clause (ii), information to show that the conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i) of this section) prescribed, recommended, or suggested in the labeling proposed for the new animal drug have been previously approved for a new animal drug listed under paragraph (4) (hereinafter in this subsection referred to as an “approved new animal drug”), and

(ii) information to show that the withdrawal period at which residues of the new animal drug will be consistent with the tolerances established for the approved new animal drug is the same as the withdrawal period previously established for the approved new animal drug or, if the withdrawal period is proposed to be different, information showing that the residues of the new animal drug at the proposed different withdrawal period will be consistent with the tolerances established for the approved new animal drug;

(B)(i) information to show that the active ingredients of the new animal drug are the same as those of the approved new animal drug, and

(ii) if the approved new animal drug has more than one active ingredient, and if one of the active ingredients of the new animal drug is different from one of the active ingredients of the approved new animal drug and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show that the other active ingredients of the new animal drug are the same as the active ingredients of the approved new animal drug,

(II) information to show either that the different active ingredient is an active ingredient of another approved new animal drug

or of an animal drug which does not meet the requirements of section 321(v) of this title, and

(III) such other information respecting the different active ingredients as the Secretary may require;

(C)(i) if the approved new animal drug is permitted to be used with one or more animal drugs in animal feed, information to show that the proposed uses of the new animal drug with other animal drugs in animal feed are the same as the uses of the approved new animal drug, and

(ii) if the approved new animal drug is permitted to be used with one or more other animal drugs in animal feed, and one of the other animal drugs proposed for use with the new animal drug in animal feed is different from one of the other animal drugs permitted to be used in animal feed with the approved new animal drug, and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show either that the different animal drug proposed for use with the approved new animal drug in animal feed is an approved new animal drug permitted to be used in animal feed or does not meet the requirements of section 321(v) of this title when used with another animal drug in animal feed,

(II) information to show that other animal drugs proposed for use with the new animal drug in animal feed are the same as the other animal drugs permitted to be used with the approved new animal drug, and

(III) such other information respecting the different animal drug or combination with respect to which the petition was filed as the Secretary may require,

(D) information to show that the route of administration, the dosage form, and the strength of the new animal drug are the same as those of the approved new animal drug or, if the route of administration, the dosage form, or the strength of the new animal drug is different and the application is filed pursuant to the approval of a petition filed under paragraph (3), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(E) information to show that the new animal drug is bioequivalent to the approved new animal drug, except that if the application is filed pursuant to the approval of a petition filed under paragraph (3) for the purposes described in subparagraph (B) or (C), information to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(F) information to show that the labeling proposed for the new animal drug is the same as the labeling approved for the approved new animal drug except for changes required be-

cause of differences approved under a petition filed under paragraph (3), because of a different withdrawal period, or because the new animal drug and the approved new animal drug are produced or distributed by different manufacturers;

(G) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(H) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the approved new animal drug or which claims a use for such approved new animal drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b)(1) or (c)(3) of this section—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new animal drug for which the application is filed; and

(I) if with respect to the approved new animal drug information was filed under subsection (b)(1) or (c)(3) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval of an application under subsection (c)(2) of this section, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by subparagraphs (A) through (I).

(2)(A) An applicant who makes a certification described in paragraph (1)(G)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to—

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (c)(1) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application, which contains data from bioequivalence studies, has been filed under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (1)(G)(iv), the notice required by subparagraph (B) shall be given when the amended application is filed.

(3) If a person wants to submit an abbreviated application for a new animal drug—

(A) whose active ingredients, route of administration, dosage form, or strength differ from that of an approved new animal drug, or

(B) whose use with other animal drugs in animal feed differs from that of an approved new animal drug,

such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve a petition for a new animal drug unless the Secretary finds that—

(C) investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which differ from the approved new animal drug, or

(D) investigations must be conducted to show the safety for human consumption of any residues in food resulting from the proposed active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed for the new animal drug which is different from the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug.

The Secretary shall approve or disapprove a petition submitted under this paragraph within 90 days of the date the petition is submitted.

(4)(A)(i) Within 60 days of November 16, 1988, the Secretary shall publish and make available to the public a list in alphabetical order of the official and proprietary name of each new animal drug which has been approved for safety and effectiveness before November 16, 1988.

(ii) Every 30 days after the publication of the first list under clause (i) the Secretary shall revise the list to include each new animal drug which has been approved for safety and effectiveness under subsection (c) of this section during the 30 day period.

(iii) When patent information submitted under subsection (b)(1) or (c)(3) of this section respecting a new animal drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A new animal drug approved for safety and effectiveness before November 16, 1988, or approved for safety and effectiveness under subsection (c) of this section shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or November 16, 1988, whichever is later.

(C) If the approval of a new animal drug was withdrawn or suspended under subsection (c)(2)(G) of this section or for grounds described in subsection (e) of this section or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (c)(2)(G) or (e) of this section, or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(5) If an application contains the information required by clauses (A), (G), and (H) of subsection (b)(1) of this section and such information—

(A) is relied on by the applicant for the approval of the application, and

(B) is not information derived either from investigations, studies, or tests conducted by or for the applicant or for which the applicant had obtained a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted,

such application shall be considered to be an application filed under subsection (b)(2) of this section.

(o) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

(p) Safety and effectiveness data

(1) Safety and effectiveness data and information which has been submitted in an application filed under subsection (b)(1) of this section or section 360ccc(a) of this title for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application filed under subsection (b)(2) of this section which refers to such drug or upon the date upon which the approval of an application filed under subsection (b)(2) of this section which refers to such drug could be made effective if such an application had been filed.

(2) Any request for data and information pursuant to paragraph (1) shall include a verified statement by the person making the request that any data or information received under such paragraph shall not be disclosed by such person to any other person—

(A) for the purpose of, or as part of a plan, scheme, or device for, obtaining the right to make, use, or market, or making, using, or marketing, outside the United States, the drug identified in the application filed under subsection (b)(1) of this section or section 360ccc(a) of this title, and

(B) without obtaining from any person to whom the data and information are disclosed

an identical verified statement, a copy of which is to be provided by such person to the Secretary, which meets the requirements of this paragraph.

(June 25, 1938, ch. 675, §512, as added Pub. L. 90-399, §101(b), July 13, 1968, 82 Stat. 343; amended Pub. L. 100-670, title I, §§101, 102, 104, 107(a)(2), Nov. 16, 1988, 102 Stat. 3971, 3981, 3982, 3984; Pub. L. 102-108, §2(e), Aug. 17, 1991, 105 Stat. 550; Pub. L. 103-80, §3(r), Aug. 13, 1993, 107 Stat. 777; Pub. L. 103-396, §2(a), (b)(2), (3), Oct. 22, 1994, 108 Stat. 4153, 4154; Pub. L. 104-250, §§2(a)-(d), 3, 4, 5(c), 6(a), (b), Oct. 9, 1996, 110 Stat. 3151-3153, 3155-3157; Pub. L. 105-115, title I, §124(b), Nov. 21, 1997, 111 Stat. 2325; Pub. L. 105-277, div. A, §101(a) [title VII, §737], Oct. 21, 1998, 112 Stat. 2681, 2681-30; Pub. L. 106-113, div. B, §1000(a)(9) [title IV, §4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A-584; Pub. L. 108-282, title I, §102(b)(2), (3), (5)(I)-(S), Aug. 2, 2004, 118 Stat. 892, 903, 904; Pub. L. 110-316, title I, §105(a), Aug. 14, 2008, 122 Stat. 3513.)

REFERENCES IN TEXT

Section 342(a)(2) of this title, referred to in subsec. (a)(6), was amended by Pub. L. 104-170, title IV, §404, Aug. 3, 1996, 110 Stat. 1514, and, as so amended, no longer contains a subcl. (D). See section 342(a)(2)(C)(ii) of this title.

AMENDMENTS

2008—Subsec. (l)(3). Pub. L. 110-316 added par. (3).

2004—Subsec. (a)(1), (2). Pub. L. 108-282, §102(b)(5)(I), added pars. (1) and (2) and struck out former pars. (1) and (2) which deemed as unsafe new animal drugs and animal feed bearing or containing a new animal drug which did not have in effect certain approvals.

Subsec. (b)(3). Pub. L. 108-282, §102(b)(5)(J), substituted “under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j)” for “under paragraph (1) or a request for an investigational exemption under subsection (j)”.

Subsec. (c)(2)(F)(ii), (iii), (v). Pub. L. 108-282, §102(b)(2), substituted “(other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species)” for “(other than bioequivalence or residue studies)”.

Subsec. (d)(4). Pub. L. 108-282, §102(b)(5)(K), substituted “have previously been separately approved pursuant to an application submitted under subsection (b)(1) of this section” for “have previously been separately approved” in introductory provisions.

Subsec. (d)(5). Pub. L. 108-282, §102(b)(3), added par. (5).

Subsec. (f). Pub. L. 108-282, §102(b)(5)(L), substituted “subsection (d), (e), or (m) of this section, or section 360ccc(c), (d), or (e) of this title” for “subsection (d), (e), or (m) of this section”.

Subsec. (g). Pub. L. 108-282, §102(b)(5)(M), substituted “this section, or section 360ccc of this title” for “this section”.

Subsec. (i). Pub. L. 108-282, §102(b)(5)(N), substituted “subsection (b) of this section or section 360ccc of this title” for “subsection (b) of this section” and inserted “or upon failure to renew a conditional approval under section 360ccc of this title” after “or upon its suspension”.

Subsec. (l)(1). Pub. L. 108-282, §102(b)(5)(O), substituted “subsection (b) of this section or section 360ccc of this title” for “subsection (b) of this section”.

Subsec. (m)(1)(C). Pub. L. 108-282, §102(b)(5)(P), substituted “applicable regulations published pursuant to subsection (i) of this section or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc-1(e)(2) of this title and the

labeling requirements set forth in section 360ccc-1(h) of this title” for “applicable regulations published pursuant to subsection (i) of this section”.

Subsec. (m)(3). Pub. L. 108-282, §102(b)(5)(Q), inserted “or an index listing pursuant to section 360ccc-1(e) of this title” after “subsection (i) of this section” in subpar. (C) and concluding provisions.

Subsec. (p)(1), (2)(A). Pub. L. 108-282, §102(b)(5)(R), (S), substituted “subsection (b)(1) of this section or section 360ccc(a) of this title” for “subsection (b)(1) of this section”.

1999—Subsec. (o). Pub. L. 106-113 substituted “United States Patent and Trademark Office” for “Patent and Trademark Office of the Department of Commerce”.

1998—Subsec. (d)(4)(D)(iii). Pub. L. 105-277 inserted before semicolon “, except that for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs”.

1997—Subsec. (c)(4). Pub. L. 105-115 added par. (4).

1996—Subsec. (a)(1). Pub. L. 104-250, §6(a), amended par. (1) generally. Prior to amendment, par. (1) read as follows: “A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for the purposes of section 351(a)(5) and section 342(a)(2)(D) of this title unless—

“(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug, and
“(B) such drug, its labeling, and such use conform to such approved application.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee—

“(i) is the holder of an approved application under subsection (m) of this section; or
“(ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved application under subsection (m) of this section.”

Subsec. (a)(2). Pub. L. 104-250, §6(a), amended par. (2) generally. Prior to amendment, par. (2) read as follows: “An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed, be deemed unsafe for the purposes of section 351(a)(6) of this title unless—

“(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such drugs, as used in such animal feed,

“(B) there is in effect an approval of an application pursuant to subsection (m)(1) of this section with respect to such animal feed, and

“(C) such animal feed, its labeling, and such use conform to the conditions and indications of use published pursuant to subsection (i) of this section and to the application with respect thereto approved under subsection (m) of this section.”

Subsec. (a)(6). Pub. L. 104-250, §4, added par. (6).

Subsec. (b)(3). Pub. L. 104-250, §2(d), added par. (3).

Subsec. (c)(2)(F)(ii), (iii). Pub. L. 104-250, §2(b)(1), substituted “substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or,” for “reports of new clinical or field investigations (other than bioequivalence or residue studies) and,” and “required for the approval” for “essential to the approval”.

Subsec. (c)(2)(F)(v). Pub. L. 104-250, §2(b)(2), substituted “clause (iv)” for “subparagraph (B)(iv)” in two places, “substantial evidence of the effectiveness of the drug involved, any studies of animal safety,” for “reports of clinical or field investigations” and “required for the new approval” for “essential to the new approval”.

Subsec. (d)(1)(F). Pub. L. 104-250, §3, amended subpar. (F) generally. Prior to amendment, subpar. (F) read as

follows: “upon the basis of the information submitted to him as part of the application or any other information before him with respect to such drug, the tolerance limitation proposed, if any, exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended;”.

Subsec. (d)(3). Pub. L. 104-250, §2(a), amended par. (3) generally. Prior to amendment, par. (3) read as follows: “As used in this subsection and subsection (e) of this section, the term ‘substantial evidence’ means evidence consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.”

Subsec. (d)(4). Pub. L. 104-250, §2(c), added par. (4).

Subsec. (i). Pub. L. 104-250, §5(c), inserted “and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian” after “(including special labeling requirements”.

Subsec. (m). Pub. L. 104-250, §6(b), amended subsec. (m) generally, substituting provisions relating to application for feed mill licenses, including approval, refusal, revocation, and suspension of such licenses, and provisions for record and reporting requirements for, as well as exemption from, such licenses, for provisions relating to application for uses of animal feed containing new animal drug, including required contents, approval, refusal, and withdrawal of approval or suspension of such usage applications, and provisions for record and reporting requirements of such usage applications.

1994—Subsec. (a)(4), (5). Pub. L. 103-396, §2(a), added pars. (4) and (5).

Subsec. (e)(1)(A). Pub. L. 103-396, §2(b)(2), inserted before semicolon at end “or the condition of use authorized under subsection (a)(4)(A) of this section”.

Subsec. (l)(1). Pub. L. 103-396, §2(b)(3), substituted “relating to experience, including experience with uses authorized under subsection (a)(4)(A) of this section,” for “relating to experience”.

1993—Subsec. (c)(2)(A)(ii). Pub. L. 103-80, §3(r)(1), inserted “in” after “except as provided”.

Subsec. (c)(2)(F)(i). Pub. L. 103-80, §3(r)(2), substituted “subparagraph (D)(iii)” for “subparagraph (C)(iii)”.

Subsec. (c)(2)(H)(ii). Pub. L. 103-80, §3(r)(3), substituted “subclauses” for “subclause” after “bioequivalency information described in” in concluding provisions.

Subsec. (d)(1). Pub. L. 103-80, §3(r)(4), substituted “subparagraphs (A) through (I)” for “subparagraphs (A) through (G)” in concluding provisions.

Subsec. (n)(1). Pub. L. 103-80, §3(r)(5), substituted “section 321(v) of this title” for “section 321(w) of this title” in subpars. (B)(ii)(II) and (C)(ii)(I) and substituted “through (I)” for “through (H)” in concluding provisions.

1991—Subsec. (e)(1)(B). Pub. L. 102-108 substituted “(I)” for “(H)”.

1988—Subsec. (a)(1)(C). Pub. L. 100-670, §107(a)(2), struck out subpar. (C) which read as follows: “in the case of a new animal drug subject to subsection (n) of this section and not exempted therefrom by regulations it is from a batch with respect to which a certificate or release issued pursuant to subsection (n) of this section is in effect with respect to such drug.”

Subsec. (b). Pub. L. 100-670, §§101(a), 102(a), designated existing provisions as par. (1), redesignated cls. (1) to (8) as cls. (A) to (H), respectively, added par. (2), and inserted provisions at end of par. (1) which require applicant to file with application, patent number and expiration date of any patent which claims new animal drug, to amend application to include such information if patent which claims such drug or method of using such drug is issued after filing date but before approval

of application, and to publish such information upon approval.

Subsec. (c). Pub. L. 100-670, §§101(c), 102(b)(1), designated existing provisions as par. (1), redesignated cls. (1) and (2) as cls. (A) and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(1). Pub. L. 100-670, §102(b)(3), substituted “(G)” for “(H)” in last sentence.

Subsec. (d)(1)(G) to (I). Pub. L. 100-670, §102(b)(2), added subpar. (G) and redesignated former subpars. (G) and (H) as (H) and (I), respectively.

Subsec. (e)(1)(D) to (F). Pub. L. 100-670, §102(b)(4), added subpar. (D) and redesignated former subpars. (D) and (E) as (E) and (F), respectively.

Subsecs. (n) to (p). Pub. L. 100-670, §101(b), added subsecs. (n) to (p) and struck out former subsec. (n) which related to certification of new drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, and release prior to certification.

EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106-113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, §4731] of Pub. L. 106-113, set out as a note under section 1 of Title 35, Patents.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1994 AMENDMENT

Pub. L. 103-396, §2(d), Oct. 22, 1994, 108 Stat. 4154, provided that: “The amendments made by this section [amending this section and section 331 of this title] shall take effect upon the adoption of the final regulations under subsection (c) [set out below].” [Final regulations were dated Oct. 22, 1996, filed Nov. 6, 1996, published Nov. 7, 1996, 61 F.R. 57732, and effective Dec. 9, 1996.]

EFFECTIVE DATE OF 1988 AMENDMENT

Pub. L. 100-670, title I, §108, Nov. 16, 1988, 102 Stat. 3984, provided that: “The Secretary of Health and Human Services may not make an approval of an application submitted under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(b)(2)) effective before January 1, 1991.”

EFFECTIVE DATE AND TRANSITIONAL PROVISIONS

Pub. L. 90-399, §108, July 13, 1968, 82 Stat. 353, as amended by Pub. L. 108-282, title I, §102(b)(5)(T), Aug. 2, 2004, 118 Stat. 905, provided that:

“(a) Except as otherwise provided in this section, the amendments made by the foregoing sections [see Short Title of 1968 Amendment note set out under section 301 of this title] shall take effect on the first day of the thirteenth calendar month which begins after the date of enactment of this Act [July 13, 1968].

“(b)(1) As used in this subsection, the term ‘effective date’ means the effective date specified in subsection (a) of this section; the term ‘basic Act’ means the Federal Food, Drug, and Cosmetic Act [this chapter]; and other terms used both in this section and the basic Act shall have the same meaning as they have, or had, at the time referred to in the context, under the basic Act.

“(2) Any approval, prior to the effective date, of a new animal drug or of an animal feed bearing or containing a new animal drug, whether granted by approval of a new-drug application, master file, antibiotic regulation, or food additive regulations, shall continue in effect, and shall be subject to change in accordance with the provisions of the basic Act as amended by this Act [see Short Title of 1968 Amendment note set out under section 301 of this title].

“(3) In the case of any drug (other than a drug subject to section 512(n) of the basic Act as amended by this

Act) [subsection (n) of this section] intended for use in animals other than man which, on October 9, 1962, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act [section 321(p) of this title] as then in force, and (C) was not covered by an effective application under section 505 of that Act [section 355 of this title], the words 'effectiveness' and 'effective' contained in section 201(v) to the basic Act [sic] [section 321(v) of this title] shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

"(4) Regulations providing for fees (and advance deposits to cover fees) which on the day preceding the effective date applicable under subsection (a) of this section were in effect pursuant to section 507 of the basic Act [section 357 of this title] shall, except as the Secretary may otherwise prescribe, be deemed to apply also under section 512(n) of the basic Act [subsection (n) of this section], and appropriations of fees (and of advance deposits to cover fees) available for the purposes specified in such section 507 [section 357 of this title] as in effect prior to the effective date shall also be available for the purposes specified in section 512(n) [subsection (n) of this section], including preparatory work or proceedings prior to that date."

REGULATIONS

Pub. L. 104-250, §2(e), Oct. 9, 1996, 110 Stat. 3154, provided that:

"(1) IN GENERAL.—Not later than 6 months after the date of enactment of this Act [Oct. 9, 1996], the Secretary of Health and Human Services shall issue proposed regulations implementing the amendments made by this Act as described in paragraph (2)(A) of this subsection, and not later than 18 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments. Not later than 12 months after the date of enactment of this Act, the Secretary shall issue proposed regulations implementing the other amendments made by this Act as described in paragraphs (2)(B) and (2)(C) of this subsection, and not later than 24 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments.

"(2) CONTENTS.—In issuing regulations implementing the amendments made by this Act [see Short Title of 1996 Amendments note set out under section 301 of this title], and in taking an action to review an application for approval of a new animal drug under section 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b), or a request for an investigational exemption for a new animal drug under subsection (j) of such section, that is pending or has been submitted prior to the effective date of the regulations, the Secretary shall—

"(A) further define the term 'adequate and well controlled', as used in subsection (d)(3) of section 512 of such Act, to require that field investigations be designed and conducted in a scientifically sound manner, taking into account practical conditions in the field and differences between field conditions and laboratory conditions;

"(B) further define the term 'substantial evidence', as defined in subsection (d)(3) of such section, in a manner that encourages the submission of applications and supplemental applications; and

"(C) take into account the proposals contained in the citizen petition (FDA Docket No. 91P-0434/CP) jointly submitted by the American Veterinary Medical Association and the Animal Health Institute, dated October 21, 1991.

Until the regulations required by subparagraph (A) are issued, nothing in the regulations published at 21 C.F.R. 514.111(a)(5) (April 1, 1996) shall be construed to compel the Secretary of Health and Human Services to require a field investigation under section 512(d)(1)(E) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(d)(1)(E)) or to apply any of its provisions in a manner inconsistent with the considerations for scientific

ically sound field investigations set forth in subparagraph (A)."

Pub. L. 103-396, §2(c), Oct. 22, 1994, 108 Stat. 4154, provided that: "Not later than 2 years after the date of the enactment of this Act [Oct. 22, 1994], the Secretary of Health and Human Services shall promulgate regulations to implement paragraphs (4)(A) and (5) of section 512(a) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(a)(4)(A), (5)] (as amended by subsection (a))."

Pub. L. 100-670, title I, §103, Nov. 16, 1988, 102 Stat. 3982, provided that:

"(a) GENERAL RULE.—The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b], as amended by sections 101 through 103 of this title, within one year of the date of enactment of this Act [Nov. 16, 1988].

"(b) TRANSITION.—During the period beginning 60 days after the date of enactment of this Act [Nov. 16, 1988] and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new animal drug applications may be submitted in accordance with the provisions of section 314.55 and part 320 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 512(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(c)] before the date of enactment of this Act. If any such provision of section 314.55 or part 320 is inconsistent with the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (as amended by this title), the Secretary shall consider the application under the applicable requirements of section 512 (as so amended)."

ANTIMICROBIAL ANIMAL DRUG DISTRIBUTION REPORTS

Pub. L. 110-316, title I, §105(b), (c), Aug. 14, 2008, 122 Stat. 3514, provided that:

"(b) FIRST REPORT.—For each new animal drug that is subject to the reporting requirement under section 512(l)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(l)(3)], as added by subsection (a), and for which an approval of an application filed pursuant to section 512(b) or 571 of such Act [21 U.S.C. 360b(b), 360ccc] is in effect on the date of the enactment of this title [Aug. 14, 2008], the Secretary of Health and Human Services shall require the sponsor of the drug to submit the first report under such section 512(l)(3) for the drug not later than March 31, 2010.

"(c) SEPARATE REPORT.—The reports required under section 512(l)(3) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), shall be separate from periodic drug experience reports that are required under section 514.80(b)(4) of title 21, Code of Federal Regulations (as in effect on the date of the enactment of this title)."

DRUGS INTENDED FOR MINOR SPECIES AND MINOR USES

Pub. L. 104-250, §2(f), Oct. 9, 1996, 110 Stat. 3154, provided that: "The Secretary of Health and Human Services shall consider legislative and regulatory options for facilitating the approval under section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b] of animal drugs intended for minor species and for minor uses and, within 18 months after the date of enactment of this Act [Oct. 9, 1996], announce proposals for legislative or regulatory change to the approval process under such section for animal drugs intended for use in minor species or for minor uses."

TRANSITIONAL PROVISION REGARDING IMPLEMENTATION OF PUB. L. 104-250; APPROVED MEDICATED FEED APPLICATION DEEMED LICENSE

Pub. L. 104-250, §6(c), Oct. 9, 1996, 110 Stat. 3160, provided that: "A person engaged in the manufacture of

animal feeds bearing or containing new animal drugs who holds at least one approved medicated feed application for an animal feed bearing or containing new animal drugs, the manufacture of which was not otherwise exempt from the requirement for an approved medicated feed application on the date of the enactment of this Act [Oct. 9, 1996], shall be deemed to hold a license for the manufacturing site identified in the approved medicated feed application. The revocation of license provisions of section 512(m)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(m)(4)], as amended by this Act, shall apply to such licenses. Such license shall expire within 18 months from the date of enactment of this Act unless the person submits to the Secretary a completed license application for the manufacturing site accompanied by a copy of an approved medicated feed application for such site, which license application shall be deemed to be approved upon receipt by the Secretary."

DRUGS PRIMARILY MANUFACTURED USING
BIOTECHNOLOGY

Pub. L. 100-670, title I, §106, Nov. 16, 1988, 102 Stat. 3984, provided that: "Notwithstanding section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(b)(2)], the Secretary of Health and Human Services may not approve an abbreviated application submitted under such section for a new animal drug which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques."

§ 360c. Classification of devices intended for human use

(a) Classes of devices

(1) There are established the following classes of devices intended for human use:

(A) CLASS I, GENERAL CONTROLS.—

(i) A device for which the controls authorized by or under section 351, 352, 360, 360f, 360h, 360i, or 360j of this title or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.

(ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it—

(I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

(II) does not present a potential unreasonable risk of illness or injury,

is to be regulated by the controls referred to in clause (i).

(B) CLASS II, SPECIAL CONTROLS.—A device which cannot be classified as a class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in pre-

market notification submissions in accordance with section 360(k) of this title), recommendations, and other appropriate actions as the Secretary deems necessary to provide such assurance. For a device that is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall examine and identify the special controls, if any, that are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide such assurance.

(C) CLASS III, PREMARKET APPROVAL.—A device which because—

(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and

(ii)(I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or

(II) presents a potential unreasonable risk of illness or injury,

is to be subject, in accordance with section 360e of this title, to premarket approval to provide reasonable assurance of its safety and effectiveness.

If there is not sufficient information to establish a performance standard for a device to provide reasonable assurance of its safety and effectiveness, the Secretary may conduct such activities as may be necessary to develop or obtain such information.

(2) For purposes of this section and sections 360d and 360e of this title, the safety and effectiveness of a device are to be determined—

(A) with respect to the persons for whose use the device is represented or intended,

(B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

(C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

(3)(A) Except as authorized by subparagraph (B), the effectiveness of a device is, for purposes of this section and sections 360d and 360e of this title, to be determined, in accordance with regulations promulgated by the Secretary, on the basis of well-controlled investigations, including 1 or more clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

(B) If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations described in subparagraph (A))—

(i) which is sufficient to determine the effectiveness of a device, and

(ii) from which it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device,

then, for purposes of this section and sections 360d and 360e of this title, the Secretary may authorize the effectiveness of the device to be determined on the basis of such evidence.

(C) In making a determination of a reasonable assurance of the effectiveness of a device for which an application under section 360e of this title has been submitted, the Secretary shall consider whether the extent of data that otherwise would be required for approval of the application with respect to effectiveness can be reduced through reliance on postmarket controls.

(D)(i) The Secretary, upon the written request of any person intending to submit an application under section 360e of this title, shall meet with such person to determine the type of valid scientific evidence (within the meaning of subparagraphs (A) and (B)) that will be necessary to demonstrate for purposes of approval of an application the effectiveness of a device for the conditions of use proposed by such person. The written request shall include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance from the device. Within 30 days after such meeting, the Secretary shall specify in writing the type of valid scientific evidence that will provide a reasonable assurance that a device is effective under the conditions of use proposed by such person.

(ii) Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval.

(iii) For purposes of clause (ii), the term “necessary” means the minimum required information that would support a determination by the Secretary that an application provides reasonable assurance of the effectiveness of the device.

(iv) Nothing in this subparagraph shall alter the criteria for evaluating an application for premarket approval of a device.

(v) The determination of the Secretary with respect to the specification of valid scientific evidence under clauses (i) and (ii) shall be binding upon the Secretary, unless such determination by the Secretary could be contrary to the public health.

(b) Classification panels

(1) For purposes of—

(A) determining which devices intended for human use should be subject to the require-

ments of general controls, performance standards, or premarket approval, and

(B) providing notice to the manufacturers and importers of such devices to enable them to prepare for the application of such requirements to devices manufactured or imported by them,

the Secretary shall classify all such devices (other than devices classified by subsection (f) of this section) into the classes established by subsection (a) of this section. For the purpose of securing recommendations with respect to the classification of devices, the Secretary shall establish panels of experts or use panels of experts established before May 28, 1976, or both. Section 14 of the Federal Advisory Committee Act shall not apply to the duration of a panel established under this paragraph.

(2) The Secretary shall appoint to each panel established under paragraph (1) persons who are qualified by training and experience to evaluate the safety and effectiveness of the devices to be referred to the panel and who, to the extent feasible, possess skill in the use of, or experience in the development, manufacture, or utilization of, such devices. The Secretary shall make appointments to each panel so that each panel shall consist of members with adequately diversified expertise in such fields as clinical and administrative medicine, engineering, biological and physical sciences, and other related professions. In addition, each panel shall include as non-voting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(3) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, but not at rates exceeding the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day so engaged, including traveltime; and while so serving away from their homes or regular places of business each member may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(4) The Secretary shall furnish each panel with adequate clerical and other necessary assistance.

(5) Classification panels covering each type of device shall be scheduled to meet at such times as may be appropriate for the Secretary to meet applicable statutory deadlines.

(6)(A) Any person whose device is specifically the subject of review by a classification panel shall have—

(i) the same access to data and information submitted to a classification panel (except for

data and information that are not available for public disclosure under section 552 of title 5) as the Secretary;

(ii) the opportunity to submit, for review by a classification panel, information that is based on the data or information provided in the application submitted under section 360e of this title by the person, which information shall be submitted to the Secretary for prompt transmittal to the classification panel; and

(iii) the same opportunity as the Secretary to participate in meetings of the panel.

(B) Any meetings of a classification panel shall provide adequate time for initial presentations and for response to any differing views by persons whose devices are specifically the subject of a classification panel review, and shall encourage free and open participation by all interested persons.

(7) After receiving from a classification panel the conclusions and recommendations of the panel on a matter that the panel has reviewed, the Secretary shall review the conclusions and recommendations, shall make a final decision on the matter in accordance with section 360e(d)(2) of this title, and shall notify the affected persons of the decision in writing and, if the decision differs from the conclusions and recommendations of the panel, shall include the reasons for the difference.

(8) A classification panel under this subsection shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.

(c) Classification panel organization and operation

(1) The Secretary shall organize the panels according to the various fields of clinical medicine and fundamental sciences in which devices intended for human use are used. The Secretary shall refer a device to be classified under this section to an appropriate panel established or authorized to be used under subsection (b) of this section for its review and for its recommendation respecting the classification of the device. The Secretary shall by regulation prescribe the procedure to be followed by the panels in making their reviews and recommendations. In making their reviews of devices, the panels, to the maximum extent practicable, shall provide an opportunity for interested persons to submit data and views on the classification of the devices.

(2)(A) Upon completion of a panel's review of a device referred to it under paragraph (1), the panel shall, subject to subparagraphs (B) and (C), submit to the Secretary its recommendation for the classification of the device. Any such recommendation shall (i) contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the recommendation is made, and (ii) to the extent practicable, include a recommendation for the assignment of a priority for the application of the requirements of section 360d or 360e of this title to a device recommended to be classified in class II or class III.

(B) A recommendation of a panel for the classification of a device in class I shall include a recommendation as to whether the device should be exempted from the requirements of section 360, 360i, or 360j(f) of this title.

(C) In the case of a device which has been referred under paragraph (1) to a panel, and which—

(i) is intended to be implanted in the human body or is purported or represented to be for a use in supporting or sustaining human life, and

(ii)(I) has been introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or

(II) is within a type of device which was so introduced or delivered before such date and is substantially equivalent to another device within that type,

such panel shall recommend to the Secretary that the device be classified in class III unless the panel determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. If a panel does not recommend that such a device be classified in class III, it shall in its recommendation to the Secretary for the classification of the device set forth the reasons for not recommending classification of the device in such class.

(3) The panels shall submit to the Secretary within one year of the date funds are first appropriated for the implementation of this section their recommendations respecting all devices of a type introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976.

(d) Panel recommendation; publication; priorities

(1) Upon receipt of a recommendation from a panel respecting a device, the Secretary shall publish in the Federal Register the panel's recommendation and a proposed regulation classifying such device and shall provide interested persons an opportunity to submit comments on such recommendation and the proposed regulation. After reviewing such comments, the Secretary shall, subject to paragraph (2), by regulation classify such device.

(2)(A) A regulation under paragraph (1) classifying a device in class I shall prescribe which, if any, of the requirements of section 360, 360i, or 360j(f) of this title shall not apply to the device. A regulation which makes a requirement of section 360, 360i, or 360j(f) of this title inapplicable to a device shall be accompanied by a statement of the reasons of the Secretary for making such requirement inapplicable.

(B) A device described in subsection (c)(2)(C) of this section shall be classified in class III unless the Secretary determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. A proposed regulation under paragraph (1) classifying such a device in a class other than class III shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for not classifying such device in such class and an identi-

fication of the risks to health (if any) presented by such device.

(3) In the case of devices classified in class II and devices classified under this subsection in class III and described in section 360e(b)(1) of this title the Secretary may establish priorities which, in his discretion, shall be used in applying sections 360d and 360e of this title, as appropriate, to such devices.

(e) Classification changes

(1)(A)(i) Based on new information respecting a device, the Secretary may, upon the initiative of the Secretary or upon petition of an interested person, change the classification of such device, and revoke, on account of the change in classification, any regulation or requirement in effect under section 360d or 360e of this title with respect to such device, by administrative order published in the Federal Register following publication of a proposed reclassification order in the Federal Register, a meeting of a device classification panel described in subsection (b), and consideration of comments to a public docket, notwithstanding subchapter II of chapter 5 of title 5. The proposed reclassification order published in the Federal Register shall set forth the proposed reclassification, and a substantive summary of the valid scientific evidence concerning the proposed reclassification, including—

(I) the public health benefit of the use of the device, and the nature and, if known, incidence of the risk of the device;

(II) in the case of a reclassification from class II to class III, why general controls pursuant to subsection (a)(1)(A) and special controls pursuant to subsection (a)(1)(B) together are not sufficient to provide a reasonable assurance of safety and effectiveness for such device; and

(III) in the case of reclassification from class III to class II, why general controls pursuant to subsection (a)(1)(A) and special controls pursuant to subsection (a)(1)(B) together are sufficient to provide a reasonable assurance of safety and effectiveness for such device.

(ii) An order under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 360d of this title for such device.

(B) Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.

(2) By an order issued under paragraph (1), the Secretary may change the classification of a device from class III—

(A) to class II if the Secretary determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls would not provide reasonable assurance of the safety and effectiveness of the device, or

(B) to class I if the Secretary determines that general controls would provide reasonable assurance of the safety and effectiveness of the device.

(f) Initial classification and reclassification of certain devices

(1) Any device intended for human use which was not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, is classified in class III unless—

(A) the device—

(i) is within a type of device (I) which was introduced or delivered for introduction into interstate commerce for commercial distribution before such date and which is to be classified pursuant to subsection (b) of this section, or (II) which was not so introduced or delivered before such date and has been classified in class I or II, and

(ii) is substantially equivalent to another device within such type;

(B) the Secretary in response to a petition submitted under paragraph (3) has classified such device in class I or II; or

(C) the device is classified pursuant to a request submitted under paragraph (2).

A device classified in class III under this paragraph shall be classified in that class until the effective date of an order of the Secretary under paragraph (2) or (3) classifying the device in class I or II.

(2)(A)(i) Any person who submits a report under section 360(k) of this title for a type of device that has not been previously classified under this chapter, and that is classified into class III under paragraph (1), may request, within 30 days after receiving written notice of such a classification, the Secretary to classify the device.

(ii) In lieu of submitting a report under section 360(k) of this title and submitting a request for classification under clause (i) for a device, if a person determines there is no legally marketed device upon which to base a determination of substantial equivalence (as defined in subsection (i)), a person may submit a request under this clause for the Secretary to classify the device.

(iii) Upon receipt of a request under clause (i) or (ii), the Secretary shall classify the device subject to the request under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1) within 120 days.

(iv) Notwithstanding clause (iii), the Secretary may decline to undertake a classification request submitted under clause (ii) if the Secretary identifies a legally marketed device that could provide a reasonable basis for review of substantial equivalence under paragraph (1), or when the Secretary determines that the device submitted is not of low-moderate risk or that general controls would be inadequate to control the risks and special controls to mitigate the risks cannot be developed.

(v) The person submitting the request for classification under this subparagraph may recommend to the Secretary a classification for the device and shall, if recommending classification in class II, include in the request an initial draft proposal for applicable special controls, as described in subsection (a)(1)(B), that are necessary, in conjunction with general controls, to provide reasonable assurance of safety and effec-

tiveness and a description of how the special controls provide such assurance. Any such request shall describe the device and provide detailed information and reasons for the recommended classification.

(B)(i) The Secretary shall by written order classify the device involved. Such classification shall be the initial classification of the device for purposes of paragraph (1) and any device classified under this paragraph shall be a predicate device for determining substantial equivalence under paragraph (1).

(ii) A device that remains in class III under this subparagraph shall be deemed to be adulterated within the meaning of section 351(f)(1)(B) of this title until approved under section 360e of this title or exempted from such approval under section 360j(g) of this title.

(C) Within 30 days after the issuance of an order classifying a device under this paragraph, the Secretary shall publish a notice in the Federal Register announcing such classification.

(3)(A) The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition.

(B)(i) Upon determining that a petition does not contain any deficiency which prevents the Secretary from making a decision on the petition, the Secretary may for good cause shown refer the petition to an appropriate panel established or authorized to be used under subsection (b) of this section. A panel to which such a petition has been referred shall not later than ninety days after the referral of the petition make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed. In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the panel shall recommend that the petition be denied unless the panel determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. If the panel recommends that such petition be approved, it shall in its recommendation to the Secretary set forth its reasons for such recommendation.

(ii) The requirements of paragraphs (1) and (2) of subsection (c) of this section (relating to opportunities for submission of data and views and recommendations respecting priorities and exemptions from sections 360, 360i, and 360j(f) of this title) shall apply with respect to consideration by panels of petitions submitted under subparagraph (A).

(C)(i) Within ninety days from the date the Secretary receives the recommendation of a panel respecting a petition (but not later than 210 days after the filing of such petition) the Secretary shall by order deny or approve the petition. If the Secretary approves the petition, the Secretary shall order the classification of the device into class I or class II in accordance with the criteria prescribed by subsection (a)(1)(A) or (a)(1)(B) of this section. In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall deny the petition unless the Secretary determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. An order approving such petition shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for approving the petition and an identification of the risks to health (if any) presented by the device to which such order applies.

(ii) The requirements of paragraphs (1) and (2)(A) of subsection (d) of this section (relating to publication of recommendations, opportunity for submission of comments, and exemption from sections 360, 360i, and 360j(f) of this title) shall apply with respect to action by the Secretary on petitions submitted under subparagraph (A).

(4) If a manufacturer reports to the Secretary under section 360(k) of this title that a device is substantially equivalent to another device—

(A) which the Secretary has classified as a class III device under subsection (b) of this section,

(B) which was introduced or delivered for introduction into interstate commerce for commercial distribution before December 1, 1990, and

(C) for which no final regulation requiring premarket approval has been promulgated under section 360e(b) of this title,

the manufacturer shall certify to the Secretary that the manufacturer has conducted a reasonable search of all information known or otherwise available to the manufacturer respecting such other device and has included in the report under section 360(k) of this title a summary of and a citation to all adverse safety and effectiveness data respecting such other device and respecting the device for which the section 360(k) report is being made and which has not been submitted to the Secretary under section 360i of this title. The Secretary may require the manufacturer to submit the adverse safety and effectiveness data described in the report.

(5) The Secretary may not withhold a determination of the initial classification of a device under paragraph (1) because of a failure to comply with any provision of this chapter unrelated to a substantial equivalence decision, including a finding that the facility in which the device is manufactured is not in compliance with good manufacturing requirements as set forth in regulations of the Secretary under section 360j(f) of this title (other than a finding that there is a substantial likelihood that the failure to comply with such regulations will potentially present a serious risk to human health).

(g) Information

Within sixty days of the receipt of a written request of any person for information respecting the class in which a device has been classified or the requirements applicable to a device under this chapter, the Secretary shall provide such person a written statement of the classification (if any) of such device and the requirements of this chapter applicable to the device.

(h) Definitions

For purposes of this section and sections 351, 360, 360d, 360e, 360f, 360i, and 360j of this title

(1) a reference to “general controls” is a reference to the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title,

(2) a reference to “class I”, “class II”, or “class III” is a reference to a class of medical devices described in subparagraph (A), (B), or (C) of subsection (a)(1) of this section, and

(3) a reference to a “panel under section 360c of this title” is a reference to a panel established or authorized to be used under this section.

(i) Substantial equivalence

(1)(A) For purposes of determinations of substantial equivalence under subsection (f) of this section and section 360j(l) of this title, the term “substantially equivalent” or “substantial equivalence” means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and that the Secretary by order has found that the device—

(i) has the same technological characteristics as the predicate device, or

(ii)(I) has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including appropriate clinical or scientific data if deemed necessary by the Secretary or a person accredited under section 360m of this title, that demonstrates that the device is as safe and effective as a legally marketed device, and (II) does not raise different questions of safety and effectiveness than the predicate device.

(B) For purposes of subparagraph (A), the term “different technological characteristics” means, with respect to a device being compared to a predicate device, that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device.

(C) To facilitate reviews of reports submitted to the Secretary under section 360(k) of this title, the Secretary shall consider the extent to which reliance on postmarket controls may expedite the classification of devices under subsection (f)(1) of this section.

(D)(i) Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such request, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly.

(ii) For purposes of clause (i), the term “necessary” means the minimum required information that would support a determination of substantial equivalence between a new device and a predicate device.

(iii) Nothing in this subparagraph shall alter the standard for determining substantial equivalence between a new device and a predicate device.

(E)(i) Any determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under section 360(k) of this title. However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices (in this subparagraph referred to as the “Director”) may require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an opportunity for consultation with the person who submitted such report, the Director determines and states in writing—

(I) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device; and

(II) that such use could cause harm.

(ii) Such determination shall—

(I) be provided to the person who submitted the report within 10 days from the date of the notification of the Director’s concerns regarding the proposed labeling;

(II) specify the limitations on the use of the device not included in the proposed labeling; and

(III) find the device substantially equivalent if the requirements of subparagraph (A) are met and if the labeling for such device conforms to the limitations specified in subclause (II).

(iii) The responsibilities of the Director under this subparagraph may not be delegated.

(F) Not later than 270 days after November 21, 1997, the Secretary shall issue guidance specifying the general principles that the Secretary will consider in determining when a specific intended use of a device is not reasonably included within a general use of such device for purposes of a determination of substantial equivalence under subsection (f) of this section or section 360j(l) of this title.

(2) A device may not be found to be substantially equivalent to a predicate device that has been removed from the market at the initiative of the Secretary or that has been determined to be misbranded or adulterated by a judicial order.

(3)(A) As part of a submission under section 360(k) of this title respecting a device, the person required to file a premarket notification under such section shall provide an adequate summary of any information respecting safety and effectiveness or state that such information will be made available upon request by any person.

(B) Any summary under subparagraph (A) respecting a device shall contain detailed information regarding data concerning adverse health

effects and shall be made available to the public by the Secretary within 30 days of the issuance of a determination that such device is substantially equivalent to another device.

(June 25, 1938, ch. 675, §513, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 540; amended Pub. L. 101-629, §§4(a), 5(a)-(c)(1), (3), 12(a), 18(a), Nov. 28, 1990, 104 Stat. 4515, 4517, 4518, 4523, 4528; Pub. L. 102-300, §6(e), June 16, 1992, 106 Stat. 240; Pub. L. 103-80, §3(s), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105-115, title II, §§205(a), (b), 206(b), (c), 207, 208, 217, Nov. 21, 1997, 111 Stat. 2336, 2337, 2339, 2340, 2350; Pub. L. 107-250, title II, §208, Oct. 26, 2002, 116 Stat. 1613; Pub. L. 112-144, title VI, §§602, 607-608(a)(2)(A), July 9, 2012, 126 Stat. 1051, 1054-1056.)

REFERENCES IN TEXT

The Federal Advisory Committee Act, referred to in subsec. (b)(1), (8), is Pub. L. 92-463, Oct. 6, 1972, 86 Stat. 770, as amended, which is set out in the Appendix to Title 5, Government Organization and Employees.

AMENDMENTS

2012—Subsec. (a)(3)(D)(iii) to (v). Pub. L. 112-144, §602(a), added cls. (iii) and (iv) and redesignated former cl. (iii) as (v).

Subsec. (e)(1). Pub. L. 112-144, §608(a)(1), amended par. (1) generally. Prior to amendment, par. (1) read as follows: “Based on new information respecting a device, the Secretary may, upon his own initiative or upon petition of an interested person, by regulation (A) change such device’s classification, and (B) revoke, because of the change in classification, any regulation or requirement in effect under section 360d or 360e of this title with respect to such device. In the promulgation of such a regulation respecting a device’s classification, the Secretary may secure from the panel to which the device was last referred pursuant to subsection (c) of this section a recommendation respecting the proposed change in the device’s classification and shall publish in the Federal Register any recommendation submitted to the Secretary by the panel respecting such change. A regulation under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 360d of this title for such device.”

Subsec. (e)(2). Pub. L. 112-144, §608(a)(2)(A), substituted “an order issued” for “regulation promulgated” in introductory provisions.

Subsec. (f)(1)(C). Pub. L. 112-144, §607(b), added subpar. (C).

Subsec. (f)(2)(A). Pub. L. 112-144, §607(a)(1)-(3), designated existing provisions as cl. (i), struck out “under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1) of this section. The person may, in the request, recommend to the Secretary a classification for the device. Any such request shall describe the device and provide detailed information and reasons for the recommended classification” before period at end, and added cls. (ii) to (v).

Subsec. (f)(2)(B)(i). Pub. L. 112-144, §607(a)(4), substituted “The Secretary” for “Not later than 60 days after the date of the submission of the request under subparagraph (A), the Secretary”.

Subsec. (i)(1)(D). Pub. L. 112-144, §602(b), designated existing provisions as cl. (i) and added cls. (ii) and (iii).

2002—Subsec. (i)(1)(E)(iv). Pub. L. 107-250 struck out cl. (iv) which read as follows: “This subparagraph has no legal effect after the expiration of the five-year period beginning on November 21, 1997.”

1997—Subsec. (a)(3)(A). Pub. L. 105-115, §217, substituted “1 or more clinical investigations” for “clinical investigations”.

Subsec. (a)(3)(C), (D). Pub. L. 105-115, §205(a), added subpars. (C) and (D).

Subsec. (b)(5) to (8). Pub. L. 105-115, §208, added pars. (5) to (8).

Subsec. (f)(1). Pub. L. 105-115, §207(1)(B), substituted “paragraph (2) or (3)” for “paragraph (2)” in closing provisions.

Subsec. (f)(1)(B). Pub. L. 105-115, §207(1)(A), substituted “paragraph (3)” for “paragraph (2)”.

Subsec. (f)(2) to (4). Pub. L. 105-115, §207(2), (3), added par. (2) and redesignated former pars. (2) and (3) as (3) and (4), respectively.

Subsec. (f)(5). Pub. L. 105-115, §206(b), added par. (5).

Subsec. (i)(1)(A)(ii). Pub. L. 105-115, §206(c)(1), substituted “appropriate clinical or scientific data” for “clinical data”, inserted “or a person accredited under section 360m of this title” after “Secretary”, and substituted “effectiveness” for “efficacy”.

Subsec. (i)(1)(C) to (E). Pub. L. 105-115, §205(b), added subpars. (C) to (E).

Subsec. (i)(1)(F). Pub. L. 105-115, §206(c)(2), added subpar. (F).

1993—Subsec. (b)(3). Pub. L. 103-80 substituted “5703” for “5703(b)”.

1992—Subsec. (f)(3). Pub. L. 102-300 redesignated clauses (i) to (iii) as subpars. (A) to (C), respectively, and substituted “the section 360(k) report” for “the 360(k) report” in closing provisions.

1990—Subsec. (a)(1)(A)(ii). Pub. L. 101-629, §5(a)(1), substituted “or to establish special controls” for “or to establish a performance standard”.

Subsec. (a)(1)(B). Pub. L. 101-629, §5(a)(2), amended subpar. (B) generally. Prior to amendment, subpar. (B) read as follows: “CLASS II, PERFORMANCE STANDARDS.— A device which cannot be classified as a class I device because the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, for which there is sufficient information to establish a performance standard to provide such assurance, and for which it is therefore necessary to establish for the device a performance standard under section 360d of this title to provide reasonable assurance of its safety and effectiveness.”

Subsec. (a)(1)(C)(i). Pub. L. 101-629, §5(a)(3), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: “it (I) cannot be classified as a class I device because insufficient information exists to determine that the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title are sufficient to provide reasonable assurance of the safety and effectiveness of the device and (II) cannot be classified as a class II device because insufficient information exists for the establishment of a performance standard to provide reasonable assurance of its safety and effectiveness, and”.

Subsec. (e). Pub. L. 101-629, §5(b), designated existing provisions as par. (1), redesignated cls. (1) and (2) as (A) and (B), respectively, and added par. (2).

Subsec. (f). Pub. L. 101-629, §5(c)(3), inserted “and reclassification” before “of” in heading.

Subsec. (f)(2)(A). Pub. L. 101-629, §5(c)(1), substituted “The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer” for “The manufacturer”.

Subsec. (f)(2)(B)(i). Pub. L. 101-629, §18(a), substituted “the Secretary may for good cause shown” for “the Secretary shall”.

Subsec. (f)(3). Pub. L. 101-629, §4(a), added par. (3).

Subsec. (i). Pub. L. 101-629, §12(a), added subsec. (i).

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

SHORT TITLE OF 1976 AMENDMENT

Pub. L. 94-295, §1(a), May 28, 1976, 90 Stat. 539, provided that: “This Act [enacting sections 360c to 360k,

379, and 379a of this title and section 3512 of Title 42, The Public Health and Welfare, and amending sections 321, 331, 334, 351, 352, 358, 360, 374, 379e, and 381 of this title and section 55 of Title 15, Commerce and Trade] may be cited as the ‘Medical Device Amendments of 1976’.”

REGULATIONS

Pub. L. 101-629, §12(b), Nov. 28, 1990, 104 Stat. 4524, provided that: “Within 12 months of the date of the enactment of this Act [Nov. 28, 1990], the Secretary of Health and Human Services shall issue regulations establishing the requirements of the summaries under section 513(i)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(i)(3)], as added by the amendment made by subsection (a).”

DEVICES RECLASSIFIED PRIOR TO JULY 9, 2012

Pub. L. 112-144, title VI, §608(a)(3), July 9, 2012, 126 Stat. 1056, provided that:

“(A) IN GENERAL.—The amendments made by this subsection [amending this section and sections 360d and 360g of this title] shall have no effect on a regulation promulgated with respect to the classification of a device under section 513(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(e)] prior to the date of enactment of this Act [July 9, 2012].

“(B) APPLICABILITY OF OTHER PROVISIONS.—In the case of a device reclassified under section 513(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360c(e)] by regulation prior to the date of enactment of this Act [July 9, 2012], section 517(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360g(a)(1)) shall apply to such regulation promulgated under section 513(e) of such Act with respect to such device in the same manner such section 517(a)(1) applies to an administrative order issued with respect to a device reclassified after the date of enactment of this Act.”

DAILY WEAR SOFT OR DAILY WEAR NONHYDROPHILIC PLASTIC CONTACT LENSES

Pub. L. 101-629, §4(b)(3), Nov. 28, 1990, 104 Stat. 4517, provided that:

“(A) Notwithstanding section 520(l)(5) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360j(l)(5)], the Secretary of Health and Human Services shall not retain any daily wear soft or daily wear nonhydrophilic plastic contact lens in class III under such Act [this chapter] unless the Secretary finds that it meets the criteria set forth in section 513(a)(1)(C) of such Act [21 U.S.C. 360c(a)(1)(C)]. The finding and the grounds for the finding shall be published in the Federal Register. For any such lens, the Secretary shall make the determination respecting reclassification required in section 520(l)(5)(B) of such Act within 24 months of the date of the enactment of this paragraph [Nov. 28, 1990].

“(B) The Secretary of Health and Human Services may by notice published in the Federal Register extend the two-year period prescribed by subparagraph (A) for a lens for an additional period not to exceed one year.

“(C)(i) Before classifying a lens in class II pursuant to subparagraph (A), the Secretary of Health and Human Services shall pursuant to section 513(a)(1)(B) of such Act assure that appropriate regulatory safeguards are in effect which provide reasonable assurance of the safety and effectiveness of such lens, including clinical and preclinical data if deemed necessary by the Secretary.

“(ii) Prior to classifying a lens in class I pursuant to subparagraph (A), the Secretary shall assure that appropriate regulatory safeguards are in effect which provide reasonable assurance of the safety and effectiveness of such lens, including clinical and preclinical data if deemed necessary by the Secretary.

“(D) Notwithstanding section 520(l)(5) of such Act, if the Secretary of Health and Human Services has not made the finding and published the finding required by subparagraph (A) within 36 months of the date of the enactment of this subparagraph [Nov. 28, 1990], the Secretary shall issue an order placing the lens in class II.

“(E) Any person adversely affected by a final regulation under this paragraph revising the classification of a lens may challenge the revision of the classification of such lens only by filing a petition under section 513(e) for a classification change.”

REFERENCES IN OTHER LAWS TO GS-16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS-16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, §101(c)(1)] of Pub. L. 101-509, set out in a note under section 5376 of Title 5.

§ 360c-1. Reporting

The Secretary of Health and Human Services shall annually post on the Internet Web site of the Food and Drug Administration—

(1) the number and type of class I and class II devices reclassified as class II or class III in the previous calendar year under section 360c(e)(1) of this title;

(2) the number and type of class II and class III devices reclassified as class I or class II in the previous calendar year under such section 360c(e)(1) of this title; and

(3) the number and type of devices reclassified in the previous calendar year under section 360e of this title.

(Pub. L. 112-144, title VI, §608(c), July 9, 2012, 126 Stat. 1059.)

CODIFICATION

Section was enacted as part of the Food and Drug Administration Safety and Innovation Act, and not as part of the Federal Food, Drug, and Cosmetic Act which comprises this chapter.

§ 360d. Performance standards

(a) Reasonable assurance of safe and effective performance; periodic evaluation

(1) The special controls required by section 360c(a)(1)(B) of this title shall include performance standards for a class II device if the Secretary determines that a performance standard is necessary to provide reasonable assurance of the safety and effectiveness of the device. A class III device may also be considered a class II device for purposes of establishing a standard for the device under subsection (b) of this section if the device has been reclassified as a class II device under an administrative order under section 360c(e) of this title (or a regulation promulgated under such section prior to July 9, 2012) but such order (or regulation) provides that the reclassification is not to take effect until the effective date of such a standard for the device.

(2) A performance standard established under subsection (b) of this section for a device—

(A) shall include provisions to provide reasonable assurance of its safe and effective performance;

(B) shall, where necessary to provide reasonable assurance of its safe and effective performance, include—

(i) provisions respecting the construction, components, ingredients, and properties of the device and its compatibility with power systems and connections to such systems,

(ii) provisions for the testing (on a sample basis or, if necessary, on an individual basis) of the device or, if it is determined that no other more practicable means are available to the Secretary to assure the conformity of the device to the standard, provisions for the testing (on a sample basis or, if necessary, on an individual basis) by the Secretary or by another person at the direction of the Secretary,

(iii) provisions for the measurement of the performance characteristics of the device,

(iv) provisions requiring that the results of each or of certain of the tests of the device required to be made under clause (ii) show that the device is in conformity with the portions of the standard for which the test or tests were required, and

(v) a provision requiring that the sale and distribution of the device be restricted but only to the extent that the sale and distribution of a device may be restricted under a regulation under section 360j(e) of this title; and

(C) shall, where appropriate, require the use and prescribe the form and content of labeling for the proper installation, maintenance, operation, and use of the device.

(3) The Secretary shall provide for periodic evaluation of performance standards established under subsection (b) of this section to determine if such standards should be changed to reflect new medical, scientific, or other technological data.

(4) In carrying out his duties under this subsection and subsection (b) of this section, the Secretary shall, to the maximum extent practicable—

(A) use personnel, facilities, and other technical support available in other Federal agencies,

(B) consult with other Federal agencies concerned with standard-setting and other nationally or internationally recognized standard-setting entities, and

(C) invite appropriate participation, through joint or other conferences, workshops, or other means, by informed persons representative of scientific, professional, industry, or consumer organizations who in his judgment can make a significant contribution.

(b) Establishment of a standard

(1)(A) The Secretary shall publish in the Federal Register a notice of proposed rulemaking for the establishment, amendment, or revocation of any performance standard for a device.

(B) A notice of proposed rulemaking for the establishment or amendment of a performance standard for a device shall—

(i) set forth a finding with supporting justification that the performance standard is appropriate and necessary to provide reasonable assurance of the safety and effectiveness of the device,

(ii) set forth proposed findings with respect to the risk of illness or injury that the performance standard is intended to reduce or eliminate,

(iii) invite interested persons to submit to the Secretary, within 30 days of the publica-

tion of the notice, requests for changes in the classification of the device pursuant to section 360c(e) of this title based on new information relevant to the classification, and

(iv) invite interested persons to submit an existing performance standard for the device, including a draft or proposed performance standard, for consideration by the Secretary.

(C) A notice of proposed rulemaking for the revocation of a performance standard shall set forth a finding with supporting justification that the performance standard is no longer necessary to provide reasonable assurance of the safety and effectiveness of a device.

(D) The Secretary shall provide for a comment period of not less than 60 days.

(2) If, after publication of a notice in accordance with paragraph (1), the Secretary receives a request for a change in the classification of the device, the Secretary shall, within 60 days of the publication of the notice, after consultation with the appropriate panel under section 360c of this title, either deny the request or give notice of an intent to initiate such change under section 360c(e) of this title.

(3)(A) After the expiration of the period for comment on a notice of proposed rulemaking published under paragraph (1) respecting a performance standard and after consideration of such comments and any report from an advisory committee under paragraph (5), the Secretary shall (i) promulgate a regulation establishing a performance standard and publish in the Federal Register findings on the matters referred to in paragraph (1), or (ii) publish a notice terminating the proceeding for the development of the standard together with the reasons for such termination. If a notice of termination is published, the Secretary shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

(B) A regulation establishing a performance standard shall set forth the date or dates upon which the standard shall take effect, but no such regulation may take effect before one year after the date of its publication unless (i) the Secretary determines that an earlier effective date is necessary for the protection of the public health and safety, or (ii) such standard has been established for a device which, effective upon the effective date of the standard, has been reclassified from class III to class II. Such date or dates shall be established so as to minimize, consistent with the public health and safety, economic loss to, and disruption or dislocation of, domestic and international trade.

(4)(A) The Secretary, upon his own initiative or upon petition of an interested person may by regulation, promulgated in accordance with the requirements of paragraphs (1), (2), and (3)(B) of this subsection, amend or revoke a performance standard.

(B) The Secretary may declare a proposed amendment of a performance standard to be effective on and after its publication in the Federal Register and until the effective date of any final action taken on such amendment if he determines that making it so effective is in the

public interest. A proposed amendment of a performance standard made so effective under the preceding sentence may not prohibit, during the period in which it is so effective, the introduction or delivery for introduction into interstate commerce of a device which conforms to such standard without the change or changes provided by such proposed amendment.

(5)(A) The Secretary—

(i) may on his own initiative refer a proposed regulation for the establishment, amendment, or revocation of a performance standard, or

(ii) shall, upon the request of an interested person which demonstrates good cause for referral and which is made before the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation,

to an advisory committee of experts, established pursuant to subparagraph (B), for a report and recommendation with respect to any matter involved in the proposed regulation which requires the exercise of scientific judgment. If a proposed regulation is referred under this subparagraph to an advisory committee, the Secretary shall provide the advisory committee with the data and information on which such proposed regulation is based. The advisory committee shall, within sixty days of the referral of a proposed regulation and after independent study of the data and information furnished to it by the Secretary and other data and information before it, submit to the Secretary a report and recommendation respecting such regulation, together with all underlying data and information and a statement of the reason or basis for the recommendation. A copy of such report and recommendation shall be made public by the Secretary.

(B) The Secretary shall establish advisory committees (which may not be panels under section 360c of this title) to receive referrals under subparagraph (A). The Secretary shall appoint as members of any such advisory committee persons qualified in the subject matter to be referred to the committee and of appropriately diversified professional background, except that the Secretary may not appoint to such a committee any individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter. Each such committee shall include as nonvoting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Members of an advisory committee who are not officers or employees of the United States, while attending conferences or meetings of their committee or otherwise serving at the request of the Secretary, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall

designate one of the members of each advisory committee to serve as chairman thereof. The Secretary shall furnish each advisory committee with clerical and other assistance, and shall by regulation prescribe the procedures to be followed by each such committee in acting on referrals made under subparagraph (A).

(c) Recognition of standard

(1)(A) In addition to establishing a performance standard under this section, the Secretary shall, by publication in the Federal Register, recognize all or part of an appropriate standard established by a nationally or internationally recognized standard development organization for which a person may submit a declaration of conformity in order to meet a premarket submission requirement or other requirement under this chapter to which such standard is applicable.

(B) If a person elects to use a standard recognized by the Secretary under subparagraph (A) to meet the requirements described in such subparagraph, the person shall provide a declaration of conformity to the Secretary that certifies that the device is in conformity with such standard. A person may elect to use data, or information, other than data required by a standard recognized under subparagraph (A) to meet any requirement regarding devices under this chapter.

(2) The Secretary may withdraw such recognition of a standard through publication of a notice in the Federal Register if the Secretary determines that the standard is no longer appropriate for meeting a requirement regarding devices under this chapter.

(3)(A) Subject to subparagraph (B), the Secretary shall accept a declaration of conformity that a device is in conformity with a standard recognized under paragraph (1) unless the Secretary finds—

(i) that the data or information submitted to support such declaration does not demonstrate that the device is in conformity with the standard identified in the declaration of conformity; or

(ii) that the standard identified in the declaration of conformity is not applicable to the particular device under review.

(B) The Secretary may request, at any time, the data or information relied on by the person to make a declaration of conformity with respect to a standard recognized under paragraph (1).

(C) A person making a declaration of conformity with respect to a standard recognized under paragraph (1) shall maintain the data and information demonstrating conformity of the device to the standard for a period of two years after the date of the classification or approval of the device by the Secretary or a period equal to the expected design life of the device, whichever is longer.

(June 25, 1938, ch. 675, §514, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 546; amended Pub. L. 94-460, title III, §304, Oct. 8, 1976, 90 Stat. 1960; Pub. L. 101-629, §§6(a), (b)(1), 18(b), Nov. 28, 1990, 104 Stat. 4519, 4528; Pub. L. 102-300, §6(g), June 16, 1992, 106 Stat. 241; Pub. L. 103-80,

§4(a)(1), Aug. 13, 1993, 107 Stat. 779; Pub. L. 105-115, title II, §204(a), (d), Nov. 21, 1997, 111 Stat. 2335, 2336; Pub. L. 112-144, title VI, §608(a)(2)(B), July 9, 2012, 126 Stat. 1056.)

AMENDMENTS

2012—Subsec. (a)(1). Pub. L. 112-144 substituted “under an administrative order under section 360c(e) of this title (or a regulation promulgated under such section prior to July 9, 2012) but such order (or regulation)” for “under a regulation under section 360c(e) of this title but such regulation”.

1997—Subsec. (a)(1). Pub. L. 105-115, §204(d)(1), substituted “under subsection (b) of this section” for “under this section”.

Subsec. (a)(2). Pub. L. 105-115, §204(d)(2), substituted “under subsection (b) of this section” for “under this section” in introductory provisions.

Subsec. (a)(3). Pub. L. 105-115, §204(d)(3), substituted “under subsection (b) of this section” for “under this section”.

Subsec. (a)(4). Pub. L. 105-115, §204(d)(4), substituted “this subsection and subsection (b) of this section” for “this section” in introductory provisions.

Subsec. (c). Pub. L. 105-115, §204(a), added subsec. (c).
1993—Subsec. (b)(4)(B), (5)(A)(ii). Pub. L. 103-80 amended directory language of Pub. L. 101-619, §18(b), identical to amendment by Pub. L. 102-300, §6(g)(1). See 1992 and 1990 Amendment notes below.

1992—Subsec. (b)(4)(B), (5)(A)(ii). Pub. L. 102-300 made technical corrections to directory language of Pub. L. 101-629, §18(b)(1), (2). See 1990 Amendment note below.

1990—Subsec. (a)(1). Pub. L. 101-629, §6(a)(1), substituted “The special controls required by section 360c(a)(1)(B) of this title shall include performance standards for a class II device if the Secretary determines that a performance standard is necessary to provide reasonable assurance of the safety and effectiveness of the device.” for “The Secretary may by regulation, promulgated in accordance with this section, establish a performance standard for a class II device.”

Subsec. (b). Pub. L. 101-629, §6(a)(2), (3), redesignated subsec. (g) as (b) and struck out former subsec. (b) which read as follows:

“(1) A proceeding for the development of a performance standard for a device shall be initiated by the Secretary by the publication in the Federal Register of notice of the opportunity to submit to the Secretary a request (within fifteen days of the date of the publication of the notice) for a change in the classification of the device based on new information relevant to its classification.

“(2) If, after publication of a notice pursuant to paragraph (1) the Secretary receives a request for a change in the device’s classification, he shall, within sixty days of the publication of such notice and after consultation with the appropriate panel under section 360c of this title, by order published in the Federal Register, either deny the request for change in classification or give notice of his intent to initiate such a change under section 360c(e) of this title.”

Subsec. (b)(1), (2). Pub. L. 101-629, §6(a)(4), amended pars. (1) and (2) generally. Prior to amendment, pars. (1) and (2) read as follows:

“(1)(A) After publication pursuant to subsection (c) of this section of a notice respecting a performance standard for a device, the Secretary shall either—

“(i) publish, in the Federal Register in a notice of proposed rulemaking, a proposed performance standard for the device (I) developed by an offeror under such notice and accepted by the Secretary, (II) developed under subsection (c)(4) of this section, (III) accepted by the Secretary under subsection (d) of this section, or (IV) developed by him under subsection (f) of this section, or

“(ii) issue a notice in the Federal Register that the proceeding is terminated together with the reasons for such termination.

“(B) If the Secretary issues under subparagraph (A)(ii) a notice of termination of a proceeding to estab-

lish a performance standard for a device, he shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

“(2) A notice of proposed rulemaking for the establishment of a performance standard for a device published under paragraph (1)(A)(i) shall set forth proposed findings with respect to the degree of the risk of illness or injury designed to be eliminated or reduced by the proposed standard and the benefit to the public from the device.”

Subsec. (b)(3)(A)(i). Pub. L. 101-629, §6(b)(1)(A), substituted “paragraph (1)” for “paragraph (2)”.

Subsec. (b)(4)(A). Pub. L. 101-629, §6(b)(1)(B), substituted “paragraphs (1), (2), and (3)(B)” for “paragraphs (2) and (3)(B)”.

Subsec. (b)(4)(B). Pub. L. 101-629, §18(b)(1), as amended by Pub. L. 102-300, §6(g)(1), (2), and Pub. L. 103-80, §4(a)(1), struck out “, after affording all interested persons an opportunity for an informal hearing,” after “if he determines”.

Subsec. (b)(5)(A)(ii). Pub. L. 101-629, §18(b)(2), as amended by Pub. L. 102-300, §6(g)(1), (3), and Pub. L. 103-80, §4(a)(1), substituted “which demonstrates good cause for referral and which is made before the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation,” for “unless the Secretary finds the request to be without good cause or the request is made after the expiration of the period for submission of comments on such proposed regulation refer such proposed regulation.”

Subsecs. (c) to (f). Pub. L. 101-629, §6(a)(2), struck out subsec. (c) relating to invitations for standards, subsec. (d) relating to acceptance of certain existing standards, subsec. (e) relating to acceptance of offers to develop standards, and subsec. (f) relating to development of standards by the Secretary after publication of notice inviting submissions or offers of standards.

Subsec. (g). Pub. L. 101-629, §6(a)(3), redesignated subsec. (g) as (b).

1976—Subsec. (a). Pub. L. 94-460 redesignated pars. (4) and (5) as (3) and (4), respectively. Section as originally enacted contained no par. (3).

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

REFERENCES IN OTHER LAWS TO GS-16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS-16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, §101(c)(1)] of Pub. L. 101-509, set out in a note under section 5376 of Title 5.

TERMINATION OF ADVISORY COMMITTEES

Advisory committees in existence on Jan. 5, 1973, to terminate not later than the expiration of the 2-year period following Jan. 5, 1973, and advisory committees established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless in the case of a committee established by the President or an officer of the Federal Government, such committee is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a committee established by Congress, its duration is otherwise provided by law. See section 14 of Pub. L. 92-463, Oct. 6, 1972, 86 Stat. 776, set out in the Appendix to Title 5, Government Organization and Employees.

§360e. Premarket approval

(a) General requirement

A class III device—

(1) which is subject to a¹ an order issued under subsection (b) (or a regulation promulgated under such subsection prior to July 9, 2012) ; or

(2) which is a class III device because of section 360c(f) of this title,

is required to have, unless exempt under section 360j(g) of this title, an approval under this section of an application for premarket approval or, as applicable, an approval under subsection (c)(2) of this section of a report seeking premarket approval.

(b) Order to require premarket approval

(1) In the case of a class III device which—

(A) was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976; or

(B) is (i) of a type so introduced or delivered, and (ii) is substantially equivalent to another device within that type,

the Secretary shall by administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5, require that such device have an approval under this section of an application for premarket approval. Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.

(2) A proposed order required under paragraph (1) shall contain—

(A) the proposed order;

(B) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved application for premarket approval and the benefit to the public from use of the device;

(C) opportunity for the submission of comments on the proposed order and the proposed findings; and

(D) opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

(3) After the expiration of the period for comment on a proposed order and proposed findings published under paragraph (2), consideration of comments submitted on such proposed order and findings, and a meeting of a device classification panel described in section 360c(b) of this title, the Secretary shall (A) issue an administrative order under paragraph (1) and publish in the Federal Register findings on the matters referred to in paragraph (2)(B), or (B) publish a notice terminating the proceeding for the issuance of the administrative order together with the reasons for such termination. If a notice of termination is published, the Secretary shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of

this title to reclassify the device subject to the proceeding terminated by such notice.

(c) Application for premarket approval

(1) Any person may file with the Secretary an application for premarket approval for a class III device. Such an application for a device shall contain—

(A) full reports of all information, published or known to or which should reasonably be known to the applicant, concerning investigations which have been made to show whether or not such device is safe and effective;

(B) a full statement of the components, ingredients, and properties and of the principle or principles of operation, of such device;

(C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device;

(D) an identifying reference to any performance standard under section 360d of this title which would be applicable to any aspect of such device if it were a class II device, and either adequate information to show that such aspect of such device fully meets such performance standard or adequate information to justify any deviation from such standard;

(E) such samples of such device and of components thereof as the Secretary may reasonably require, except that where the submission of such samples is impracticable or unduly burdensome, the requirement of this subparagraph may be met by the submission of complete information concerning the location of one or more such devices readily available for examination and testing;

(F) specimens of the labeling proposed to be used for such device;

(G) the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application); and

(H) such other information relevant to the subject matter of the application as the Secretary, with the concurrence of the appropriate panel under section 360c of this title, may require.

(2)(A) Any person may file with the Secretary a report seeking premarket approval for a class III device referred to in subsection (a) of this section that is a reprocessed single-use device. Such a report shall contain the following:

(i) The device name, including both the trade or proprietary name and the common or usual name.

(ii) The establishment registration number of the owner or operator submitting the report.

(iii) Actions taken to comply with performance standards under section 360d of this title.

(iv) Proposed labels, labeling, and advertising sufficient to describe the device, its intended use, and directions for use.

(v) Full reports of all information, published or known to or which should be reasonably known to the applicant, concerning investigations which have been made to show whether or not the device is safe or effective.

(vi) A description of the device's components, ingredients, and properties.

(vii) A full description of the methods used in, and the facilities and controls used for, the reprocessing and packing of the device.

¹ So in original.

(viii) Such samples of the device that the Secretary may reasonably require.

(ix) A financial certification or disclosure statement or both, as required by part 54 of title 21, Code of Federal Regulations.

(x) A statement that the applicant believes to the best of the applicant's knowledge that all data and information submitted to the Secretary are truthful and accurate and that no material fact has been omitted in the report.

(xi) Any additional data and information, including information of the type required in paragraph (1) for an application under such paragraph, that the Secretary determines is necessary to determine whether there is reasonable assurance of safety and effectiveness for the reprocessed device.

(xii) Validation data described in section 360(o)(1)(A) of this title that demonstrates that the reasonable assurance of the safety or effectiveness of the device will remain after the maximum number of times the device is reprocessed as intended by the person submitting such report.

(B) In the case of a class III device referred to in subsection (a) of this section that is a reprocessed single-use device:

(i) Subparagraph (A) of this paragraph applies in lieu of paragraph (1).

(ii) Subject to clause (i), the provisions of this section apply to a report under subparagraph (A) to the same extent and in the same manner as such provisions apply to an application under paragraph (1).

(iii) Each reference in other sections of this chapter to an application under this section, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a report under subparagraph (A).

(iv) Each reference in other sections of this chapter to a device for which an application under this section has been approved, or has been denied, suspended, or withdrawn, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a device for which a report under subparagraph (A) has been approved, or has been denied, suspended, or withdrawn, respectively.

(3) Upon receipt of an application meeting the requirements set forth in paragraph (1), the Secretary—

(A) may on the Secretary's own initiative, or

(B) shall, upon the request of an applicant unless the Secretary finds that the information in the application which would be reviewed by a panel substantially duplicates information which has previously been reviewed by a panel appointed under section 360c of this title,

refer such application to the appropriate panel under section 360c of this title for study and for submission (within such period as he may establish) of a report and recommendation respecting approval of the application, together with all underlying data and the reasons or basis for the recommendation. Where appropriate, the Secretary shall ensure that such panel includes, or consults with, one or more pediatric experts.

(4)(A) Prior to the submission of an application under this subsection, the Secretary shall

accept and review any portion of the application that the applicant and the Secretary agree is complete, ready, and appropriate for review, except that such requirement does not apply, and the Secretary has discretion whether to accept and review such portion, during any period in which, under section 379j(h) of this title, the Secretary does not have the authority to collect fees under section 379j(a) of this title.

(B) Each portion of a submission reviewed under subparagraph (A) and found acceptable by the Secretary shall not be further reviewed after receipt of an application that satisfies the requirements of paragraph (1), unless a significant issue of safety or effectiveness provides the Secretary reason to review such accepted portion.

(C) Whenever the Secretary determines that a portion of a submission under subparagraph (A) is unacceptable, the Secretary shall, in writing, provide to the applicant a description of any deficiencies in such portion and identify the information that is required to correct these deficiencies, unless the applicant is no longer pursuing the application.

(d) Action on application for premarket approval

(1)(A) As promptly as possible, but in no event later than one hundred and eighty days after the receipt of an application under subsection (c) of this section (except as provided in section 360j(l)(3)(D)(ii) of this title or unless, in accordance with subparagraph (B)(i), an additional period as agreed upon by the Secretary and the applicant), the Secretary, after considering the report and recommendation submitted under paragraph (2) of such subsection, shall—

(i) issue an order approving the application if he finds that none of the grounds for denying approval specified in paragraph (2) of this subsection applies; or

(ii) deny approval of the application if he finds (and sets forth the basis for such finding as part of or accompanying such denial) that one or more grounds for denial specified in paragraph (2) of this subsection apply.

In making the determination whether to approve or deny the application, the Secretary shall rely on the conditions of use included in the proposed labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, if the proposed labeling is neither false nor misleading. In determining whether or not such labeling is false or misleading, the Secretary shall fairly evaluate all material facts pertinent to the proposed labeling.

(B)(i) The Secretary may not enter into an agreement to extend the period in which to take action with respect to an application submitted for a device subject to a regulation promulgated under subsection (b) of this section unless he finds that the continued availability of the device is necessary for the public health.

(ii) An order approving an application for a device may require as a condition to such approval that the sale and distribution of the device be restricted but only to the extent that the sale and distribution of a device may be restricted under a regulation under section 360j(e) of this title.

(iii) The Secretary shall accept and review statistically valid and reliable data and any other

information from investigations conducted under the authority of regulations required by section 360j(g) of this title to make a determination of whether there is a reasonable assurance of safety and effectiveness of a device subject to a pending application under this section if—

(I) the data or information is derived from investigations of an earlier version of the device, the device has been modified during or after the investigations (but prior to submission of an application under subsection (c) of this section) and such a modification of the device does not constitute a significant change in the design or in the basic principles of operation of the device that would invalidate the data or information; or

(II) the data or information relates to a device approved under this section, is available for use under this chapter, and is relevant to the design and intended use of the device for which the application is pending.

(2) The Secretary shall deny approval of an application for a device if, upon the basis of the information submitted to the Secretary as part of the application and any other information before him with respect to such device, the Secretary finds that—

(A) there is a lack of a showing of reasonable assurance that such device is safe under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(B) there is a lack of a showing of reasonable assurance that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(C) the methods used in, or the facilities or controls used for, the manufacture, processing, packing, or installation of such device do not conform to the requirements of section 360j(f) of this title;

(D) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular; or

(E) such device is not shown to conform in all respects to a performance standard in effect under section 360d of this title compliance with which is a condition to approval of the application and there is a lack of adequate information to justify the deviation from such standard.

Any denial of an application shall, insofar as the Secretary determines to be practicable, be accompanied by a statement informing the applicant of the measures required to place such application in approvable form (which measures may include further research by the applicant in accordance with one or more protocols prescribed by the Secretary).

(3)(A)(i) The Secretary shall, upon the written request of an applicant, meet with the applicant, not later than 100 days after the receipt of an application that has been filed as complete under subsection (c) of this section, to discuss the review status of the application.

(ii) The Secretary shall, in writing and prior to the meeting, provide to the applicant a description of any deficiencies in the application that, at that point, have been identified by the Secretary based on an interim review of the en-

tire application and identify the information that is required to correct those deficiencies.

(iii) The Secretary shall notify the applicant promptly of—

(I) any additional deficiency identified in the application, or

(II) any additional information required to achieve completion of the review and final action on the application,

that was not described as a deficiency in the written description provided by the Secretary under clause (ii).

(B) The Secretary and the applicant may, by mutual consent, establish a different schedule for a meeting required under this paragraph.

(4) An applicant whose application has been denied approval may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such denial, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section, and any interested person may obtain review, in accordance with paragraph (1) or (2) of subsection (g) of this section, of an order of the Secretary approving an application.

(5) In order to provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions, the Secretary shall provide review priority for devices—

(A) representing breakthrough technologies,

(B) for which no approved alternatives exist,

(C) which offer significant advantages over existing approved alternatives, or

(D) the availability of which is in the best interest of the patients.

(6)(A)(i) A supplemental application shall be required for any change to a device subject to an approved application under this subsection that affects safety or effectiveness, unless such change is a modification in a manufacturing procedure or method of manufacturing and the holder of the approved application submits a written notice to the Secretary that describes in detail the change, summarizes the data or information supporting the change, and informs the Secretary that the change has been made under the requirements of section 360j(f) of this title.

(ii) The holder of an approved application who submits a notice under clause (i) with respect to a manufacturing change of a device may distribute the device 30 days after the date on which the Secretary receives the notice, unless the Secretary within such 30-day period notifies the holder that the notice is not adequate and describes such further information or action that is required for acceptance of such change. If the Secretary notifies the holder that a supplemental application is required, the Secretary shall review the supplement within 135 days after the receipt of the supplement. The time used by the Secretary to review the notice of the manufacturing change shall be deducted from the 135-day review period if the notice meets appropriate content requirements for pre-market approval supplements.

(B)(i) Subject to clause (ii), in reviewing a supplement to an approved application, for an incremental change to the design of a device that affects safety or effectiveness, the Secretary shall approve such supplement if—

(I) nonclinical data demonstrate that the design modification creates the intended additional capacity, function, or performance of the device; and

(II) clinical data from the approved application and any supplement to the approved application provide a reasonable assurance of safety and effectiveness for the changed device.

(ii) The Secretary may require, when necessary, additional clinical data to evaluate the design modification of the device to provide a reasonable assurance of safety and effectiveness.

(e) Withdrawal and temporary suspension of approval of application

(1) The Secretary shall, upon obtaining, where appropriate, advice on scientific matters from a panel or panels under section 360c of this title, and after due notice and opportunity for informal hearing to the holder of an approved application for a device, issue an order withdrawing approval of the application if the Secretary finds—

(A) that such device is unsafe or ineffective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(B) on the basis of new information before him with respect to such device, evaluated together with the evidence available to him when the application was approved, that there is a lack of a showing of reasonable assurance that the device is safe or effective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(C) that the application contained or was accompanied by an untrue statement of a material fact;

(D) that the applicant (i) has failed to establish a system for maintaining records, or has repeatedly or deliberately failed to maintain records or to make reports, required by an applicable regulation under section 360i(a) of this title, (ii) has refused to permit access to, or copying or verification of, such records as required by section 374 of this title, or (iii) has not complied with the requirements of section 360 of this title;

(E) on the basis of new information before him with respect to such device, evaluated together with the evidence before him when the application was approved, that the methods used in, or the facilities and controls used for, the manufacture, processing, packing, or installation of such device do not conform with the requirements of section 360j(f) of this title and were not brought into conformity with such requirements within a reasonable time after receipt of written notice from the Secretary of nonconformity;

(F) on the basis of new information before him, evaluated together with the evidence before him when the application was approved, that the labeling of such device, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary of such fact; or

(G) on the basis of new information before him, evaluated together with the evidence be-

fore him when the application was approved, that such device is not shown to conform in all respects to a performance standard which is in effect under section 360d of this title compliance with which was a condition to approval of the application and that there is a lack of adequate information to justify the deviation from such standard.

(2) The holder of an application subject to an order issued under paragraph (1) withdrawing approval of the application may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such withdrawal, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section.

(3) If, after providing an opportunity for an informal hearing, the Secretary determines there is reasonable probability that the continuation of distribution of a device under an approved application would cause serious, adverse health consequences or death, the Secretary shall by order temporarily suspend the approval of the application approved under this section. If the Secretary issues such an order, the Secretary shall proceed expeditiously under paragraph (1) to withdraw such application.

(f) Product development protocol

(1) In the case of a class III device which is required to have an approval of an application submitted under subsection (c) of this section, such device shall be considered as having such an approval if a notice of completion of testing conducted in accordance with a product development protocol approved under paragraph (4) has been declared completed under paragraph (6).

(2) Any person may submit to the Secretary a proposed product development protocol with respect to a device. Such a protocol shall be accompanied by data supporting it. If, within thirty days of the receipt of such a protocol, the Secretary determines that it appears to be appropriate to apply the requirements of this subsection to the device with respect to which the protocol is submitted, the Secretary—

(A) may, at the initiative of the Secretary, refer the proposed protocol to the appropriate panel under section 360c of this title for its recommendation respecting approval of the protocol; or

(B) shall so refer such protocol upon the request of the submitter, unless the Secretary finds that the proposed protocol and accompanying data which would be reviewed by such panel substantially duplicate a product development protocol and accompanying data which have previously been reviewed by such a panel.

(3) A proposed product development protocol for a device may be approved only if—

(A) the Secretary determines that it is appropriate to apply the requirements of this subsection to the device in lieu of the requirement of approval of an application submitted under subsection (c) of this section; and

(B) the Secretary determines that the proposed protocol provides—

(i) a description of the device and the changes which may be made in the device,

(ii) a description of the preclinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the commencement of clinical trials of the device, and (II) any permissible variations in preclinical trials and the results therefrom,

(iii) a description of the clinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the filing of a notice of completion of the requirements of the protocol, and (II) any permissible variations in such trials and the results therefrom,

(iv) a description of the methods to be used in, and the facilities and controls to be used for, the manufacture, processing, and, when relevant, packing and installation of the device,

(v) an identifying reference to any performance standard under section 360d of this title to be applicable to any aspect of such device,

(vi) if appropriate, specimens of the labeling proposed to be used for such device,

(vii) such other information relevant to the subject matter of the protocol as the Secretary, with the concurrence of the appropriate panel or panels under section 360c of this title, may require, and

(viii) a requirement for submission of progress reports and, when completed, records of the trials conducted under the protocol which records are adequate to show compliance with the protocol.

(4) The Secretary shall approve or disapprove a proposed product development protocol submitted under paragraph (2) within one hundred and twenty days of its receipt unless an additional period is agreed upon by the Secretary and the person who submitted the protocol. Approval of a protocol or denial of approval of a protocol is final agency action subject to judicial review under chapter 7 of title 5.

(5) At any time after a product development protocol for a device has been approved pursuant to paragraph (4), the person for whom the protocol was approved may submit a notice of completion—

(A) stating (i) his determination that the requirements of the protocol have been fulfilled and that, to the best of his knowledge, there is no reason bearing on safety or effectiveness why the notice of completion should not become effective, and (ii) the data and other information upon which such determination was made, and

(B) setting forth the results of the trials required by the protocol and all the information required by subsection (c)(1) of this section.

(6)(A) The Secretary may, after providing the person who has an approved protocol and opportunity for an informal hearing and at any time prior to receipt of notice of completion of such protocol, issue a final order to revoke such protocol if he finds that—

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ so substantially from the

results required by the protocol that further trials cannot be justified, or

(iii) the results of the trials conducted under the protocol or available new information do not demonstrate that the device tested under the protocol does not present an unreasonable risk to health and safety.

(B) After the receipt of a notice of completion of an approved protocol the Secretary shall, within the ninety-day period beginning on the date such notice is received, by order either declare the protocol completed or declare it not completed. An order declaring a protocol not completed may take effect only after the Secretary has provided the person who has the protocol opportunity for an informal hearing on the order. Such an order may be issued only if the Secretary finds—

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ substantially from the results required by the protocol, or

(iii) there is a lack of a showing of reasonable assurance of the safety and effectiveness of the device under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.

(C) A final order issued under subparagraph (A) or (B) shall be in writing and shall contain the reasons to support the conclusions thereof.

(7) At any time after a notice of completion has become effective, the Secretary may issue an order (after due notice and opportunity for an informal hearing to the person for whom the notice is effective) revoking the approval of a device provided by a notice of completion which has become effective as provided in subparagraph (B) if he finds that any of the grounds listed in subparagraphs (A) through (G) of subsection (e)(1) of this section apply. Each reference in such subparagraphs to an application shall be considered for purposes of this paragraph as a reference to a protocol and the notice of completion of such protocol, and each reference to the time when an application was approved shall be considered for purposes of this paragraph as a reference to the time when a notice of completion took effect.

(8) A person who has an approved protocol subject to an order issued under paragraph (6)(A) revoking such protocol, a person who has an approved protocol with respect to which an order under paragraph (6)(B) was issued declaring that the protocol had not been completed, or a person subject to an order issued under paragraph (7) revoking the approval of a device may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such order, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section.

(g) Review

(1) Upon petition for review of—

(A) an order under subsection (d) of this section approving or denying approval of an application or an order under subsection (e) of this section withdrawing approval of an application, or

(B) an order under subsection (f)(6)(A) of this section revoking an approved protocol, under subsection (f)(6)(B) of this section declaring that an approved protocol has not been completed, or under subsection (f)(7) of this section revoking the approval of a device,

the Secretary shall, unless he finds the petition to be without good cause or unless a petition for review of such order has been submitted under paragraph (2), hold a hearing, in accordance with section 554 of title 5, on the order. The panel or panels which considered the application, protocol, or device subject to such order shall designate a member to appear and testify at any such hearing upon request of the Secretary, the petitioner, or the officer conducting the hearing, but this requirement does not preclude any other member of the panel or panels from appearing and testifying at any such hearing. Upon completion of such hearing and after considering the record established in such hearing, the Secretary shall issue an order either affirming the order subject to the hearing or reversing such order and, as appropriate, approving or denying approval of the application, reinstating the application's approval, approving the protocol, or placing in effect a notice of completion.

(2)(A) Upon petition for review of—

(i) an order under subsection (d) of this section approving or denying approval of an application or an order under subsection (e) of this section withdrawing approval of an application, or

(ii) an order under subsection (f)(6)(A) of this section revoking an approved protocol, under subsection (f)(6)(B) of this section declaring that an approved protocol has not been completed, or under subsection (f)(7) of this section revoking the approval of a device,

the Secretary shall refer the application or protocol subject to the order and the basis for the order to an advisory committee of experts established pursuant to subparagraph (B) for a report and recommendation with respect to the order. The advisory committee shall, after independent study of the data and information furnished to it by the Secretary and other data and information before it, submit to the Secretary a report and recommendation, together with all underlying data and information and a statement of the reasons or basis for the recommendation. A copy of such report shall be promptly supplied by the Secretary to any person who petitioned for such referral to the advisory committee.

(B) The Secretary shall establish advisory committees (which may not be panels under section 360c of this title) to receive referrals under subparagraph (A). The Secretary shall appoint as members of any such advisory committee persons qualified in the subject matter to be referred to the committee and of appropriately diversified professional backgrounds, except that the Secretary may not appoint to such a committee any individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter. Members of an advisory committee (other than officers or employees of the United States), while attending conferences or meetings of their committee

or otherwise serving at the request of the Secretary, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent for grade GS-18 of the General Schedule for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall designate the chairman of an advisory committee from its members. The Secretary shall furnish each advisory committee with clerical and other assistance, and shall by regulation prescribe the procedures to be followed by each such committee in acting on referrals made under subparagraph (A).

(C) The Secretary shall make public the report and recommendation made by an advisory committee with respect to an application and shall by order, stating the reasons therefor, either affirm the order referred to the advisory committee or reverse such order and, if appropriate, approve or deny approval of the application, reinstate the application's approval, approve the protocol, or place in effect a notice of completion.

(h) Service of orders

Orders of the Secretary under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary, or (2) by mailing the order by registered mail or certified mail addressed to the applicant at his last known address in the records of the Secretary.

(i) Revision

(1) Before December 1, 1995, the Secretary shall by order require manufacturers of devices, which were introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, and which are subject to revision of classification under paragraph (2), to submit to the Secretary a summary of and citation to any information known or otherwise available to the manufacturer respecting such devices, including adverse safety or effectiveness information which has not been submitted under section 360i of this title. The Secretary may require the manufacturer to submit the adverse safety or effectiveness data for which a summary and citation were submitted, if such data are available to the manufacturer.

(2) After the issuance of an order under paragraph (1) but before the date that is 2 years after July 9, 2012, the Secretary shall issue an administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5, for each device—

(A) which the Secretary has classified as a class III device, and

(B) for which no administrative order has been issued under subsection (b) (or no regulation has been promulgated under such subsection prior to July 9, 2012),

revising the classification of the device so that the device is classified into class I or class II, unless the administrative order issued under this paragraph requires the device to remain in class III. In determining whether to revise the classification of a device or to require a device to remain in class III, the Secretary shall apply the criteria set forth in section 360c(a) of this title.

(3) The Secretary shall, as promptly as is reasonably achievable, but not later than 12 months after the effective date of the order requiring a device to remain in class III, establish a schedule for the issuance of an administrative order under subsection (b) for each device which is subject to the order requiring the device to remain in class III.

(June 25, 1938, ch. 675, §515, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 552; amended Pub. L. 101-629, §§4(b)(1), 9(a), 18(c), Nov. 28, 1990, 104 Stat. 4515, 4521, 4528; Pub. L. 103-80, §3(t), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105-115, title II, §§201(b), 202, 205(c), 209(b), 216(b), Nov. 21, 1997, 111 Stat. 2334, 2338, 2341, 2349; Pub. L. 107-250, title II, §§209, 210, title III, §302(c), Oct. 26, 2002, 116 Stat. 1613, 1614, 1618; Pub. L. 108-214, §2(d)(1), Apr. 1, 2004, 118 Stat. 576; Pub. L. 110-85, title VIII, §801(b)(3)(D), Sept. 27, 2007, 121 Stat. 921; Pub. L. 112-144, title II, §203(g), title VI, §608(b)(1), July 9, 2012, 126 Stat. 1006, 1056.)

AMENDMENTS

2012—Subsec. (a)(1). Pub. L. 112-144, §608(b)(1)(A), substituted “an order issued under subsection (b) (or a regulation promulgated under such subsection prior to July 9, 2012)” for “regulation promulgated under subsection (b)”.

Subsec. (b). Pub. L. 112-144, §608(b)(1)(B)(i)(I), which directed substitution of “Order” for “Regulation” in the heading of par. (1) of subsec. (b), was executed by making the substitution in the heading of subsec. (b), to reflect the probable intent of Congress.

Subsec. (b)(1). Pub. L. 112-144, §608(b)(1)(B)(i)(II), in concluding provisions, substituted “by administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5” for “by regulation, promulgated in accordance with this subsection” and inserted at end “Authority to issue such administrative order shall not be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the Commissioner.”

Subsec. (b)(2). Pub. L. 112-144, §608(b)(1)(B)(ii), struck out subpar. (A) designation after “(2)” and substituted “A proposed order required under paragraph (1) shall contain—” for “A proceeding for the promulgation of a regulation under paragraph (1) respecting a device shall be initiated by the publication in the Federal Register of a notice of proposed rulemaking. Such notice shall contain—” in introductory provisions, redesignated cls. (i) to (iv) as subpars. (A) to (D), respectively, substituted “order” for “regulation” in subpars. (A) and (C), and struck out former subpar. (B) which read as follows: “If, within fifteen days after publication of a notice under subparagraph (A), the Secretary receives a request for a change in the classification of a device, he shall, within sixty days of the publication of such notice and after consultation with the appropriate panel under section 360c of this title, by order published in the Federal Register, either deny the request for change in classification or give notice of his intent to

initiate such a change under section 360c(e) of this title.”

Subsec. (b)(3). Pub. L. 112-144, §608(b)(1)(B)(iii)(I), (II), (IV), (V), substituted “proposed order” for “proposed regulation” in two places, “paragraph (2),” for “paragraph (2) and after”, “(A) issue an administrative order under paragraph (1)” for “(A) promulgate such regulation”, “paragraph (2)(B)” for “paragraph (2)(A)(ii)”, and “issuance of the administrative order” for “promulgation of the regulation”.

Pub. L. 112-144, §608(b)(1)(B)(iii)(III), which directed insertion of “and a meeting of a device classification panel described in section 360c(b) of this title,” after “such proposed regulation and findings,” was inserted after “such proposed order and findings,” to reflect the probable intent of Congress and amendment by Pub. L. 112-144, §608(b)(1)(B)(iii)(I). See above.

Subsec. (b)(4). Pub. L. 112-144, §608(b)(1)(B)(iv), struck out par. (4) which read as follows: “The Secretary, upon his own initiative or upon petition of an interested person, may by regulation amend or revoke any regulation promulgated under this subsection. A regulation to amend or revoke a regulation under this subsection shall be promulgated in accordance with the requirements prescribed by this subsection for the promulgation of the regulation to be amended or revoked.”

Subsec. (c)(4)(A). Pub. L. 112-144, §203(g), substituted “379j(h)” for “379j(g)”.

Subsec. (i)(2). Pub. L. 112-144, §608(b)(1)(C)(i)(III), (IV), in concluding provisions, substituted “administrative order issued under this paragraph requires” for “regulation requires” and struck out at end “Before the publication of a regulation requiring a device to remain in class III or revising its classification, the Secretary shall publish a proposed regulation respecting the classification of a device under this paragraph and provide reasonable opportunity for the submission of comments on any such regulation. No regulation requiring a device to remain in class III or revising its classification may take effect before the expiration of 90 days from the date of its publication in the Federal Register as a proposed regulation.”

Pub. L. 112-144, §608(b)(1)(C)(i)(I), in introductory provisions, substituted “the date that is 2 years after July 9, 2012” for “December 1, 1995” and “issue an administrative order following publication of a proposed order in the Federal Register, a meeting of a device classification panel described in section 360c(b) of this title, and consideration of comments from all affected stakeholders, including patients, payors, and providers, notwithstanding subchapter II of chapter 5 of title 5,” for “publish a regulation in the Federal Register”.

Subsec. (i)(2)(B). Pub. L. 112-144, §608(b)(1)(C)(i)(II), substituted “administrative order has been issued under subsection (b) (or no regulation has been promulgated under such subsection prior to July 9, 2012)” for “final regulation has been promulgated under subsection (b) of this section”.

Subsec. (i)(3). Pub. L. 112-144, §608(b)(1)(C)(ii), substituted “order requiring” for “regulation requiring” in two places and “issuance of an administrative order under subsection (b)” for “promulgation of a subsection (b) of this section regulation”.

2007—Subsec. (c)(1)(G), (H). Pub. L. 110-85 added subpar. (G) and redesignated former subpar. (G) as (H).

2004—Subsec. (c)(3). Pub. L. 108-214, §2(d)(1)(B), amended directory language of Pub. L. 107-250, §210. See 2002 Amendment note below.

Pub. L. 108-214, §2(d)(1)(A)(i), redesignated par. (3) relating to acceptance and review of any portion of the application prior to submission as (4).

Subsec. (c)(4). Pub. L. 108-214, §2(d)(1)(A), redesignated par. (3) relating to acceptance and review of any portion of the application prior to submission as (4) and substituted “unless a significant issue of safety” for “unless an issue of safety” in subpar. (B).

2002—Subsec. (a). Pub. L. 107-250, §302(c)(1), inserted “or, as applicable, an approval under subsection (c)(2) of this section of a report seeking premarket approval” before period in concluding provisions.

Subsec. (c)(2). Pub. L. 107-250, §302(c)(2)(B), added par. (2). Former par. (2) redesignated (3).

Subsec. (c)(3). Pub. L. 107-250, §302(c)(2)(A), redesignated par. (2) relating to Secretary's referral of application to appropriate panel as (3).

Pub. L. 107-250, §210, as amended by Pub. L. 108-214, §2(d)(1)(B), inserted "Where appropriate, the Secretary shall ensure that such panel includes, or consults with, one or more pediatric experts." at the end of the concluding provisions of par. (3) as redesignated by Pub. L. 107-250, §302(c)(2)(A).

Pub. L. 107-250, §209, added par. (3) relating to acceptance and review of any portion of the application prior to submission.

1997—Subsec. (d)(1)(A). Pub. L. 105-115, §205(c)(1), inserted at end "In making the determination whether to approve or deny the application, the Secretary shall rely on the conditions of use included in the proposed labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, if the proposed labeling is neither false nor misleading. In determining whether or not such labeling is false or misleading, the Secretary shall fairly evaluate all material facts pertinent to the proposed labeling."

Subsec. (d)(1)(B)(iii). Pub. L. 105-115, §201(b), added cl. (iii).

Subsec. (d)(3), (4). Pub. L. 105-115, §202(1), 209(b), added par. (3) and redesignated former par. (3) as (4).

Subsec. (d)(5). Pub. L. 105-115, §202(2), added par. (5).

Subsec. (d)(6). Pub. L. 105-115, §205(c)(2), added par. (6).

Subsec. (f)(2). Pub. L. 105-115, §216(b), substituted "the Secretary—" and subpars. (A) and (B) for "he shall refer the proposed protocol to the appropriate panel under section 360c of this title for its recommendation respecting approval of the protocol."

1993—Subsec. (c)(2)(A). Pub. L. 103-80 struck out "refer such application" after "own initiative".

1990—Subsec. (c)(2). Pub. L. 101-629, §18(c), substituted "the Secretary—" for "the Secretary shall" and added subpars. (A) and (B).

Subsec. (e). Pub. L. 101-629, §9(a)(2), inserted "and temporary suspension" after "Withdrawal" in heading.

Subsec. (e)(3). Pub. L. 101-629, §9(a)(1), added par. (3).

Subsec. (i). Pub. L. 101-629, §4(b)(1), added subsec. (i).

EFFECTIVE DATE OF 2012 AMENDMENT

Amendment by section 203(g) of Pub. L. 112-144 effective Oct. 1, 2012, with additional provision for assessment of certain fees, see section 206 of Pub. L. 112-144, set out as a note under section 379i of this title.

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

TERMINATION OF ADVISORY COMMITTEES

Advisory committees in existence on Jan. 5, 1973, to terminate not later than the expiration of the 2-year period following Jan. 5, 1973, and advisory committees established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless in the case of a committee established by the President or an officer of the Federal Government, such committee is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a committee established by Congress, its duration is otherwise provided by law. See section 14 of Pub. L. 92-463, Oct. 6, 1972, 86 Stat. 776, set out in the Appendix to Title 5, Government Organization and Employees.

REPORT ON CERTAIN DEVICES

Pub. L. 107-250, title II, §205, Oct. 26, 2002, 116 Stat. 1612, directed the Secretary of Health and Human Services, not later than one year after Oct. 26, 2002, to report to the appropriate committees of Congress on the

timeliness and effectiveness of device premarket reviews by centers other than the Center for Devices and Radiological Health, including information on the times required to log in and review original submissions and supplements, times required to review manufacturers' replies to submissions, times to approve or clear such devices, and recommendations on improvement of performance and reassignment of responsibility for regulating such devices.

REFERENCES IN OTHER LAWS TO GS-16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS-16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, §101(c)(1)] of Pub. L. 101-509, set out in a note under section 5376 of Title 5.

§ 360e-1. Pediatric uses of devices

(a) New devices

(1) In general

A person that submits to the Secretary an application under section 360j(m) of this title, or an application (or supplement to an application) or a product development protocol under section 360e of this title, shall include in the application or protocol the information described in paragraph (2).

(2) Required information

The application or protocol described in paragraph (1) shall include, with respect to the device for which approval is sought and if readily available—

(A) a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure; and

(B) the number of affected pediatric patients.

(3) Annual report

Not later than 18 months after September 27, 2007, and annually thereafter, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report that includes—

(A) the number of devices approved in the year preceding the year in which the report is submitted, for which there is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose, or cure;

(B) the number of devices approved in the year preceding the year in which the report is submitted, labeled for use in pediatric patients;

(C) the number of pediatric devices approved in the year preceding the year in which the report is submitted, exempted from a fee pursuant to section 379j(a)(2)(B)(v) of this title; and

(D) the review time for each device described in subparagraphs (A), (B), and (C).

(b) Determination of pediatric effectiveness based on similar course of disease or condition or similar effect of device on adults

(1) In general

If the course of the disease or condition and the effects of the device are sufficiently simi-

lar in adults and pediatric patients, the Secretary may conclude that adult data may be used to support a determination of a reasonable assurance of effectiveness in pediatric populations, as appropriate.

(2) Extrapolation between subpopulations

A study may not be needed in each pediatric subpopulation if data from one subpopulation can be extrapolated to another subpopulation.

(c) Pediatric subpopulation

For purposes of this section, the term “pediatric subpopulation” has the meaning given the term in section 360j(m)(6)(E)(ii) of this title.

(June 25, 1938, ch. 675, §515A, as added Pub. L. 110-85, title III, §302, Sept. 27, 2007, 121 Stat. 859.)

FINAL RULE RELATING TO TRACKING OF PEDIATRIC USES OF DEVICES

Pub. L. 112-144, title VI, §620(b), July 9, 2012, 126 Stat. 1064, provided that: “The Secretary of Health and Human Services shall issue—

“(1) a proposed rule implementing section 515A(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e-1(a)(2)) not later than December 31, 2012; and

“(2) a final rule implementing such section not later than December 31, 2013.”

§ 360f. Banned devices

(a) General rule

Whenever the Secretary finds, on the basis of all available data and information, that—

(1) a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury; and

(2) in the case of substantial deception or an unreasonable and substantial risk of illness or injury which the Secretary determined could be corrected or eliminated by labeling or change in labeling and with respect to which the Secretary provided written notice to the manufacturer specifying the deception or risk of illness or injury, the labeling or change in labeling to correct the deception or eliminate or reduce such risk, and the period within which such labeling or change in labeling was to be done, such labeling or change in labeling was not done within such period;

he may initiate a proceeding to promulgate a regulation to make such device a banned device.

(b) Special effective date

The Secretary may declare a proposed regulation under subsection (a) of this section to be effective upon its publication in the Federal Register and until the effective date of any final action taken respecting such regulation if (1) he determines, on the basis of all available data and information, that the deception or risk of illness or injury associated with the use of the device which is subject to the regulation presents an unreasonable, direct, and substantial danger to the health of individuals, and (2) before the date of the publication of such regulation, the Secretary notifies the manufacturer of such device that such regulation is to be made so effective. If the Secretary makes a proposed regulation so effective, he shall, as expeditiously as possible, give interested persons prompt notice of his action under this subsection, provide

reasonable opportunity for an informal hearing on the proposed regulation, and either affirm, modify, or revoke such proposed regulation.

(June 25, 1938, ch. 675, §516, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 560; amended Pub. L. 101-629, §18(d), Nov. 28, 1990, 104 Stat. 4529.)

AMENDMENTS

1990—Subsec. (a). Pub. L. 101-629 struck out “and after consultation with the appropriate panel or panels under section 360c of this title” after “data and information” in introductory provisions and struck out at end “The Secretary shall afford all interested persons opportunity for an informal hearing on a regulation proposed under this subsection.”

§ 360g. Judicial review

(a) Petition; record

Not later than thirty days after—

(1) the promulgation of a regulation under section 360c of this title classifying a device in class I, an administrative order changing the classification of a device to class I, or an order under subsection (f)(2) of such section reclassifying a device or denying a petition for reclassification of a device,

(2) the promulgation of a regulation under section 360d of this title establishing, amending, or revoking a performance standard for a device,

(3) the issuance of an order under section 360d(b)(2) or 360e(b)(2)(B) of this title denying a request for reclassification of a device,

(4) the promulgation of a regulation under paragraph (3) of section 360e(b) of this title requiring a device to have an approval of a pre-market application, a regulation under paragraph (4) of that section amending or revoking a regulation under paragraph (3), or an order pursuant to section 360e(g)(1) or 360e(g)(2)(C) of this title,

(5) the promulgation of a regulation under section 360f of this title (other than a proposed regulation made effective under subsection (b) of such section upon the regulation’s publication) making a device a banned device,

(6) the issuance of an order under section 360j(f)(2) of this title,

(7) an order under section 360j(g)(4) of this title disapproving an application for an exemption of a device for investigational use or an order under section 360j(g)(5) of this title withdrawing such an exemption for a device,

(8) an order pursuant to section 360c(i) of this title, or

(9) a regulation under section 360e(i)(2) or 360j(l)(5)(B) of this title,

any person adversely affected by such regulation or order may file a petition with the United States Court of Appeals for the District of Columbia or for the circuit wherein such person resides or has his principal place of business for judicial review of such regulation or order. A copy of the petition shall be transmitted by the clerk of the court to the Secretary or other officer designated by him for that purpose. The Secretary shall file in the court the record of the proceedings on which the Secretary based his regulation or order as provided in section 2112 of

title 28. For purposes of this section, the term “record” means all notices and other matter published in the Federal Register with respect to the regulation or order reviewed, all information submitted to the Secretary with respect to such regulation or order, proceedings of any panel or advisory committee with respect to such regulation or order, any hearing held with respect to such regulation or order, and any other information identified by the Secretary, in the administrative proceeding held with respect to such regulation or order, as being relevant to such regulation or order.

(b) Additional data, views, and arguments

If the petitioner applies to the court for leave to adduce additional data, views, or arguments respecting the regulation or order being reviewed and shows to the satisfaction of the court that such additional data, views, or arguments are material and that there were reasonable grounds for the petitioner’s failure to adduce such data, views, or arguments in the proceedings before the Secretary, the court may order the Secretary to provide additional opportunity for the oral presentation of data, views, or arguments and for written submissions. The Secretary may modify his findings, or make new findings by reason of the additional data, views, or arguments so taken and shall file with the court such modified or new findings, and his recommendation, if any, for the modification or setting aside of the regulation or order being reviewed, with the return of such additional data, views, or arguments.

(c) Standard for review

Upon the filing of the petition under subsection (a) of this section for judicial review of a regulation or order, the court shall have jurisdiction to review the regulation or order in accordance with chapter 7 of title 5 and to grant appropriate relief, including interim relief, as provided in such chapter. A regulation described in paragraph (2) or (5) of subsection (a) of this section and an order issued after the review provided by section 360e(g) of this title shall not be affirmed if it is found to be unsupported by substantial evidence on the record taken as a whole.

(d) Finality of judgments

The judgment of the court affirming or setting aside, in whole or in part, any regulation or order shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification, as provided in section 1254 of title 28.

(e) Remedies

The remedies provided for in this section shall be in addition to and not in lieu of any other remedies provided by law.

(f) Statement of reasons

To facilitate judicial review under this section or under any other provision of law of a regulation or order issued under section 360c, 360d, 360e, 360f, 360h, 360i, 360j, or 360k of this title each such regulation or order shall contain a statement of the reasons for its issuance and the basis, in the record of the proceedings held in connection with its issuance, for its issuance.

(June 25, 1938, ch. 675, §517, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 560; amended Pub. L. 101-629, §13, Nov. 28, 1990, 104 Stat. 4524; Pub. L. 102-300, §6(f), June 16, 1992, 106 Stat. 240; Pub. L. 105-115, title II, §216(a)(2), Nov. 21, 1997, 111 Stat. 2349; Pub. L. 112-144, title VI, §608(a)(2)(C), July 9, 2012, 126 Stat. 1056.)

AMENDMENTS

2012—Subsec. (a)(1). Pub. L. 112-144 substituted “, an administrative order changing the classification of a device to class I,” for “or changing the classification of a device to class I”.

1997—Subsec. (a)(8). Pub. L. 105-115, §216(a)(2)(A), inserted “or” at end.

Subsec. (a)(9). Pub. L. 105-115, §216(a)(2)(B), substituted comma for “, or” at end.

Subsec. (a)(10). Pub. L. 105-115, §216(a)(2)(C), struck out par. (10) which read as follows: “an order under section 360j(h)(4)(B) of this title.”

1992—Subsec. (a)(10). Pub. L. 102-300 substituted “360j(h)(4)(B)” for “360j(c)(4)(B)”.

1990—Subsec. (a)(8) to (10). Pub. L. 101-629 added pars. (8) to (10).

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

§ 360g-1. Agency documentation and review of significant decisions regarding devices

(a) Documentation of rationale for significant decisions

(1) In general

The Secretary shall provide a substantive summary of the scientific and regulatory rationale for any significant decision of the Center for Devices and Radiological Health regarding submission or review of a report under section 360(k) of this title, an application under section 360e of this title, or an application for an exemption under section 360j(g) of this title, including documentation of significant controversies or differences of opinion and the resolution of such controversies or differences of opinion.

(2) Provision of documentation

Upon request, the Secretary shall furnish such substantive summary to the person who is seeking to submit, or who has submitted, such report or application.

(b) Review of significant decisions

(1) Request for supervisory review of significant decision

Any person may request a supervisory review of the significant decision described in subsection (a)(1). Such review may be conducted at the next supervisory level or higher above the individual who made the significant decision.

(2) Submission of request

A person requesting a supervisory review under paragraph (1) shall submit such request to the Secretary not later than 30 days after such decision and shall indicate in the request whether such person seeks an in-person meeting or a teleconference review.

(3) Timeframe**(A) In general**

Except as provided in subparagraph (B), the Secretary shall schedule an in-person or teleconference review, if so requested, not later than 30 days after such request is made. The Secretary shall issue a decision to the person requesting a review under this subsection not later than 45 days after the request is made under paragraph (1), or, in the case of a person who requests an in-person meeting or teleconference, 30 days after such meeting or teleconference.

(B) Exception

Subparagraph (A) shall not apply in cases that are referred to experts outside of the Food and Drug Administration.

(June 25, 1938, ch. 675, §517A, as added Pub. L. 112-144, title VI, §603, July 9, 2012, 126 Stat. 1051.)

§ 360h. Notification and other remedies**(a) Notification**

If the Secretary determines that—

(1) a device intended for human use which is introduced or delivered for introduction into interstate commerce for commercial distribution presents an unreasonable risk of substantial harm to the public health, and

(2) notification under this subsection is necessary to eliminate the unreasonable risk of such harm and no more practicable means is available under the provisions of this chapter (other than this section) to eliminate such risk,

the Secretary may issue such order as may be necessary to assure that adequate notification is provided in an appropriate form, by the persons and means best suited under the circumstances involved, to all health professionals who prescribe or use the device and to any other person (including manufacturers, importers, distributors, retailers, and device users) who should properly receive such notification in order to eliminate such risk. An order under this subsection shall require that the individuals subject to the risk with respect to which the order is to be issued be included in the persons to be notified of the risk unless the Secretary determines that notice to such individuals would present a greater danger to the health of such individuals than no such notification. If the Secretary makes such a determination with respect to such individuals, the order shall require that the health professionals who prescribe or use the device provide for the notification of the individuals whom the health professionals treated with the device of the risk presented by the device and of any action which may be taken by or on behalf of such individuals to eliminate or reduce such risk. Before issuing an order under this subsection, the Secretary shall consult with the persons who are to give notice under the order.

(b) Repair, replacement, or refund

(1)(A) If, after affording opportunity for an informal hearing, the Secretary determines that—

(i) a device intended for human use which is introduced or delivered for introduction into

interstate commerce for commercial distribution presents an unreasonable risk of substantial harm to the public health,

(ii) there are reasonable grounds to believe that the device was not properly designed or manufactured with reference to the state of the art as it existed at the time of its design or manufacture,

(iii) there are reasonable grounds to believe that the unreasonable risk was not caused by failure of a person other than a manufacturer, importer, distributor, or retailer of the device to exercise due care in the installation, maintenance, repair, or use of the device, and

(iv) the notification authorized by subsection (a) of this section would not by itself be sufficient to eliminate the unreasonable risk and action described in paragraph (2) of this subsection is necessary to eliminate such risk,

the Secretary may order the manufacturer, importer, or any distributor of such device, or any combination of such persons, to submit to him within a reasonable time a plan for taking one or more of the actions described in paragraph (2). An order issued under the preceding sentence which is directed to more than one person shall specify which person may decide which action shall be taken under such plan and the person specified shall be the person who the Secretary determines bears the principal, ultimate financial responsibility for action taken under the plan unless the Secretary cannot determine who bears such responsibility or the Secretary determines that the protection of the public health requires that such decision be made by a person (including a device user or health professional) other than the person he determines bears such responsibility.

(B) The Secretary shall approve a plan submitted pursuant to an order issued under subparagraph (A) unless he determines (after affording opportunity for an informal hearing) that the action or actions to be taken under the plan or the manner in which such action or actions are to be taken under the plan will not assure that the unreasonable risk with respect to which such order was issued will be eliminated. If the Secretary disapproves a plan, he shall order a revised plan to be submitted to him within a reasonable time. If the Secretary determines (after affording opportunity for an informal hearing) that the revised plan is unsatisfactory or if no revised plan or no initial plan has been submitted to the Secretary within the prescribed time, the Secretary shall (i) prescribe a plan to be carried out by the person or persons to whom the order issued under subparagraph (A) was directed, or (ii) after affording an opportunity for an informal hearing, by order prescribe a plan to be carried out by a person who is a manufacturer, importer, distributor, or retailer of the device with respect to which the order was issued but to whom the order under subparagraph (A) was not directed.

(2) The actions which may be taken under a plan submitted under an order issued under paragraph (1) are as follows:

(A) To repair the device so that it does not present the unreasonable risk of substantial harm with respect to which the order under paragraph (1) was issued.

(B) To replace the device with a like or equivalent device which is in conformity with all applicable requirements of this chapter.

(C) To refund the purchase price of the device (less a reasonable allowance for use if such device has been in the possession of the device user for one year or more—

(i) at the time of notification ordered under subsection (a) of this section, or

(ii) at the time the device user receives actual notice of the unreasonable risk with respect to which the order was issued under paragraph (1),

whichever first occurs).

(3) No charge shall be made to any person (other than a manufacturer, importer, distributor or retailer) for availing himself of any remedy, described in paragraph (2) and provided under an order issued under paragraph (1), and the person subject to the order shall reimburse each person (other than a manufacturer, importer, distributor, or retailer) who is entitled to such a remedy for any reasonable and foreseeable expenses actually incurred by such person in availing himself of such remedy.

(c) Reimbursement

An order issued under subsection (b) of this section with respect to a device may require any person who is a manufacturer, importer, distributor, or retailer of the device to reimburse any other person who is a manufacturer, importer, distributor, or retailer of such device for such other person's expenses actually incurred in connection with carrying out the order if the Secretary determines such reimbursement is required for the protection of the public health. Any such requirement shall not affect any rights or obligations under any contract to which the person receiving reimbursement or the person making such reimbursement is a party.

(d) Effect on other liability

Compliance with an order issued under this section shall not relieve any person from liability under Federal or State law. In awarding damages for economic loss in an action brought for the enforcement of any such liability, the value to the plaintiff in such action of any remedy provided him under such order shall be taken into account.

(e) Recall authority

(1) If the Secretary finds that there is a reasonable probability that a device intended for human use would cause serious, adverse health consequences or death, the Secretary shall issue an order requiring the appropriate person (including the manufacturers, importers, distributors, or retailers of the device)—

(A) to immediately cease distribution of such device, and

(B) to immediately notify health professionals and device user facilities of the order and to instruct such professionals and facilities to cease use of such device.

The order shall provide the person subject to the order with an opportunity for an informal hearing, to be held not later than 10 days after the date of the issuance of the order, on the actions

required by the order and on whether the order should be amended to require a recall of such device. If, after providing an opportunity for such a hearing, the Secretary determines that inadequate grounds exist to support the actions required by the order, the Secretary shall vacate the order.

(2)(A) If, after providing an opportunity for an informal hearing under paragraph (1), the Secretary determines that the order should be amended to include a recall of the device with respect to which the order was issued, the Secretary shall, except as provided in subparagraphs (B) and (C), amend the order to require a recall. The Secretary shall specify a timetable in which the device recall will occur and shall require periodic reports to the Secretary describing the progress of the recall.

(B) An amended order under subparagraph (A)—

(i) shall—

(I) not include recall of a device from individuals, and

(II) not include recall of a device from device user facilities if the Secretary determines that the risk of recalling such device from the facilities presents a greater health risk than the health risk of not recalling the device from use, and

(ii) shall provide for notice to individuals subject to the risks associated with the use of such device.

In providing the notice required by clause (ii), the Secretary may use the assistance of health professionals who prescribed or used such a device for individuals. If a significant number of such individuals cannot be identified, the Secretary shall notify such individuals pursuant to section 375(b) of this title.

(3) The remedy provided by this subsection shall be in addition to remedies provided by subsections (a), (b), and (c) of this section.

(June 25, 1938, ch. 675, §518, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 562; amended Pub. L. 101-629, §8, Nov. 28, 1990, 104 Stat. 4520; Pub. L. 102-300, §4, June 16, 1992, 106 Stat. 239.)

AMENDMENTS

1992—Subsec. (b)(1)(A)(ii). Pub. L. 102-300 substituted “or” for “and” after “properly designed” and “time of its design”.

1990—Subsec. (e). Pub. L. 101-629 added subsec. (e).

§ 360h-1. Program to improve the device recall system

(a) In general

The Secretary shall—

(1) establish a program to routinely and systematically assess information relating to device recalls and use such information to proactively identify strategies for mitigating health risks presented by defective or unsafe devices;

(2) clarify procedures for conducting device recall audit checks to improve the ability of investigators to perform those checks in a consistent manner;

(3) develop detailed criteria for assessing whether a person performing a device recall

has performed an effective correction or action plan for the recall; and

(4) document the basis for each termination by the Food and Drug Administration of a device recall.

(b) Assessment content

The program established under subsection (a)(1) shall, at a minimum, identify—

(1) trends in the number and types of device recalls;

(2) devices that are most frequently the subject of a recall; and

(3) underlying causes of device recalls.

(c) Termination of recalls

The Secretary shall document the basis for the termination by the Food and Drug Administration of a device recall.

(d) Definition

In this section, the term “recall” means—

(1) the removal from the market of a device pursuant to an order of the Secretary under subsection (b) or (e) of section 360h of this title; or

(2) the correction or removal from the market of a device at the initiative of the manufacturer or importer of the device that is required to be reported to the Secretary under section 360i(g) of this title.

(June 25, 1938, ch. 675, §518A, as added Pub. L. 112-144, title VI, §605, July 9, 2012, 126 Stat. 1053.)

§ 360i. Records and reports on devices

(a) General rule

Every person who is a manufacturer or importer of a device intended for human use shall establish and maintain such records, make such reports, and provide such information, as the Secretary may by regulation reasonably require to assure that such device is not adulterated or misbranded and to otherwise assure its safety and effectiveness. Regulations prescribed under the preceding sentence—

(1) shall require a device manufacturer or importer to report to the Secretary whenever the manufacturer or importer receives or otherwise becomes aware of information that reasonably suggests that one of its marketed devices—

(A) may have caused or contributed to a death or serious injury, or

(B) has malfunctioned and that such device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, which report under this subparagraph—

(i) shall be submitted in accordance with part 803 of title 21, Code of Federal Regulations (or successor regulations), unless the Secretary grants an exemption or variance from, or an alternative to, a requirement under such regulations pursuant to section 803.19 of such part, if the device involved is—

(I) a class III device;

(II) a class II device that is permanently implantable, is life supporting, or is life sustaining; or

(III) a type of device which the Secretary has, by notice published in the Federal Register or letter to the person who is the manufacturer or importer of the device, indicated should be subject to such part 803 in order to protect the public health;

(ii) shall, if the device is not subject to clause (i), be submitted in accordance with criteria established by the Secretary for reports made pursuant to this clause, which criteria shall require the reports to be in summary form and made on a quarterly basis; or

(iii) shall, if the device is imported into the United States and for which part 803 of title 21, Code of Federal Regulations (or successor regulations) requires an importer to submit a report to the manufacturer, be submitted by the importer to the manufacturer in accordance with part 803 of title 21, Code of Federal Regulations (or successor regulations)¹

(2) shall define the term “serious injury” to mean an injury that—

(A) is life threatening,

(B) results in permanent impairment of a body function or permanent damage to a body structure, or

(C) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure;

(3) shall require reporting of other significant adverse device experiences as determined by the Secretary to be necessary to be reported;

(4) shall not impose requirements unduly burdensome to a device manufacturer or importer taking into account his cost of complying with such requirements and the need for the protection of the public health and the implementation of this chapter;

(5) which prescribe the procedure for making requests for reports or information shall require that each request made under such regulations for submission of a report or information to the Secretary state the reason or purpose for such request and identify to the fullest extent practicable such report or information;

(6) which require submission of a report or information to the Secretary shall state the reason or purpose for the submission of such report or information and identify to the fullest extent practicable such report or information;

(7) may not require that the identity of any patient be disclosed in records, reports, or information required under this subsection unless required for the medical welfare of an individual, to determine the safety or effectiveness of a device, or to verify a record, report, or information submitted under this chapter; and

(8) may not require a manufacturer or importer of a class I device to—

¹ So in original. Probably should be followed by a semicolon.

(A) maintain for such a device records respecting information not in the possession of the manufacturer or importer, or

(B) to submit for such a device to the Secretary any report or information—

- (i) not in the possession of the manufacturer or importer, or
- (ii) on a periodic basis,

unless such report or information is necessary to determine if the device should be reclassified or if the device is adulterated or misbranded, and²

In prescribing such regulations, the Secretary shall have due regard for the professional ethics of the medical profession and the interests of patients. The prohibitions of paragraph (7) of this subsection continue to apply to records, reports, and information concerning any individual who has been a patient, irrespective of whether or when he ceases to be a patient. The Secretary shall by regulation require distributors to keep records and make such records available to the Secretary upon request. Paragraphs (4) and (8) apply to distributors to the same extent and in the same manner as such paragraphs apply to manufacturers and importers.

(b) User reports

(1)(A) Whenever a device user facility receives or otherwise becomes aware of information that reasonably suggests that a device has or may have caused or contributed to the death of a patient of the facility, the facility shall, as soon as practicable but not later than 10 working days after becoming aware of the information, report the information to the Secretary and, if the identity of the manufacturer is known, to the manufacturer of the device. In the case of deaths, the Secretary may by regulation prescribe a shorter period for the reporting of such information.

(B) Whenever a device user facility receives or otherwise becomes aware of—

- (i) information that reasonably suggests that a device has or may have caused or contributed to the serious illness of, or serious injury to, a patient of the facility, or
- (ii) other significant adverse device experiences as determined by the Secretary by regulation to be necessary to be reported,

the facility shall, as soon as practicable but not later than 10 working days after becoming aware of the information, report the information to the manufacturer of the device or to the Secretary if the identity of the manufacturer is not known.

(C) Each device user facility shall submit to the Secretary on an annual basis a summary of the reports made under subparagraphs (A) and (B). Such summary shall be submitted on January 1 of each year. The summary shall be in such form and contain such information from such reports as the Secretary may require and shall include—

- (i) sufficient information to identify the facility which made the reports for which the summary is submitted,
- (ii) in the case of any product which was the subject of a report, the product name, serial number, and model number,

(iii) the name and the address of the manufacturer of such device, and

(iv) a brief description of the event reported to the manufacturer.

(D) For purposes of subparagraphs (A), (B), and (C), a device user facility shall be treated as having received or otherwise become aware of information with respect to a device of that facility when medical personnel who are employed by or otherwise formally affiliated with the facility receive or otherwise become aware of information with respect to that device in the course of their duties.

(2) The Secretary may not disclose the identity of a device user facility which makes a report under paragraph (1) except in connection with—

(A) an action brought to enforce section 331(q) of this title, or

(B) a communication to a manufacturer of a device which is the subject of a report under paragraph (1).

This paragraph does not prohibit the Secretary from disclosing the identity of a device user facility making a report under paragraph (1) or any information in such a report to employees of the Department of Health and Human Services, to the Department of Justice, or to the duly authorized committees and subcommittees of the Congress.

(3) No report made under paragraph (1) by—

- (A) a device user facility,
- (B) an individual who is employed by or otherwise formally affiliated with such a facility, or
- (C) a physician who is not required to make such a report,

shall be admissible into evidence or otherwise used in any civil action involving private parties unless the facility, individual, or physician who made the report had knowledge of the falsity of the information contained in the report.

(4) A report made under paragraph (1) does not affect any obligation of a manufacturer who receives the report to file a report as required under subsection (a) of this section.

(5) With respect to device user facilities:

(A) The Secretary shall by regulation plan and implement a program under which the Secretary limits user reporting under paragraphs (1) through (4) to a subset of user facilities that constitutes a representative profile of user reports for device deaths and serious illnesses or serious injuries.

(B) During the period of planning the program under subparagraph (A), paragraphs (1) through (4) continue to apply.

(C) During the period in which the Secretary is providing for a transition to the full implementation of the program, paragraphs (1) through (4) apply except to the extent that the Secretary determines otherwise.

(D) On and after the date on which the program is fully implemented, paragraphs (1) through (4) do not apply to a user facility unless the facility is included in the subset referred to in subparagraph (A).

(E) Not later than 2 years after November 21, 1997, the Secretary shall submit to the Committee on Commerce of the House of Rep-

²So in original. The word "and" probably should not appear.

representatives, and to the Committee on Labor and Human Resources of the Senate, a report describing the plan developed by the Secretary under subparagraph (A) and the progress that has been made toward the implementation of the plan.

(6) For purposes of this subsection:

(A) The term “device user facility” means a hospital, ambulatory surgical facility, nursing home, or outpatient treatment facility which is not a physician’s office. The Secretary may by regulation include an outpatient diagnostic facility which is not a physician’s office in such term.

(B) The terms “serious illness” and “serious injury” mean illness or injury, respectively, that—

- (i) is life threatening,
- (ii) results in permanent impairment of a body function or permanent damage to a body structure, or
- (iii) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

(c) Persons exempt

Subsection (a) of this section shall not apply to—

(1) any practitioner who is licensed by law to prescribe or administer devices intended for use in humans and who manufactures or imports devices solely for use in the course of his professional practice;

(2) any person who manufactures or imports devices intended for use in humans solely for such person’s use in research or teaching and not for sale (including any person who uses a device under an exemption granted under section 360j(g) of this title); and

(3) any other class of persons as the Secretary may by regulation exempt from subsection (a) of this section upon a finding that compliance with the requirements of such subsection by such class with respect to a device is not necessary to (A) assure that a device is not adulterated or misbranded or (B) otherwise to assure its safety and effectiveness.

(d) Repealed. Pub. L. 105-115, title II, § 213(a)(2), Nov. 21, 1997, 111 Stat. 2347

(e) Device tracking

(1) The Secretary may by order require a manufacturer to adopt a method of tracking a class II or class III device—

(A) the failure of which would be reasonably likely to have serious adverse health consequences; or

(B) which is—

- (i) intended to be implanted in the human body for more than one year, or
- (ii) a life sustaining or life supporting device used outside a device user facility.

(2) Any patient receiving a device subject to tracking under paragraph (1) may refuse to release, or refuse permission to release, the patient’s name, address, social security number, or other identifying information for the purpose of tracking.

(f) Unique device identification system

Not later than December 31, 2012, the Secretary shall issue proposed regulations estab-

lishing a unique device identification system for medical devices requiring the label of devices to bear a unique identifier, unless the Secretary requires an alternative placement or provides an exception for a particular device or type of device. The unique identifier shall adequately identify the device through distribution and use, and may include information on the lot or serial number. The Secretary shall finalize the proposed regulations not later than 6 months after the close of the comment period and shall implement the final regulations with respect to devices that are implantable, life-saving, and life sustaining not later than 2 years after the regulations are finalized, taking into account patient access to medical devices and therapies.

(g) Reports of removals and corrections

(1) Except as provided in paragraph (2), the Secretary shall by regulation require a manufacturer or importer of a device to report promptly to the Secretary any correction or removal of a device undertaken by such manufacturer or importer if the removal or correction was undertaken—

(A) to reduce a risk to health posed by the device, or

(B) to remedy a violation of this chapter caused by the device which may present a risk to health.

A manufacturer or importer of a device who undertakes a correction or removal of a device which is not required to be reported under this paragraph shall keep a record of such correction or removal.

(2) No report of the corrective action or removal of a device may be required under paragraph (1) if a report of the corrective action or removal is required and has been submitted under subsection (a) of this section.

(3) For purposes of paragraphs (1) and (2), the terms “correction” and “removal” do not include routine servicing.

(h) Inclusion of devices in the postmarket risk identification and analysis system

(1) In general

(A) Application to devices

The Secretary shall amend the procedures established and maintained under clauses (i), (ii), (iii), and (v) of section 355(k)(3)(C) of this title in order to expand the postmarket risk identification and analysis system established under such section to include and apply to devices.

(B) Exception

Subclause (II) of clause (i) of section 355(k)(3)(C) of this title shall not apply to devices.

(C) Clarification

With respect to devices, the private sector health-related electronic data provided under section 355(k)(3)(C)(i)(III)(bb) of this title may include medical device utilization data, health insurance claims data, and procedure and device registries.

(2) Data

In expanding the system as described in paragraph (1)(A), the Secretary shall use rel-

evant data with respect to devices cleared under section 360(k) of this title or approved under section 360e of this title, including claims data, patient survey data, and any other data deemed appropriate by the Secretary.

(3) Stakeholder input

To help ensure effective implementation of the system as described in paragraph (1) with respect to devices, the Secretary shall engage outside stakeholders in development of the system, and gather information from outside stakeholders regarding the content of an effective sentinel program, through a public hearing, advisory committee meeting, maintenance of a public docket, or other similar public measures.

(4) Voluntary surveys

Chapter 35 of title 44 shall not apply to the collection of voluntary information from health care providers, such as voluntary surveys or questionnaires, initiated by the Secretary for purposes of postmarket risk identification, mitigation, and analysis for devices.

(June 25, 1938, ch. 675, §519, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 564; amended Pub. L. 101-629, §§2(a), 3(a)(1), (b)(1), 7, Nov. 28, 1990, 104 Stat. 4511, 4513, 4514, 4520; Pub. L. 102-300, §5(a), June 16, 1992, 106 Stat. 239; Pub. L. 103-80, §3(u), Aug. 13, 1993, 107 Stat. 778; Pub. L. 105-115, title II, §§211, 213(a), (c), Nov. 21, 1997, 111 Stat. 2345-2347; Pub. L. 110-85, title II, §§226(a), 227, Sept. 27, 2007, 121 Stat. 854; Pub. L. 112-144, title VI, §§614, 615, July 9, 2012, 126 Stat. 1061.)

AMENDMENTS

2012—Subsec. (f). Pub. L. 112-144, §614, substituted “Not later than December 31, 2012, the Secretary shall issue proposed” for “The Secretary shall promulgate” and inserted at end “The Secretary shall finalize the proposed regulations not later than 6 months after the close of the comment period and shall implement the final regulations with respect to devices that are implantable, life-saving, and life sustaining not later than 2 years after the regulations are finalized, taking into account patient access to medical devices and therapies.”

Subsec. (h). Pub. L. 112-144, §615, added subsec. (h).

2007—Subsec. (a)(1)(B). Pub. L. 110-85, §227, substituted “were to recur, which report under this subparagraph—” for “were to recur;” and added cls. (i) to (iii).

Subsecs. (f), (g). Pub. L. 110-85, §226(a), added subsec. (f) and redesignated former subsec. (f) as (g).

1997—Subsec. (a). Pub. L. 105-115, §213(a)(1)(A), (F), in introductory provisions, substituted “manufacturer or importer” for “manufacturer, importer, or distributor” and, in closing provisions, inserted at end “The Secretary shall by regulation require distributors to keep records and make such records available to the Secretary upon request. Paragraphs (4) and (8) apply to distributors to the same extent and in the same manner as such paragraphs apply to manufacturers and importers.”

Subsec. (a)(4). Pub. L. 105-115, §213(a)(1)(B), substituted “manufacturer or importer” for “manufacturer, importer, or distributor”.

Subsec. (a)(7). Pub. L. 105-115, §213(a)(1)(C), inserted “and” after semicolon at end.

Subsec. (a)(8). Pub. L. 105-115, §213(a)(1)(D), substituted “manufacturer or importer” for “manufacturer, importer, or distributor” wherever appearing and substituted period for semicolon after “misbranded”.

Subsec. (a)(9). Pub. L. 105-115, §213(a)(1)(E), struck out par. (9) which read as follows: “shall require distributors who submit such reports to submit copies of the reports to the manufacturer of the device for which the report was made.”

Subsec. (b)(1)(C). Pub. L. 105-115, §213(c)(1)(A), in introductory provisions, substituted “on an annual basis” for “on a semi-annual basis” and struck out “and July 1” after “January 1” and struck out closing provisions which read as follows: “The Secretary may by regulation alter the frequency and timing of reports required by this subparagraph.”

Subsec. (b)(2)(A). Pub. L. 105-115, §213(c)(1)(B)(i), inserted “or” after comma at end.

Subsec. (b)(2)(B). Pub. L. 105-115, §213(c)(1)(B)(ii), substituted period for “, or” at end.

Subsec. (b)(2)(C). Pub. L. 105-115, §213(c)(1)(B)(iii), struck out subpar. (C) which read as follows: “a disclosure required under subsection (a) of this section.”

Subsec. (b)(5), (6). Pub. L. 105-115, §213(c)(2), added par. (5) and redesignated former par. (5) as (6).

Subsec. (d). Pub. L. 105-115, §213(a)(2), struck out heading and text of subsec. (d). Text read as follows: “Each manufacturer, importer, and distributor required to make reports under subsection (a) of this section shall submit to the Secretary annually a statement certifying that—

“(1) the manufacturer, importer, or distributor did file a certain number of such reports, or

“(2) the manufacturer, importer, or distributor did not file any report under subsection (a) of this section.”

Subsec. (e). Pub. L. 105-115, §211, amended heading and text of subsec. (e) generally. Prior to amendment, text read as follows: “Every person who registers under section 360 of this title and is engaged in the manufacture of—

“(1) a device the failure of which would be reasonably likely to have serious adverse health consequences and which is (A) a permanently implantable device, or (B) a life sustaining or life supporting device used outside a device user facility, or

“(2) any other device which the Secretary may designate, shall adopt a method of device tracking.”

Subsec. (f)(1). Pub. L. 105-115, §213(a)(3), substituted “or importer” for “, importer, or distributor” wherever appearing.

1993—Subsec. (a). Pub. L. 103-80 substituted “paragraph (7)” for “paragraph (4)” in last sentence.

1992—Subsec. (a). Pub. L. 102-300, §5(a)(1), added pars. (1) to (3) and redesignated former pars. (1) to (6) as (4) to (9), respectively.

Subsec. (b)(1)(A). Pub. L. 102-300, §5(a)(2)(A), substituted “a device has or may have” for “there is a probability that a device has”.

Subsec. (b)(1)(B). Pub. L. 102-300, §5(a)(2)(A), (B), substituted “a device has or may have” for “there is a probability that a device has”, designated existing provisions as cl. (i), and added cl. (ii).

Subsec. (b)(5)(B)(iii). Pub. L. 102-300, §5(a)(2)(C), struck out “immediate” before “medical”.

1990—Subsec. (a)(6). Pub. L. 101-629, §3(a)(1), added par. (6).

Subsecs. (b), (c). Pub. L. 101-629, §2(a), added subsec. (b) and redesignated former subsec. (b) as (c).

Subsecs. (d), (e). Pub. L. 101-629, §3(b)(1), added subsecs. (d) and (e).

Subsec. (f). Pub. L. 101-629, §7, added subsec. (f).

CHANGE OF NAME

Committee on Labor and Human Resources of Senate changed to Committee on Health, Education, Labor, and Pensions of Senate by Senate Resolution No. 20, One Hundred Sixth Congress, Jan. 19, 1999.

EFFECTIVE DATE OF 1997 AMENDMENT

Pub. L. 105-115, title II, §211, Nov. 21, 1997, 111 Stat. 2345, provided in part that the amendment made by that section is effective 90 days after Nov. 21, 1997.

Amendment by section 213(a), (c) of Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1992 AMENDMENT

Pub. L. 102-300, §2(b), June 16, 1992, 106 Stat. 238, provided that: "The amendments made by subsection (a) [amending sections 3(b)(3) and 3(c) of Pub. L. 101-629, set out as notes below] shall take effect as of May 27, 1992 and any rule to implement section 519(e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(e)] proposed under section 3(c)(2) of the Safe Medical Devices Act of 1990 [Pub. L. 101-629, set out as a note below] shall revert to its proposed status as of such date."

Pub. L. 102-300, §5(b), June 16, 1992, 106 Stat. 240, provided that: "The amendments made by subsection (a) [amending this section] shall take effect—

- "(1) 1 year after the date of the enactment of this Act [June 16, 1992]; or
- "(2) on the effective date of regulations of the Secretary to implement such amendments, whichever occurs first."

EFFECTIVE DATE OF 1990 AMENDMENT

Pub. L. 101-629, §2(c), Nov. 28, 1990, 104 Stat. 4513, provided that: "Section 519(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(b)], as added by the amendment made by subsection (a), shall take effect—

- "(1) upon the effective date of regulations promulgated under subsection (b) [set out below], or
- "(2) upon the expiration of 12 months from the date of the enactment of this Act [Nov. 28, 1990], whichever occurs first."

Pub. L. 101-629, §3(a)(2), Nov. 28, 1990, 104 Stat. 4514, provided that: "Section 519(a)(6) [21 U.S.C. 360i(a)(6)], as added by the amendment made by paragraph (1), shall take effect upon the effective date of final regulations under subsection (c) [set out below]."

Pub. L. 101-629, §3(b)(3), Nov. 28, 1990, 104 Stat. 4514, as amended by Pub. L. 102-300, §2(a)(1), June 16, 1992, 106 Stat. 238, provided that: "Section 519(e) [21 U.S.C. 360i(e)], as added by the amendment made by paragraph (1), shall take effect upon the expiration of 9 months after the issuance of final regulations under subsection (c) [set out below]."

[For effective date of amendment by Pub. L. 102-300, see section 2(b) of Pub. L. 102-300, set out above as an Effective Date of 1992 Amendment note.]

REGULATIONS

Pub. L. 101-629, §2(b), Nov. 28, 1990, 104 Stat. 4512, provided that: "The Secretary of Health and Human Services shall promulgate regulations to implement section 519(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(b)], as added by the amendment made by subsection (a) (including a definition of the summary required by paragraph (1)(C) of such section) not later than 12 months after the date of enactment of this Act [Nov. 28, 1990]. In promulgating the regulations, the Secretary shall minimize the administrative burdens on device user facilities consistent with the need to assure adequate information."

Pub. L. 101-629, §3(c), Nov. 28, 1990, 104 Stat. 4514, as amended by Pub. L. 102-300, §2(a)(2), (3), June 16, 1992, 106 Stat. 238, provided that:

"(1)(A) Not later than 9 months after the date of the enactment of this Act [Nov. 28, 1990], the Secretary of Health and Human Services shall issue proposed regulations—

- "(i) to require distributors of devices to establish and maintain records and to make reports (including reports required by part 803 of title 21 of the Code of Federal Regulations) under section 519(a)(6) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360i(a)(6)], and
- "(ii) to implement section 519(e) of such Act.

The Secretary may exempt from regulations described in clause (i) classes of distributors of class I and class

II devices from whom reports are not necessary for the protection of the public health.

"(B) Regulations under subparagraph (A) shall—

"(i) require appropriate methods for maintenance of records to ensure that patients who receive devices can be provided the notification required by such Act [this chapter],

"(ii) require that manufacturers adopt effective methods of tracking devices,

"(iii) take into account the position of distributors in the device distribution process, and

"(iv) include such other requirements as the Secretary deems necessary for the adoption of an effective user tracking program under section 519(e) of such Act.

"(2) Not later than 18 months after the date of the enactment of this Act, the Secretary shall issue final regulations to implement sections [sic] 519(a)(6) of the Federal Food, Drug, and Cosmetic Act. If the Secretary does not promulgate such final regulations upon the expiration of such 18 months, the Congress finds that there is good cause for the proposed regulations to be considered as the final regulations without response to comment because the implementation of sections [sic] 519(a)(6) of such Act is essential to protect the health of patients who use such devices. Consequently, in such event, the proposed regulations issued under paragraph (1) shall become final regulations as of the expiration of such 18 months. There shall be promptly published in the Federal Register notice of the new status of the proposed regulations.

"(3) Not later than November 28, 1992, the Secretary shall issue final regulations to implement section 519(e) of the Federal Food, Drug, and Cosmetic Act. If the Secretary does not promulgate such final regulations by November 28, 1992, the Congress finds that there is good cause for the proposed regulations to be considered as the final regulations without response to comment because the implementation of section 519(e) of such Act is essential to protect the health of patients who use devices. In such event, the proposed regulations issued under paragraph (1) shall become the issued final regulations on November 29, 1992. There shall be promptly published in the Federal Register notice of the new status of the proposed regulations."

[For effective date of amendment by Pub. L. 102-300, see section 2(b) of Pub. L. 102-300, set out above as an Effective Date of 1992 Amendment note.]

INFORMATION CONCERNING REPORTING REQUIREMENTS FOR DEVICE USER FACILITIES

Pub. L. 101-629, §2(d), Nov. 28, 1990, 104 Stat. 4513, directed Secretary of Health and Human Services, during the 18-month period beginning on Nov. 28, 1990, to inform device user facilities (as defined in 21 U.S.C. 360i(b)(5)(A)) and manufacturers and distributors of devices respecting the requirements of 21 U.S.C. 360i(b), and, to the extent practicable, provide persons subject to such requirements assistance in the form of publications regarding such requirements.

STUDY OF REPORTING REQUIREMENTS; COMPLIANCE BY DEVICE USER FACILITIES; ACTIONS BY MANUFACTURERS; COST EFFECTIVENESS; RECOMMENDATIONS

Pub. L. 101-629, §2(e), Nov. 28, 1990, 104 Stat. 4513, directed Comptroller General of the United States, not more than 36 months after Nov. 28, 1990, to conduct a study of compliance by device user facilities with the requirements of 21 U.S.C. 360i(b), actions taken by manufacturers of devices in response to reports made to them, cost effectiveness of such requirements and their implementation, and any recommendations for improvements to such requirements, with Comptroller General to complete the study and submit a report on the study not later than 45 months from Nov. 28, 1990, to appropriate committees of Congress.

REPORT TO CONGRESS ON REPORTING REQUIREMENTS FOR DEVICE USER FACILITIES

Pub. L. 101-629, §2(f), Nov. 28, 1990, 104 Stat. 4513, directed Secretary of Health and Human Services, not

later than 36 months after Nov. 28, 1990, to prepare and submit to appropriate committees of Congress a report containing an evaluation of the requirements of 21 U.S.C. 360i(b), consisting of an evaluation of the safety benefits of the requirements, the burdens placed on the Food and Drug Administration and on device user facilities by the requirements, and the cost-effectiveness of the requirements and recommendations for legislative reform.

§ 360j. General provisions respecting control of devices intended for human use

(a) General rule

Any requirement authorized by or under section 351, 352, 360, or 360i of this title applicable to a device intended for human use shall apply to such device until the applicability of the requirement to the device has been changed by action taken under section 360c, 360d, or 360e of this title or under subsection (g) of this section, and any requirement established by or under section 351, 352, 360, or 360i of this title which is inconsistent with a requirement imposed on such device under section 360d or 360e of this title or under subsection (g) of this section shall not apply to such device.

(b) Custom devices

(1) In general

The requirements of sections 360d and 360e of this title shall not apply to a device that—

(A) is created or modified in order to comply with the order of an individual physician or dentist (or any other specially qualified person designated under regulations promulgated by the Secretary after an opportunity for an oral hearing);

(B) in order to comply with an order described in subparagraph (A), necessarily deviates from an otherwise applicable performance standard under section 360d of this title or requirement under section 360e of this title;

(C) is not generally available in the United States in finished form through labeling or advertising by the manufacturer, importer, or distributor for commercial distribution;

(D) is designed to treat a unique pathology or physiological condition that no other device is domestically available to treat;

(E)(i) is intended to meet the special needs of such physician or dentist (or other specially qualified person so designated) in the course of the professional practice of such physician or dentist (or other specially qualified person so designated); or

(ii) is intended for use by an individual patient named in such order of such physician or dentist (or other specially qualified person so designated);

(F) is assembled from components or manufactured and finished on a case-by-case basis to accommodate the unique needs of individuals described in clause (i) or (ii) of subparagraph (E); and

(G) may have common, standardized design characteristics, chemical and material compositions, and manufacturing processes as commercially distributed devices.

(2) Limitations

Paragraph (1) shall apply to a device only if—

(A) such device is for the purpose of treating a sufficiently rare condition, such that conducting clinical investigations on such device would be impractical;

(B) production of such device under paragraph (1) is limited to no more than 5 units per year of a particular device type, provided that such replication otherwise complies with this section; and

(C) the manufacturer of such device notifies the Secretary on an annual basis, in a manner prescribed by the Secretary, of the manufacture of such device.

(3) Guidance

Not later than 2 years after July 9, 2012, the Secretary shall issue final guidance on replication of multiple devices described in paragraph (2)(B).

(c) Trade secrets

Any information reported to or otherwise obtained by the Secretary or his representative under section 360c, 360d, 360e, 360f, 360h, 360i, or 374 of this title or under subsection (f) or (g) of this section which is exempt from disclosure pursuant to subsection (a) of section 552 of title 5 by reason of subsection (b)(4) of such section shall be considered confidential and shall not be disclosed and may not be used by the Secretary as the basis for the reclassification of a device from class III to class II or class I or as the basis for the establishment or amendment of a performance standard under section 360d of this title for a device reclassified from class III to class II, except (1) in accordance with subsection (h) of this section, and (2) that such information may be disclosed to other officers or employees concerned with carrying out this chapter or when relevant in any proceeding under this chapter (other than section 360c or 360d of this title).

(d) Notices and findings

Each notice of proposed rulemaking under section 360c, 360d, 360e, 360f, 360h, or 360i of this title, or under this section, any other notice which is published in the Federal Register with respect to any other action taken under any such section and which states the reasons for such action, and each publication of findings required to be made in connection with rulemaking under any such section shall set forth—

(1) the manner in which interested persons may examine data and other information on which the notice or findings is based, and

(2) the period within which interested persons may present their comments on the notice or findings (including the need therefor) orally or in writing, which period shall be at least sixty days but may not exceed ninety days unless the time is extended by the Secretary by a notice published in the Federal Register stating good cause therefor.

(e) Restricted devices

(1) The Secretary may by regulation require that a device be restricted to sale, distribution, or use—

(A) only upon the written or oral authorization of a practitioner licensed by law to administer or use such device, or

(B) upon such other conditions as the Secretary may prescribe in such regulation, if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the Secretary determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. No condition prescribed under subparagraph (B) may restrict the use of a device to persons with specific training or experience in its use or to persons for use in certain facilities unless the Secretary determines that such a restriction is required for the safe and effective use of the device. No such condition may exclude a person from using a device solely because the person does not have the training or experience to make him eligible for certification by a certifying board recognized by the American Board of Medical Specialties or has not been certified by such a Board. A device subject to a regulation under this subsection is a restricted device.

(2) The label of a restricted device shall bear such appropriate statements of the restrictions required by a regulation under paragraph (1) as the Secretary may in such regulation prescribe.

(f) Good manufacturing practice requirements

(1)(A) The Secretary may, in accordance with subparagraph (B), prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation (including a process to assess the performance of a device but not including an evaluation of the safety or effectiveness of a device), packing, storage, and installation of a device conform to current good manufacturing practice, as prescribed in such regulations, to assure that the device will be safe and effective and otherwise in compliance with this chapter.

(B) Before the Secretary may promulgate any regulation under subparagraph (A) he shall—

- (i) afford the advisory committee established under paragraph (3) an opportunity to submit recommendations to him with respect to the regulation proposed to be promulgated;
- (ii) afford opportunity for an oral hearing; and
- (iii) ensure that such regulation conforms, to the extent practicable, with internationally recognized standards defining quality systems, or parts of the standards, for medical devices.

The Secretary shall provide the advisory committee a reasonable time to make its recommendation with respect to proposed regulations under subparagraph (A).

(2)(A) Any person subject to any requirement prescribed by regulations under paragraph (1) may petition the Secretary for an exemption or variance from such requirement. Such a petition shall be submitted to the Secretary in such form and manner as he shall prescribe and shall—

- (i) in the case of a petition for an exemption from a requirement, set forth the basis for the petitioner's determination that compliance with the requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this chapter,
- (ii) in the case of a petition for a variance from a requirement, set forth the methods

proposed to be used in, and the facilities and controls proposed to be used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, facilities, and controls prescribed by the requirement, and

(iii) contain such other information as the Secretary shall prescribe.

(B) The Secretary may refer to the advisory committee established under paragraph (3) any petition submitted under subparagraph (A). The advisory committee shall report its recommendations to the Secretary with respect to a petition referred to it within sixty days of the date of the petition's referral. Within sixty days after—

- (i) the date the petition was submitted to the Secretary under subparagraph (A), or
- (ii) if the petition was referred to an advisory committee, the expiration of the sixty-day period beginning on the date the petition was referred to the advisory committee,

whichever occurs later, the Secretary shall by order either deny the petition or approve it.

(C) The Secretary may approve—

- (i) a petition for an exemption for a device from a requirement if he determines that compliance with such requirement is not required to assure that the device will be safe and effective and otherwise in compliance with this chapter, and
- (ii) a petition for a variance for a device from a requirement if he determines that the methods to be used in, and the facilities and controls to be used for, the manufacture, packing, storage, and installation of the device in lieu of the methods, controls, and facilities prescribed by the requirement are sufficient to assure that the device will be safe and effective and otherwise in compliance with this chapter.

An order of the Secretary approving a petition for a variance shall prescribe such conditions respecting the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of the device to be granted the variance under the petition as may be necessary to assure that the device will be safe and effective and otherwise in compliance with this chapter.

(D) After the issuance of an order under subparagraph (B) respecting a petition, the petitioner shall have an opportunity for an informal hearing on such order.

(3) The Secretary shall establish an advisory committee for the purpose of advising and making recommendations to him with respect to regulations proposed to be promulgated under paragraph (1)(A) and the approval or disapproval of petitions submitted under paragraph (2). The advisory committee shall be composed of nine members as follows:

(A) Three of the members shall be appointed from persons who are officers or employees of any State or local government or of the Federal Government.

(B) Two of the members shall be appointed from persons who are representative of interests of the device manufacturing industry; two of the members shall be appointed from persons who are representative of the interests of

physicians and other health professionals; and two of the members shall be representative of the interests of the general public.

Members of the advisory committee who are not officers or employees of the United States, while attending conferences or meetings of the committee or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of title 5 for persons in the Government service employed intermittently. The Secretary shall designate one of the members of the advisory committee to serve as its chairman. The Secretary shall furnish the advisory committee with clerical and other assistance. Section 14 of the Federal Advisory Committee Act shall not apply with respect to the duration of the advisory committee established under this paragraph.

(g) Exemption for devices for investigational use

(1) It is the purpose of this subsection to encourage, to the extent consistent with the protection of the public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose.

(2)(A) The Secretary shall, within the one hundred and twenty-day period beginning on May 28, 1976, by regulation prescribe procedures and conditions under which devices intended for human use may upon application be granted an exemption from the requirements of section 352, 360, 360d, 360e, 360f, 360i, or 379e of this title or subsection (e) or (f) of this section or from any combination of such requirements to permit the investigational use of such devices by experts qualified by scientific training and experience to investigate the safety and effectiveness of such devices.

(B) The conditions prescribed pursuant to subparagraph (A) shall include the following:

(i) A requirement that an application be submitted to the Secretary before an exemption may be granted and that the application be submitted in such form and manner as the Secretary shall specify.

(ii) A requirement that the person applying for an exemption for a device assure the establishment and maintenance of such records, and the making of such reports to the Secretary of safety or effectiveness data obtained as a result of the investigational use of the device during the exemption, as the Secretary determines will enable him to assure compliance with such conditions, review the progress of the investigation, and evaluate the safety and effectiveness of the device.

(iii) Such other requirements as the Secretary may determine to be necessary for the protection of the public health and safety.

(C) Procedures and conditions prescribed pursuant to subparagraph (A) for an exemption may

appropriately vary depending on (i) the scope and duration of clinical testing to be conducted under such exemption, (ii) the number of human subjects that are to be involved in such testing, (iii) the need to permit changes to be made in the device subject to the exemption during testing conducted in accordance with a clinical testing plan required under paragraph (3)(A), and (iv) whether the clinical testing of such device is for the purpose of developing data to obtain approval for the commercial distribution of such device.

(3) Procedures and conditions prescribed pursuant to paragraph (2)(A) shall require, as a condition to the exemption of any device to be the subject of testing involving human subjects, that the person applying for the exemption—

(A) submit a plan for any proposed clinical testing of the device and a report of prior investigations of the device (including, where appropriate, tests on animals) adequate to justify the proposed clinical testing—

(i) to the local institutional review committee which has been established in accordance with regulations of the Secretary to supervise clinical testing of devices in the facilities where the proposed clinical testing is to be conducted, or

(ii) to the Secretary, if—

(I) no such committee exists, or

(II) the Secretary finds that the process of review by such committee is inadequate (whether or not the plan for such testing has been approved by such committee),

for review for adequacy to justify the commencement of such testing; and, unless the plan and report are submitted to the Secretary, submit to the Secretary a summary of the plan and a report of prior investigations of the device (including, where appropriate, tests on animals);

(B) promptly notify the Secretary (under such circumstances and in such manner as the Secretary prescribes) of approval by a local institutional review committee of any clinical testing plan submitted to it in accordance with subparagraph (A);

(C) in the case of a device to be distributed to investigators for testing, obtain signed agreements from each of such investigators that any testing of the device involving human subjects will be under such investigator's supervision and in accordance with subparagraph (D) and submit such agreements to the Secretary; and

(D) assure that informed consent will be obtained from each human subject (or his representative) of proposed clinical testing involving such device, except where subject to such conditions as the Secretary may prescribe, the investigator conducting or supervising the proposed clinical testing of the device determines in writing that there exists a life threatening situation involving the human subject of such testing which necessitates the use of such device and it is not feasible to obtain informed consent from the subject and there is not sufficient time to obtain such consent from his representative.

The determination required by subparagraph (D) shall be concurred in by a licensed physician

who is not involved in the testing of the human subject with respect to which such determination is made unless immediate use of the device is required to save the life of the human subject of such testing and there is not sufficient time to obtain such concurrence.

(4)(A) An application, submitted in accordance with the procedures prescribed by regulations under paragraph (2), for an exemption for a device (other than an exemption from section 360f of this title) shall be deemed approved on the thirtieth day after the submission of the application to the Secretary unless on or before such day the Secretary by order disapproves the application and notifies the applicant of the disapproval of the application.

(B) The Secretary may disapprove an application only if he finds that the investigation with respect to which the application is submitted does not conform to procedures and conditions prescribed under regulations under paragraph (2). Such a notification shall contain the order of disapproval and a complete statement of the reasons for the Secretary's disapproval of the application and afford the applicant opportunity for an informal hearing on the disapproval order.

(C) Consistent with paragraph (1), the Secretary shall not disapprove an application under this subsection because the Secretary determines that—

(i) the investigation may not support a substantial equivalence or de novo classification determination or approval of the device;

(ii) the investigation may not meet a requirement, including a data requirement, relating to the approval or clearance of a device; or

(iii) an additional or different investigation may be necessary to support clearance or approval of the device.

(5) The Secretary may by order withdraw an exemption granted under this subsection for a device if the Secretary determines that the conditions applicable to the device under this subsection for such exemption are not met. Such an order may be issued only after opportunity for an informal hearing, except that such an order may be issued before the provision of an opportunity for an informal hearing if the Secretary determines that the continuation of testing under the exemption with respect to which the order is to be issued will result in an unreasonable risk to the public health.

(6)(A) Not later than 1 year after November 21, 1997, the Secretary shall by regulation establish, with respect to a device for which an exemption under this subsection is in effect, procedures and conditions that, without requiring an additional approval of an application for an exemption or the approval of a supplement to such an application, permit—

(i) developmental changes in the device (including manufacturing changes) that do not constitute a significant change in design or in basic principles of operation and that are made in response to information gathered during the course of an investigation; and

(ii) changes or modifications to clinical protocols that do not affect—

(I) the validity of data or information resulting from the completion of an approved

protocol, or the relationship of likely patient risk to benefit relied upon to approve a protocol;

(II) the scientific soundness of an investigational plan submitted under paragraph (3)(A); or

(III) the rights, safety, or welfare of the human subjects involved in the investigation.

(B) Regulations under subparagraph (A) shall provide that a change or modification described in such subparagraph may be made if—

(i) the sponsor of the investigation determines, on the basis of credible information (as defined by the Secretary) that the applicable conditions under subparagraph (A) are met; and

(ii) the sponsor submits to the Secretary, not later than 5 days after making the change or modification, a notice of the change or modification.

(7)(A) In the case of a person intending to investigate the safety or effectiveness of a class III device or any implantable device, the Secretary shall ensure that the person has an opportunity, prior to submitting an application to the Secretary or to an institutional review committee, to submit to the Secretary, for review, an investigational plan (including a clinical protocol). If the applicant submits a written request for a meeting with the Secretary regarding such review, the Secretary shall, not later than 30 days after receiving the request, meet with the applicant for the purpose of reaching agreement regarding the investigational plan (including a clinical protocol). The written request shall include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan (including a clinical protocol) for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance from the device.

(B) Any agreement regarding the parameters of an investigational plan (including a clinical protocol) that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Any such agreement shall not be changed, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (C) by the director of the office in which the device involved is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the device involved has been identified.

(C) A decision under subparagraph (B)(ii) by the director shall be in writing, and may be made only after the Secretary has provided to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant are present and at which the director documents the scientific issue involved.

(8)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B).

The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is a determination that—

(i) the device involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the device, the design of the clinical investigation, the condition for which the device is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish.

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(h) Release of information respecting safety and effectiveness

(1) The Secretary shall promulgate regulations under which a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the Secretary and which was the basis for—

(A) an order under section 360e(d)(1)(A) of this title approving an application for premarket approval for the device or denying approval of such an application or an order under section 360e(e) of this title withdrawing approval of such an application for the device,

(B) an order under section 360e(f)(6)(A) of this title revoking an approved protocol for the device, an order under section 360e(f)(6)(B) of this title declaring a protocol for the device completed or not completed, or an order under section 360e(f)(7) of this title revoking the approval of the device, or

(C) an order approving an application under subsection (g) of this section for an exemption for the device from section 360f of this title or an order disapproving, or withdrawing approval of, an application for an exemption under such subsection for the device,

shall be made available to the public upon issuance of the order. Summaries of information made available pursuant to this paragraph respecting a device shall include information respecting any adverse effects on health of the device.

(2) The Secretary shall promulgate regulations under which each advisory committee established under section 360e(g)(2)(B) of this title shall make available to the public a detailed summary of information respecting the safety and effectiveness of a device which information was submitted to the advisory committee and which was the basis for its recommendation to the Secretary made pursuant to section

360e(g)(2)(A) of this title. A summary of information upon which such a recommendation is based shall be made available pursuant to this paragraph only after the issuance of the order with respect to which the recommendation was made and each summary shall include information respecting any adverse effect on health of the device subject to such order.

(3) Except as provided in paragraph (4), any information respecting a device which is made available pursuant to paragraph (1) or (2) of this subsection (A) may not be used to establish the safety or effectiveness of another device for purposes of this chapter by any person other than the person who submitted the information so made available, and (B) shall be made available subject to subsection (c) of this section.

(4)(A) Any information contained in an application for premarket approval filed with the Secretary pursuant to section 360e(c) of this title (including information from clinical and preclinical tests or studies that demonstrate the safety and effectiveness of a device, but excluding descriptions of methods of manufacture and product composition and other trade secrets) shall be available, 6 years after the application has been approved by the Secretary, for use by the Secretary in—

(i) approving another device;

(ii) determining whether a product development protocol has been completed, under section 360e of this title for another device;

(iii) establishing a performance standard or special control under this chapter; or

(iv) classifying or reclassifying another device under section 360c of this title and subsection (l)(2) of this section.

(B) The publicly available detailed summaries of information respecting the safety and effectiveness of devices required by paragraph (1)(A) shall be available for use by the Secretary as the evidentiary basis for the agency actions described in subparagraph (A).

(i) Proceedings of advisory panels and committees

Each panel under section 360c of this title and each advisory committee established under section 360d(b)(5)(B) or 360e(g) of this title or under subsection (f) of this section shall make and maintain a transcript of any proceeding of the panel or committee. Each such panel and committee shall delete from any transcript made pursuant to this subsection information which under subsection (c) of this section is to be considered confidential.

(j) Traceability

Except as provided in section 360i(e) of this title, no regulation under this chapter may impose on a type or class of device requirements for the traceability of such type or class of device unless such requirements are necessary to assure the protection of the public health.

(k) Research and development

The Secretary may enter into contracts for research, testing, and demonstrations respecting devices and may obtain devices for research, testing, and demonstration purposes without regard to section 3324(a) and (b) of title 31 and section 6101 of title 41.

(I) Transitional provisions for devices considered as new drugs

(1) Any device intended for human use—

(A) for which on May 28, 1976 (hereinafter in this subsection referred to as the “enactment date”) an approval of an application submitted under section 355(b) of this title was in effect;

(B) for which such an application was filed on or before the enactment date and with respect to which application no order of approval or refusing to approve had been issued on such date under subsection (c) or (d) of such section;

(C) for which on the enactment date an exemption under subsection (i) of such section was in effect;

(D) which is within a type of device described in subparagraph (A), (B), or (C) and is substantially equivalent to another device within that type;

(E) which the Secretary in a notice published in the Federal Register before the enactment date has declared to be a new drug subject to section 355 of this title; or

(F) with respect to which on the enactment date an action is pending in a United States court under section 332, 333, or 334 of this title for an alleged violation of a provision of section 331 of this title which enforces a requirement of section 355 of this title or for an alleged violation of section 355(a) of this title,

is classified in class III unless the Secretary in response to a petition submitted under paragraph (2) has classified such device in class I or II.

(2) The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition. Except as provided in paragraph (3)(D)(ii), within one hundred and eighty days after the filing of a petition under this paragraph, the Secretary shall, after consultation with the appropriate panel under section 360c of this title, by order either deny the petition or order the classification, in accordance with the criteria prescribed by section 360c(a)(1)(A) of this title or 360c(a)(1)(B) of this title, of the device in class I or class II.

(3)(A) In the case of a device which is described in paragraph (1)(A) and which is in class III—

(i) such device shall on the enactment date be considered a device with an approved application under section 360e of this title, and

(ii) the requirements applicable to such device before the enactment date under section 355 of this title shall continue to apply to such device until changed by the Secretary as authorized by this chapter.

(B) In the case of a device which is described in paragraph (1)(B) and which is in class III, an application for such device shall be considered as having been filed under section 360e of this

title on the enactment date. The period in which the Secretary shall act on such application in accordance with section 360e(d)(1) of this title shall be one hundred and eighty days from the enactment date (or such greater period as the Secretary and the applicant may agree upon after the Secretary has made the finding required by section 360e(d)(1)(B)(i) of this title) less the number of days in the period beginning on the date an application for such device was filed under section 355 of this title and ending on the enactment date. After the expiration of such period such device is required, unless exempt under subsection (g) of this section, to have in effect an approved application under section 360e of this title.

(C) A device which is described in paragraph (1)(C) and which is in class III shall be considered a new drug until the expiration of the ninety-day period beginning on the date of the promulgation of regulations under subsection (g) of this section. After the expiration of such period such device is required, unless exempt under subsection (g) of this section, to have in effect an approved application under section 360e of this title.

(D)(i) Except as provided in clauses (ii) and (iii), a device which is described in subparagraph (D), (E), or (F) of paragraph (1) and which is in class III is required, unless exempt under subsection (g) of this section, to have on and after sixty days after the enactment date in effect an approved application under section 360e of this title.

(ii) If—

(I) a petition is filed under paragraph (2) for a device described in subparagraph (D), (E), or (F) of paragraph (1), or

(II) an application for premarket approval is filed under section 360e of this title for such a device,

within the sixty-day period beginning on the enactment date (or within such greater period as the Secretary, after making the finding required under section 360e(d)(1)(B) of this title, and the petitioner or applicant may agree upon), the Secretary shall act on such petition or application in accordance with paragraph (2) or section 360e of this title except that the period within which the Secretary must act on the petition or application shall be within the one hundred and twenty-day period beginning on the date the petition or application is filed. If such a petition or application is filed within such sixty-day (or greater) period, clause (i) of this subparagraph shall not apply to such device before the expiration of such one hundred and twenty-day period, or if such petition is denied or such application is denied approval, before the date of such denial, whichever occurs first.

(iii) In the case of a device which is described in subparagraph (E) of paragraph (1), which the Secretary in a notice published in the Federal Register after March 31, 1976, declared to be a new drug subject to section 355 of this title, and which is in class III—

(I) the device shall, after eighteen months after the enactment date, have in effect an approved application under section 360e of this title unless exempt under subsection (g) of this section, and

(II) the Secretary may, during the period beginning one hundred and eighty days after the enactment date and ending eighteen months after such date, restrict the use of the device to investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of such device, and to investigational use in accordance with the requirements applicable under regulations under subsection (g) of this section to investigational use of devices granted an exemption under such subsection.

If the requirements under subsection (g) of this section are made applicable to the investigational use of such a device, they shall be made applicable in such a manner that the device shall be made reasonably available to physicians meeting appropriate qualifications prescribed by the Secretary.

(4) Repealed. Pub. L. 105-115, title I, § 125(b)(2)(E), Nov. 21, 1997, 111 Stat. 2325.

(5)(A) Before December 1, 1991, the Secretary shall by order require manufacturers of devices described in paragraph (1), which are subject to revision of classification under subparagraph (B), to submit to the Secretary a summary of and citation to any information known or otherwise available to the manufacturers respecting the devices, including adverse safety or effectiveness information which has not been submitted under section 360i of this title. The Secretary may require a manufacturer to submit the adverse safety or effectiveness data for which a summary and citation were submitted, if such data are available to the manufacturer.

(B) Except as provided in subparagraph (C), after the issuance of an order under subparagraph (A) but before December 1, 1992, the Secretary shall publish a regulation in the Federal Register for each device which is classified in class III under paragraph (1) revising the classification of the device so that the device is classified into class I or class II, unless the regulation requires the device to remain in class III. In determining whether to revise the classification of a device or to require a device to remain in class III, the Secretary shall apply the criteria set forth in section 360c(a) of this title. Before the publication of a regulation requiring a device to remain in class III or revising its classification, the Secretary shall publish a proposed regulation respecting the classification of a device under this subparagraph and provide an opportunity for the submission of comments on any such regulation. No regulation under this subparagraph requiring a device to remain in class III or revising its classification may take effect before the expiration of 90 days from the date of the publication in the Federal Register of the proposed regulation.

(C) The Secretary may by notice published in the Federal Register extend the period prescribed by subparagraph (B) for a device for an additional period not to exceed 1 year.

(m) Humanitarian device exemption

(1) To the extent consistent with the protection of the public health and safety and with ethical standards, it is the purpose of this subsection to encourage the discovery and use of devices intended to benefit patients in the treat-

ment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States.

(2) The Secretary may grant a request for an exemption from the effectiveness requirements of sections 360d and 360e of this title for a device for which the Secretary finds that—

(A) the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States,

(B) the device would not be available to a person with a disease or condition referred to in subparagraph (A) unless the Secretary grants such an exemption and there is no comparable device, other than under this exemption, available to treat or diagnose such disease or condition, and

(C) the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

The request shall be in the form of an application submitted to the Secretary and such application shall include the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application). Not later than 75 days after the date of the receipt of the application, the Secretary shall issue an order approving or denying the application.

(3) Except as provided in paragraph (6), no person granted an exemption under paragraph (2) with respect to a device may sell the device for an amount that exceeds the costs of research and development, fabrication, and distribution of the device.

(4) Devices granted an exemption under paragraph (2) may only be used—

(A) in facilities that have established, in accordance with regulations of the Secretary, a local institutional review committee to supervise clinical testing of devices in the facilities, and

(B) if, before the use of a device, an institutional review committee approves the use in the treatment or diagnosis of a disease or condition referred to in paragraph (2)(A), unless a physician determines in an emergency situation that approval from a local institutional review committee can not be obtained in time to prevent serious harm or death to a patient.

In a case described in subparagraph (B) in which a physician uses a device without an approval from an institutional review committee, the physician shall, after the use of the device, notify the chairperson of the local institutional review committee of such use. Such notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.

(5) The Secretary may require a person granted an exemption under paragraph (2) to demonstrate continued compliance with the requirements of this subsection if the Secretary believes such demonstration to be necessary to protect the public health, if the Secretary has

reason to believe that the requirements of paragraph (6) are no longer met, or if the Secretary has reason to believe that the criteria for the exemption are no longer met. If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.

(6)(A) Except as provided in subparagraph (D), the prohibition in paragraph (3) shall not apply with respect to a person granted an exemption under paragraph (2) if each of the following conditions apply:

(i) The device with respect to which the exemption is granted—

(I) is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs; or

(II) is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is impossible, highly impracticable, or unsafe.

(ii) During any calendar year, the number of such devices distributed during that year under each exemption granted under this subsection does not exceed the annual distribution number for such device. In this paragraph, the term “annual distribution number” means the number of such devices reasonably needed to treat, diagnose, or cure a population of 4,000 individuals in the United States. The Secretary shall determine the annual distribution number when the Secretary grants such exemption.

(iii) Such person immediately notifies the Secretary if the number of such devices distributed during any calendar year exceeds the annual distribution number referred to in clause (ii).

(iv) The request for such exemption is submitted on or before October 1, 2017.

(B) The Secretary may inspect the records relating to the number of devices distributed during any calendar year of a person granted an exemption under paragraph (2) for which the prohibition in paragraph (3) does not apply.

(C) A person may petition the Secretary to modify the annual distribution number determined by the Secretary under subparagraph (A)(ii) with respect to a device if additional information arises, and the Secretary may modify such annual distribution number.

(D) If a person notifies the Secretary, or the Secretary determines through an inspection under subparagraph (B), that the number of devices distributed during any calendar year exceeds the annual distribution number, as required under subparagraph (A)(iii), and modified under subparagraph (C), if applicable, then the

prohibition in paragraph (3) shall apply with respect to such person for such device for any sales of such device after such notification.

(E)(i) In this subsection, the term “pediatric patients” means patients who are 21 years of age or younger at the time of the diagnosis or treatment.

(ii) In this subsection, the term “pediatric subpopulation” means 1 of the following populations:

- (I) Neonates.
- (II) Infants.
- (III) Children.
- (IV) Adolescents.

(7) The Secretary shall refer any report of an adverse event regarding a device described in paragraph (6)(A)(i)(I) for which the prohibition under paragraph (3) does not apply pursuant to paragraph (6)(A) that the Secretary receives to the Office of Pediatric Therapeutics, established under section 393a of this title. In considering the report, the Director of the Office of Pediatric Therapeutics, in consultation with experts in the Center for Devices and Radiological Health, shall provide for periodic review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this chapter in response to the report.

(8) The Secretary, acting through the Office of Pediatric Therapeutics and the Center for Devices and Radiological Health, shall provide for an annual review by the Pediatric Advisory Committee of all devices described in paragraph (6)(A)(i)(I) to ensure that the exemption under paragraph (2) remains appropriate for the pediatric populations for which it is granted.

(n) Regulation of contact lenses as devices

(1) All contact lenses shall be deemed to be devices under section 321(h) of this title.

(2) Paragraph (1) shall not be construed as bearing on or being relevant to the question of whether any product other than a contact lens is a device as defined by section 321(h) of this title or a drug as defined by section 321(g) of this title.

(June 25, 1938, ch. 675, § 520, as added Pub. L. 94-295, § 2, May 28, 1976, 90 Stat. 565; amended Pub. L. 101-629, §§ 3(b)(2), 4(b)(2), 5(c)(2), 6(b)(2), 11, 14(a), 18(e), (f), Nov. 28, 1990, 104 Stat. 4514, 4516, 4518, 4519, 4522, 4524, 4529; Pub. L. 102-571, title I, § 107(10), Oct. 29, 1992, 106 Stat. 4499; Pub. L. 105-115, title I, § 125(b)(2)(E), title II, §§ 201(a), 203, 216(a)(1), title IV, § 410(a), Nov. 21, 1997, 111 Stat. 2325, 2332, 2334, 2349, 2372; Pub. L. 109-96, § 1, Nov. 9, 2005, 119 Stat. 2119; Pub. L. 110-85, title III, § 303(a), title VIII, § 801(b)(3)(E), Sept. 27, 2007, 121 Stat. 860, 921; Pub. L. 112-144, title V, § 507(c), title VI, §§ 601, 606, 613(a), 617, July 9, 2012, 126 Stat. 1045, 1051, 1054, 1060, 1062.)

REFERENCES IN TEXT

July 9, 2012, referred to in subsec. (b)(3), was in the original “the date of enactment of this section”, which was translated as meaning the date of enactment of Pub. L. 112-144, which amended subsec. (b) generally, to reflect the probable intent of Congress.

Section 14 of the Federal Advisory Committee Act, referred to in subsec. (f)(3), is section 14 of Pub. L.

92-463, which is set out in the Appendix to Title 5, Government Organization and Employees.

CODIFICATION

In subsec. (k), “section 3324(a) and (b) of title 31 and section 6101 of title 41” substituted for “sections 3648 and 3709 of the Revised Statutes (31 U.S.C. 529, 41 U.S.C. 5)” on authority of Pub. L. 97-258, §4(b), Sept. 13, 1982, 96 Stat. 1067, which Act enacted Title 31, Money and Finance, and Pub. L. 111-350, §6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

AMENDMENTS

2012—Subsec. (b). Pub. L. 112-144, §617, amended subsec. (b) generally. Prior to amendment, subsec. (b) related to custom devices.

Subsec. (g)(2)(B)(ii). Pub. L. 112-144, §601(1), inserted “safety or effectiveness” before “data obtained”.

Subsec. (g)(4)(C). Pub. L. 112-144, §601(2), added subpar. (C).

Subsec. (g)(8). Pub. L. 112-144, §606, added par. (8).

Subsec. (m)(6)(A)(i). Pub. L. 112-144, §613(a)(1)(A)(i), added cl. (i) and struck out former cl. (i) which read as follows:

“(i)(I) The device with respect to which the exemption is granted is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs.

“(II) The device was not previously approved under this subsection for the pediatric patients or the pediatric subpopulation described in subclause (I) prior to September 27, 2007.”

Subsec. (m)(6)(A)(ii). Pub. L. 112-144, §613(a)(1)(A)(ii), added cl. (ii) and struck out former cl. (ii) which read as follows: “During any calendar year, the number of such devices distributed during that year does not exceed the annual distribution number specified by the Secretary when the Secretary grants such exemption. The annual distribution number shall be based on the number of individuals affected by the disease or condition that such device is intended to treat, diagnose, or cure, and of that number, the number of individuals likely to use the device, and the number of devices reasonably necessary to treat such individuals. In no case shall the annual distribution number exceed the number identified in paragraph (2)(A).”

Subsec. (m)(6)(A)(iv). Pub. L. 112-144, §507(c), substituted “2017” for “2012”.

Subsec. (m)(6)(C). Pub. L. 112-144, §613(a)(1)(B), amended subpar. (C) generally. Prior to amendment, subpar. (C) read as follows: “A person may petition the Secretary to modify the annual distribution number specified by the Secretary under subparagraph (A)(ii) with respect to a device if additional information on the number of individuals affected by the disease or condition arises, and the Secretary may modify such number but in no case shall the annual distribution number exceed the number identified in paragraph (2)(A).”

Subsec. (m)(7). Pub. L. 112-144, §613(a)(2), substituted “regarding a device described in paragraph (6)(A)(i)(I)” for “regarding a device”.

Subsec. (m)(8). Pub. L. 112-144, §613(a)(3), substituted “of all devices described in paragraph (6)(A)(i)(I)” for “of all devices described in paragraph (6)”.

2007—Subsec. (m)(2). Pub. L. 110-85, §801(b)(3)(E), inserted before period at end of first sentence of concluding provisions “and such application shall include the certification required under section 282(j)(5)(B) of title 42 (which shall not be considered an element of such application)”.

Subsec. (m)(3). Pub. L. 110-85, §303(a)(1), substituted “Except as provided in paragraph (6), no” for “No”.

Subsec. (m)(5). Pub. L. 110-85, §303(a)(2), inserted “, if the Secretary has reason to believe that the requirements of paragraph (6) are no longer met,” after “pub-

lic health” and inserted at end “If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.”

Subsec. (m)(6) to (8). Pub. L. 110-85, §303(a)(3), added pars. (6) to (8) and struck out former par. (6) which read as follows: “The Secretary may suspend or withdraw an exemption from the effectiveness requirements of sections 360d and 360e of this title for a humanitarian device only after providing notice and an opportunity for an informal hearing.”

2005—Subsec. (n). Pub. L. 109-96 added subsec. (n).

1997—Subsec. (f)(1)(B)(iii). Pub. L. 105-115, §410(a), added cl. (iii).

Subsec. (g)(6), (7). Pub. L. 105-115, §201(a), added pars. (6) and (7).

Subsec. (h)(4). Pub. L. 105-115, §216(a)(1), amended par. (4) generally. Prior to amendment, par. (4) related to premarket approval of devices.

Subsec. (l). Pub. L. 105-115, §125(b)(2)(E), struck out “or antibiotic drugs” after “new drugs” in heading.

Subsec. (l)(4). Pub. L. 105-115, §125(b)(2)(E), struck out par. (4) which read as follows: “Any device intended for human use which on the enactment date was subject to the requirements of section 357 of this title shall be subject to such requirements as follows:

“(A) In the case of such a device which is classified into class I, such requirements shall apply to such device until the effective date of the regulation classifying the device into such class.

“(B) In the case of such a device which is classified into class II, such requirements shall apply to such device until the effective date of a performance standard applicable to the device under section 360d of this title.

“(C) In the case of such a device which is classified into class III, such requirements shall apply to such device until the date on which the device is required to have in effect an approved application under section 360e of this title.”

Subsec. (m)(2). Pub. L. 105-115, §203(1), inserted at end “The request shall be in the form of an application submitted to the Secretary. Not later than 75 days after the date of the receipt of the application, the Secretary shall issue an order approving or denying the application.”

Subsec. (m)(4). Pub. L. 105-115, §203(2)(B), inserted at end “In a case described in subparagraph (B) in which a physician uses a device without an approval from an institutional review committee, the physician shall, after the use of the device, notify the chairperson of the local institutional review committee of such use. Such notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.”

Subsec. (m)(4)(B). Pub. L. 105-115, §203(2)(A), inserted before period at end “, unless a physician determines in an emergency situation that approval from a local institutional review committee can not be obtained in time to prevent serious harm or death to a patient”.

Subsec. (m)(5). Pub. L. 105-115, §203(3), amended par. (5) generally. Prior to amendment, par. (5) read as follows: “An exemption under paragraph (2) shall be for a term of 18 months and may only be initially granted in the 5-year period beginning on the date regulations under paragraph (6) take effect. The Secretary may extend such an exemption for a period of 18 months if the Secretary is able to make the findings set forth in paragraph (2) and if the applicant supplies information demonstrating compliance with paragraph (3). An exemption may be extended more than once and may be extended after the expiration of such 5-year period.”

Subsec. (m)(6). Pub. L. 105-115, §203(4), amended par. (6) generally. Prior to amendment, par. (6) read as follows: “Within one year of November 28, 1990, the Secretary shall issue regulations to implement this subsection.”

1992—Subsec. (g)(2)(A). Pub. L. 102-571 substituted “379e” for “376”.

1990—Subsec. (c). Pub. L. 101-629, §11(1), substituted “from class III to class II or class I” for “under section 360c of this title from class III to class II” and inserted “(1) in accordance with subsection (h) of this section, and (2)” after “except”.

Subsec. (f)(1)(A). Pub. L. 101-629, §18(e), inserted “pre-production design validation (including a process to assess the performance of a device but not including an evaluation of the safety or effectiveness of a device),” after “manufacture,”.

Subsec. (h)(3). Pub. L. 101-629, §11(2)(A), substituted “Except as provided in paragraph (4), any” for “Any”.

Subsec. (h)(4). Pub. L. 101-629, §11(2)(B), added par. (4).

Subsec. (i). Pub. L. 101-629, §6(b)(2), substituted “section 360d(b)(5)(B)” for “section 360d(g)(5)(B)”.

Subsec. (j). Pub. L. 101-629, §3(b)(2), substituted “Except as provided in section 360i(e) of this title, no” for “No”.

Subsec. (l)(2). Pub. L. 101-629, §18(f), struck out “and after affording the petitioner an opportunity for an informal hearing” after “under this paragraph”.

Pub. L. 101-629, §5(c)(2), substituted “The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer” for “The manufacturer”.

Subsec. (l)(5). Pub. L. 101-629, §4(b)(2), added par. (5).

Subsec. (m). Pub. L. 101-629, §14(a), added subsec. (m).

EFFECTIVE DATE OF 1997 AMENDMENT

Amendment by sections 201(a), 203, 216(a)(1), and 410(a) of Pub. L. 105-115 effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

EFFECTIVE DATE OF 1990 AMENDMENT

Pub. L. 101-629, §14(b), Nov. 28, 1990, 104 Stat. 4525, provided that: “Subsection (m) of section 520 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360j(m)], as added by the amendment made by subsection (a), shall take effect on the effective date of the regulations issued by the Secretary under paragraph (6) of such subsection.”

APPLICABILITY TO EXISTING DEVICES

Pub. L. 112-144, title VI, §613(b), July 9, 2012, 126 Stat. 1061, provided that: “A sponsor of a device for which an exemption was approved under paragraph (2) of section 520(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)) before the date of enactment of this Act [July 9, 2012] may seek a determination under subclause (I) or (II) of section 520(m)(6)(A)(i) (as amended by subsection (a)). If the Secretary of Health and Human Services determines that such subclause (I) or (II) applies with respect to a device, clauses (ii), (iii), and (iv) of subparagraph (A) and subparagraphs (B), (C), (D), and (E) of paragraph (6) of such section 520(m) shall apply to such device, and the Secretary shall determine the annual distribution number for purposes of clause (ii) of such subparagraph (A) when making the determination under this subsection.”

GUIDANCE

Pub. L. 110-85, title III, §303(c), Sept. 27, 2007, 121 Stat. 862, provided that: “Not later than 180 days after the date of the enactment of this Act [Sept. 27, 2007], the Commissioner of Food and Drugs shall issue guidance for institutional review committees on how to evaluate requests for approval for devices for which a humanitarian device exemption under section 520(m)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(m)(2)) has been granted.”

Pub. L. 107-250, title II, §213, Oct. 26, 2002, 116 Stat. 1614, provided that: “Not later than 270 days after the date of the enactment of this Act [Oct. 26, 2002], the Secretary of Health and Human Services shall issue guidance on the following:

“(1) The type of information necessary to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in pediatric populations.

“(2) Protections for pediatric subjects in clinical investigations of the safety or effectiveness of such devices.”

REPORT ON HUMANITARIAN DEVICE EXEMPTIONS

Pub. L. 101-629, §14(c), Nov. 28, 1990, 104 Stat. 4525, directed Secretary of Health and Human Services, within 4 years after issuance of regulations under 21 U.S.C. 360j(m)(6), to report to Congress on types of devices exempted, an evaluation of effects of such section, and a recommendation on extension of the section.

REFERENCES IN OTHER LAWS TO GS-16, 17, OR 18 PAY RATES

References in laws to the rates of pay for GS-16, 17, or 18, or to maximum rates of pay under the General Schedule, to be considered references to rates payable under specified sections of Title 5, Government Organization and Employees, see section 529 [title I, §101(c)(1)] of Pub. L. 101-509, set out in a note under section 5376 of Title 5.

§ 360k. State and local requirements respecting devices

(a) General rule

Except as provided in subsection (b) of this section, no State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement—

(1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and

(2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter.

(b) Exempt requirements

Upon application of a State or a political subdivision thereof, the Secretary may, by regulation promulgated after notice and opportunity for an oral hearing, exempt from subsection (a) of this section, under such conditions as may be prescribed in such regulation, a requirement of such State or political subdivision applicable to a device intended for human use if—

(1) the requirement is more stringent than a requirement under this chapter which would be applicable to the device if an exemption were not in effect under this subsection; or

(2) the requirement—

(A) is required by compelling local conditions, and

(B) compliance with the requirement would not cause the device to be in violation of any applicable requirement under this chapter.

(June 25, 1938, ch. 675, §521, as added Pub. L. 94-295, §2, May 28, 1976, 90 Stat. 574.)

§ 360L. Postmarket surveillance

(a) Postmarket surveillance

(1) In general

(A) Conduct

The Secretary may by order, at the time of approval or clearance of a device or at any

time thereafter, require a manufacturer to conduct postmarket surveillance for any device of the manufacturer that is a class II or class III device—

(i) the failure of which would be reasonably likely to have serious adverse health consequences;

(ii) that is expected to have significant use in pediatric populations; or

(iii) that is intended to be—

(I) implanted in the human body for more than 1 year; or

(II) a life-sustaining or life-supporting device used outside a device user facility.

(B) Condition

The Secretary may order a postmarket surveillance under subparagraph (A) as a condition to approval or clearance of a device described in subparagraph (A)(ii).

(2) Rule of construction

The provisions of paragraph (1) shall have no effect on authorities otherwise provided under the¹ chapter or regulations issued under this chapter.

(b) Surveillance approval

(1) In general

Each manufacturer required to conduct a surveillance of a device shall, within 30 days of receiving an order from the Secretary prescribing that the manufacturer is required under this section to conduct such surveillance, submit, for the approval of the Secretary, a plan for the required surveillance. The Secretary, within 60 days of the receipt of such plan, shall determine if the person designated to conduct the surveillance has appropriate qualifications and experience to undertake such surveillance and if the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. The manufacturer shall commence surveillance under this section not later than 15 months after the day on which the Secretary issues an order under this section. Except as provided in paragraph (2), the Secretary, in consultation with the manufacturer, may by order require a prospective surveillance period of up to 36 months. Except as provided in paragraph (2), any determination by the Secretary that a longer period is necessary shall be made by mutual agreement between the Secretary and the manufacturer or, if no agreement can be reached, after the completion of a dispute resolution process as described in section 360bbb-1 of this title.

(2) Longer surveillance for pediatric devices

The Secretary may by order require a prospective surveillance period of more than 36 months with respect to a device that is expected to have significant use in pediatric populations if such period of more than 36 months is necessary in order to assess the impact of the device on growth and development, or the effects of growth, development, activity level,

or other factors on the safety or efficacy of the device.

(c) Dispute resolution

A manufacturer may request review under section 360bbb-1 of this title of any order or condition requiring postmarket surveillance under this section. During the pendency of such review, the device subject to such a postmarket surveillance order or condition shall not, because of noncompliance with such order or condition, be deemed in violation of section 331(q)(1)(C) of this title, adulterated under section 351(f)(1) of this title, misbranded under section 352(t)(3) of this title, or in violation of, as applicable, section 360(k) of this title or section 360e of this title, unless deemed necessary to protect the public health.

(June 25, 1938, ch. 675, §522, as added Pub. L. 101-629, §10, Nov. 28, 1990, 104 Stat. 4521; amended Pub. L. 102-300, §3(b), June 16, 1992, 106 Stat. 239; Pub. L. 105-115, title II, §212, Nov. 21, 1997, 111 Stat. 2346; Pub. L. 110-85, title III, §307, Sept. 27, 2007, 121 Stat. 865; Pub. L. 112-144, title VI, §616, July 9, 2012, 126 Stat. 1062.)

AMENDMENTS

2012—Subsec. (a)(1)(A). Pub. L. 112-144, §616(1), inserted “, at the time of approval or clearance of a device or at any time thereafter,” after “by order” in introductory provisions.

Subsec. (b)(1). Pub. L. 112-144, §616(2), inserted “The manufacturer shall commence surveillance under this section not later than 15 months after the day on which the Secretary issues an order under this section.” after “the public health.”

2007—Pub. L. 110-85, §307(1), made technical amendment to section catchline.

Subsec. (a). Pub. L. 110-85, §307(2), added subsec. (a) and struck out former subsec. (a). Prior to amendment, text read as follows: “The Secretary may by order require a manufacturer to conduct postmarket surveillance for any device of the manufacturer which is a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences or which is intended to be—

“(1) implanted in the human body for more than one year, or

“(2) a life sustaining or life supporting device used outside a device user facility.”

Subsec. (b). Pub. L. 110-85, §307(3), designated existing provisions as par. (1), inserted par. heading, substituted “Except as provided in paragraph (2), the Secretary, in consultation” for “The Secretary, in consultation” and “Except as provided in paragraph (2), any determination” for “Any determination”, and added par. (2).

Subsec. (c). Pub. L. 110-85, §307(3)(D), added subsec. (c).

1997—Pub. L. 105-115 amended section generally, substituting present provisions for former provisions which related to required surveillance, discretionary surveillance, and surveillance approval.

1992—Subsec. (b). Pub. L. 102-300 substituted “(a)(1)” for “(a)”, inserted comma after “commerce”, and inserted after first sentence “Each manufacturer required to conduct a surveillance of a device under subsection (a)(2) of this section shall, within 30 days after receiving notice that the manufacturer is required to conduct such surveillance, submit, for the approval of the Secretary, a protocol for the required surveillance.”

EFFECTIVE DATE OF 1997 AMENDMENT

Pub. L. 105-115, title II, §212, Nov. 21, 1997, 111 Stat. 2346, provided in part that the amendment made by that section is effective 90 days after Nov. 21, 1997.

¹ So in original. Probably should be “this”.

STUDY BY INSTITUTE OF MEDICINE OF POSTMARKET SURVEILLANCE REGARDING PEDIATRIC POPULATIONS

Pub. L. 107-250, title II, §212, Oct. 26, 2002, 116 Stat. 1614, as amended by Pub. L. 108-214, §2(d)(3)(C), Apr. 1, 2004, 118 Stat. 577, provided that:

“(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this section as the ‘Secretary’) shall request the Institute of Medicine to enter into an agreement with the Secretary under which such Institute conducts a study for the purpose of determining whether the system under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] for the post-market surveillance of medical devices provides adequate safeguards regarding the use of devices in pediatric populations.

“(b) CERTAIN MATTERS.—The Secretary shall ensure that determinations made in the study under subsection (a) include determinations of—

“(1) whether postmarket surveillance studies of implanted medical devices are of long enough duration to evaluate the impact of growth and development for the number of years that the child will have the implant, and whether the studies are adequate to evaluate how children’s active lifestyles may affect the failure rate and longevity of the implant; and

“(2) whether the postmarket surveillance by the Food and Drug Administration of medical devices used in pediatric populations is sufficient to provide adequate safeguards for such populations, taking into account the Secretary’s monitoring of commitments made at the time of approval of medical devices and the Secretary’s monitoring and use of adverse reaction reports, registries, and other postmarket surveillance activities.

“(c) REPORT TO CONGRESS.—The Secretary shall ensure that, not later than four years after the date of the enactment of this Act [Oct. 26, 2002], a report describing the findings of the study under subsection (a) is submitted to the Congress. The report shall include any recommendations of the Secretary for administrative or legislative changes to the system of postmarket surveillance referred to in such subsection.”

§ 360m. Accredited persons

(a) In general

(1) Review and classification of devices

Not later than 1 year after November 21, 1997, the Secretary shall, subject to paragraph (3), accredit persons for the purpose of reviewing reports submitted under section 360(k) of this title and making recommendations to the Secretary regarding the initial classification of devices under section 360c(f)(1) of this title.

(2) Requirements regarding review

(A) In general

In making a recommendation to the Secretary under paragraph (1), an accredited person shall notify the Secretary in writing of the reasons for the recommendation.

(B) Time period for review

Not later than 30 days after the date on which the Secretary is notified under subparagraph (A) by an accredited person with respect to a recommendation of an initial classification of a device, the Secretary shall make a determination with respect to the initial classification.

(C) Special rule

The Secretary may change the initial classification under section 360c(f)(1) of this title that is recommended under paragraph (1) by an accredited person, and in such case shall

provide to such person, and the person who submitted the report under section 360(k) of this title for the device, a statement explaining in detail the reasons for the change.

(3) Certain devices

(A) In general

An accredited person may not be used to perform a review of—

(i) a class III device;

(ii) a class II device which is intended to be permanently implantable or life sustaining or life supporting; or

(iii) a class II device which requires clinical data in the report submitted under section 360(k) of this title for the device, except that the number of class II devices to which the Secretary applies this clause for a year, less the number of such reports to which clauses (i) and (ii) apply, may not exceed 6 percent of the number that is equal to the total number of reports submitted to the Secretary under such section for such year less the number of such reports to which such clauses apply for such year.

(B) Adjustment

In determining for a year the ratio described in subparagraph (A)(iii), the Secretary shall not include in the numerator class III devices that the Secretary reclassified into class II, and the Secretary shall include in the denominator class II devices for which reports under section 360(k) of this title were not required to be submitted by reason of the operation of section 360(m) of this title.

(b) Accreditation

(1) Programs

The Secretary shall provide for such accreditation through programs administered by the Food and Drug Administration, other government agencies, or by other qualified non-government organizations.

(2) Accreditation

(A) In general

Not later than 180 days after November 21, 1997, the Secretary shall establish and publish in the Federal Register criteria to accredit or deny accreditation to persons who request to perform the duties specified in subsection (a) of this section. The Secretary shall respond to a request for accreditation within 60 days of the receipt of the request. The accreditation of such person shall specify the particular activities under subsection (a) of this section for which such person is accredited.

(B) Withdrawal of accreditation

The Secretary may suspend or withdraw accreditation of any person accredited under this paragraph, after providing notice and an opportunity for an informal hearing, when such person is substantially not in compliance with the requirements of this section or poses a threat to public health or fails to act in a manner that is consistent with the purposes of this section.

(C) Performance auditing

To ensure that persons accredited under this section will continue to meet the standards of accreditation, the Secretary shall—

- (i) make onsite visits on a periodic basis to each accredited person to audit the performance of such person; and
- (ii) take such additional measures as the Secretary determines to be appropriate.

(D) Annual report

The Secretary shall include in the annual report required under section 393(g) of this title the names of all accredited persons and the particular activities under subsection (a) of this section for which each such person is accredited and the name of each accredited person whose accreditation has been withdrawn during the year.

(E) Periodic reaccreditation**(i) Period**

Subject to suspension or withdrawal under subparagraph (B), any accreditation under this section shall be valid for a period of 3 years after its issuance.

(ii) Response to reaccreditation request

Upon the submission of a request by an accredited person for reaccreditation under this section, the Secretary shall approve or deny such request not later than 60 days after receipt of the request.

(iii) Criteria

Not later than 120 days after July 9, 2012, the Secretary shall establish and publish in the Federal Register criteria to reaccredit or deny reaccreditation to persons under this section. The reaccreditation of persons under this section shall specify the particular activities under subsection (a), and the devices, for which such persons are reaccredited.

(3) Qualifications

An accredited person shall, at a minimum, meet the following requirements:

- (A) Such person may not be an employee of the Federal Government.
- (B) Such person shall be an independent organization which is not owned or controlled by a manufacturer, supplier, or vendor of devices and which has no organizational, material, or financial affiliation with such a manufacturer, supplier, or vendor.
- (C) Such person shall be a legally constituted entity permitted to conduct the activities for which it seeks accreditation.
- (D) Such person shall not engage in the design, manufacture, promotion, or sale of devices.
- (E) The operations of such person shall be in accordance with generally accepted professional and ethical business practices and shall agree in writing that as a minimum it will—
 - (i) certify that reported information accurately reflects data reviewed;
 - (ii) limit work to that for which competence and capacity are available;
 - (iii) treat information received, records, reports, and recommendations as proprietary information;

(iv) promptly respond and attempt to resolve complaints regarding its activities for which it is accredited; and

(v) protect against the use, in carrying out subsection (a) of this section with respect to a device, of any officer or employee of the person who has a financial conflict of interest regarding the device, and annually make available to the public disclosures of the extent to which the person, and the officers and employees of the person, have maintained compliance with requirements under this clause relating to financial conflicts of interest.

(4) Selection of accredited persons

The Secretary shall provide each person who chooses to use an accredited person to receive a section 360(k) of this title report a panel of at least two or more accredited persons from which the regulated person may select one for a specific regulatory function.

(5) Compensation of accredited persons

Compensation for an accredited person shall be determined by agreement between the accredited person and the person who engages the services of the accredited person, and shall be paid by the person who engages such services.

(c) Duration

The authority provided by this section terminates October 1, 2017.

(d) Report

Not later than January 10, 2007, the Secretary shall conduct a study based on the experience under the program under this section and submit to the Committee on Energy and Commerce of the House of Representatives, and the Committee on Health, Education, Labor, and Pensions of the Senate, a report describing the findings of the study. The objectives of the study shall include determining—

- (1) the number of devices reviewed under this section;
- (2) the number of devices reviewed under this section that were ultimately cleared by the Secretary;
- (3) the number of devices reviewed under this section that were ultimately not cleared by the Secretary;
- (4) the average time period for a review under this section (including the time it takes for the Secretary to review a recommendation of an accredited person under subsection (a) of this section and determine the initial device classification);
- (5) the average time period identified in paragraph (4) compared to the average time period for review of devices solely by the Secretary pursuant to section 360(k) of this title;
- (6) if there is a difference in the average time period under paragraph (4) and the average time period under paragraph (5), the reasons for such difference;
- (7) whether the quality of reviews under this section for devices for which no guidance has been issued is qualitatively inferior to reviews by the Secretary for devices for which no guidance has been issued;

(8) whether the quality of reviews under this section of devices for which no guidance has been issued is qualitatively inferior to reviews under this section of devices for which guidance has been issued;

(9) whether this section has in any way jeopardized or improved the public health;

(10) any impact of this section on resources available to the Secretary to review reports under section 360(k) of this title; and

(11) any suggestions for continuation, modification (including contraction or expansion of device eligibility), or termination of this section that the Secretary determines to be appropriate.

(June 25, 1938, ch. 675, §523, as added Pub. L. 105-115, title II, §210(a), Nov. 21, 1997, 111 Stat. 2342; amended Pub. L. 107-250, title II, §202, Oct. 26, 2002, 116 Stat. 1609; Pub. L. 110-85, title II, §221, Sept. 27, 2007, 121 Stat. 852; Pub. L. 111-31, div. A, title I, §103(f), June 22, 2009, 123 Stat. 1837; Pub. L. 112-144, title VI, §611, July 9, 2012, 126 Stat. 1059.)

AMENDMENTS

2012—Subsec. (b)(2)(E). Pub. L. 112-144, §611(a), added subpar. (E).

Subsec. (c). Pub. L. 112-144, §611(b), substituted “October 1, 2017” for “October 1, 2012”.

2009—Subsec. (b)(2)(D). Pub. L. 111-31 made technical amendment to reference in original act which appears in text as reference to section 393(g) of this title.

2007—Subsec. (c). Pub. L. 110-85 substituted “2012” for “2007”.

2002—Subsec. (c). Pub. L. 107-250, §202(1), substituted “The authority provided by this section terminates October 1, 2007.” for “The authority provided by this section terminates—

“(1) 5 years after the date on which the Secretary notifies Congress that at least 2 persons accredited under subsection (b) of this section are available to review at least 60 percent of the submissions under section 360(k) of this title, or

“(2) 4 years after the date on which the Secretary notifies Congress that the Secretary has made a determination described in paragraph (2)(B) of subsection (a) of this section for at least 35 percent of the devices that are subject to review under paragraph (1) of such subsection, whichever occurs first.”

Subsec. (d). Pub. L. 107-250, §202(2), added subsec. (d).

EFFECTIVE DATE

Section effective 90 days after Nov. 21, 1997, except as otherwise provided, see section 501 of Pub. L. 105-115, set out as a note under section 321 of this title.

REPORTS ON PROGRAM OF ACCREDITATION

Pub. L. 105-115, title II, §210(d), Nov. 21, 1997, 111 Stat. 2345, provided that:

“(1) COMPTROLLER GENERAL.—

“(A) IMPLEMENTATION OF PROGRAM.—Not later than 5 years after the date of the enactment of this Act [Nov. 21, 1997], the Comptroller General of the United States shall submit to the Committee on Commerce [now Committee on Energy and Commerce] of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report describing the extent to which the program of accreditation required by the amendment made by subsection (a) [enacting this section] has been implemented.

“(B) EVALUATION OF PROGRAM.—Not later than 6 months prior to the date on which, pursuant to subsection (c) of section 523 of the Federal Food, Drug,

and Cosmetic Act [21 U.S.C. 360m(c)] (as added by subsection (a)), the authority provided under subsection (a) of such section will terminate, the Comptroller General shall submit to the Committee on Commerce [now Committee on Energy and Commerce] of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report describing the use of accredited persons under such section 523, including an evaluation of the extent to which such use assisted the Secretary in carrying out the duties of the Secretary under such Act [21 U.S.C. 301 et seq.] with respect to devices, and the extent to which such use promoted actions which are contrary to the purposes of such Act.

“(2) INCLUSION OF CERTAIN DEVICES WITHIN PROGRAM.—Not later than 3 years after the date of the enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources [now Committee on Health, Education, Labor, and Pensions] of the Senate a report providing a determination by the Secretary of whether, in the program of accreditation established pursuant to the amendment made by subsection (a), the limitation established in clause (iii) of section 523(a)(3)(A) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360m(a)(3)(A)] (relating to class II devices for which clinical data are required in reports under section 510(k) [21 U.S.C. 360(k)]) should be removed.”

§ 360n. Priority review to encourage treatments for tropical diseases

(a) Definitions

In this section:

(1) Priority review

The term “priority review”, with respect to a human drug application as defined in section 379g(1) of this title, means review and action by the Secretary on such application not later than 6 months after receipt by the Secretary of such application, as described in the Manual of Policies and Procedures of the Food and Drug Administration and goals identified in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(2) Priority review voucher

The term “priority review voucher” means a voucher issued by the Secretary to the sponsor of a tropical disease product application that entitles the holder of such voucher to priority review of a single human drug application submitted under section 355(b)(1) of this title or section 262 of title 42 after the date of approval of the tropical disease product application.

(3) Tropical disease

The term “tropical disease” means any of the following:

- (A) Tuberculosis.
- (B) Malaria.
- (C) Blinding trachoma.
- (D) Buruli Ulcer.
- (E) Cholera.
- (F) Dengue/dengue haemorrhagic fever.
- (G) Dracunculiasis (guinea-worm disease).
- (H) Fascioliasis.
- (I) Human African trypanosomiasis.
- (J) Leishmaniasis.
- (K) Leprosy.
- (L) Lymphatic filariasis.

- (M) Onchocerciasis.
- (N) Schistosomiasis.
- (O) Soil transmitted helminthiasis.
- (P) Yaws.

(Q) Any other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations, designated by regulation by the Secretary.

(4) Tropical disease product application

The term “tropical disease product application” means an application that—

(A) is a human drug application as defined in section 379g(1) of this title—

- (i) for prevention or treatment of a tropical disease; and
- (ii) the Secretary deems eligible for priority review;

(B) is approved after September 27, 2007, by the Secretary for use in the prevention, detection, or treatment of a tropical disease; and

(C) is for a human drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under section 355(b)(1) of this title or section 262 of title 42.

(b) Priority review voucher

(1) In general

The Secretary shall award a priority review voucher to the sponsor of a tropical disease product application upon approval by the Secretary of such tropical disease product application.

(2) Transferability

The sponsor of a tropical disease product that receives a priority review voucher under this section may transfer (including by sale) the entitlement to such voucher to a sponsor of a human drug for which an application under section 355(b)(1) of this title or section 262 of title 42 will be submitted after the date of the approval of the tropical disease product application.

(3) Limitation

(A) No award for prior approved application

A sponsor of a tropical disease product may not receive a priority review voucher under this section if the tropical disease product application was submitted to the Secretary prior to September 27, 2007.

(B) One-year waiting period

The Secretary shall issue a priority review voucher to the sponsor of a tropical disease product no earlier than the date that is 1 year after September 27, 2007.

(4) Notification

The sponsor of a human drug application shall notify the Secretary not later than 365 days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug application, including the date on which the sponsor intends to submit the application. Such notification shall be a legally binding commitment to pay for the user fee to be assessed in accordance with this section.

(c) Priority review user fee

(1) In general

The Secretary shall establish a user fee program under which a sponsor of a human drug application that is the subject of a priority review voucher shall pay to the Secretary a fee determined under paragraph (2). Such fee shall be in addition to any fee required to be submitted by the sponsor under subchapter VII.

(2) Fee amount

The amount of the priority review user fee shall be determined each fiscal year by the Secretary and based on the average cost incurred by the agency in the review of a human drug application subject to priority review in the previous fiscal year.

(3) Annual fee setting

The Secretary shall establish, before the beginning of each fiscal year beginning after September 30, 2007, for that fiscal year, the amount of the priority review user fee.

(4) Payment

(A) In general

The priority review user fee required by this subsection shall be due upon the submission of a human drug application under section 355(b)(1) of this title or section 262 of title 42 for which the priority review voucher is used.

(B) Complete application

An application described under subparagraph (A) for which the sponsor requests the use of a priority review voucher shall be considered incomplete if the fee required by this subsection and all other applicable user fees are not paid in accordance with the Secretary’s procedures for paying such fees.

(C) No waivers, exemptions, reductions, or refunds

The Secretary may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section.

(5) Offsetting collections

Fees collected pursuant to this subsection for any fiscal year—

(A) shall be deposited and credited as offsetting collections to the account providing appropriations to the Food and Drug Administration; and

(B) shall not be collected for any fiscal year except to the extent provided in advance in appropriation Acts.

(June 25, 1938, ch. 675, §524, as added Pub. L. 110-85, title XI, §1102, Sept. 27, 2007, 121 Stat. 972.)

REFERENCES IN TEXT

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (a)(1), is section 101(c) of Pub. L. 110-85, which is set out as a note under section 379g of this title.

§ 360n-1. Priority review for qualified infectious disease products

If the Secretary designates a drug under section 355f(d) of this title as a qualified infectious

disease product, then the Secretary shall give priority review to any application submitted for approval for such drug under section 355(b) of this title.

(June 25, 1938, ch. 675, §524A, as added Pub. L. 112-144, title VIII, §802(a), July 9, 2012, 126 Stat. 1079.)

EFFECTIVE DATE

Pub. L. 112-144, title VIII, §802(b), July 9, 2012, 126 Stat. 1079, provided that: “Section 524A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360n-1], as added by subsection (a), applies only with respect to an application that is submitted under section 505(b) of such Act (21 U.S.C. 355(b)) on or after the date of the enactment of this Act [July 9, 2012].”

PART B—DRUGS FOR RARE DISEASES OR CONDITIONS

§ 360aa. Recommendations for investigations of drugs for rare diseases or conditions

(a) Request by sponsor; response by Secretary

The sponsor of a drug for a disease or condition which is rare in the States may request the Secretary to provide written recommendations for the non-clinical and clinical investigations which must be conducted with the drug before—

- (1) it may be approved for such disease or condition under section 355 of this title, or
- (2) if the drug is a biological product, it may be licensed for such disease or condition under section 262 of title 42.

If the Secretary has reason to believe that a drug for which a request is made under this section is a drug for a disease or condition which is rare in the States, the Secretary shall provide the person making the request written recommendations for the non-clinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request under this section, would be necessary for approval of such drug for such disease or condition under section 355 of this title or licensing of such drug for such disease or condition under section 262 of title 42.

(b) Regulations

The Secretary shall by regulation promulgate procedures for the implementation of subsection (a) of this section.

(June 25, 1938, ch. 675, §525, as added Pub. L. 97-414, §2(a), Jan. 4, 1983, 96 Stat. 2049; amended Pub. L. 99-91, §3(a)(1), Aug. 15, 1985, 99 Stat. 387; Pub. L. 105-115, title I, §125(b)(2)(F), (G), Nov. 21, 1997, 111 Stat. 2325, 2326.)

AMENDMENTS

1997—Subsec. (a). Pub. L. 105-115, §125(b)(2)(G), struck out “, certification of such drug for such disease or condition under section 357 of this title,” before “or licensing of such drug” in closing provisions.

Subsec. (a)(1) to (3). Pub. L. 105-115, §125(b)(2)(F), inserted “or” at end of par. (1), redesignated par. (3) as (2), and struck out former par. (2), which read as follows: “if the drug is an antibiotic, it may be certified for such disease or condition under section 357 of this title, or”.

1985—Subsec. (a). Pub. L. 99-91 struck out “or” at end of par. (1), inserted par. (2), redesignated former par. (2) as (3) and struck out “before” after “product,” and in last sentence inserted provisions relating to certifi-

cation of such drug for disease or condition under section 357 of this title and substituted “licensing of such drug for such disease or condition under section 262 of title 42” for “licensing under section 262 of title 42 for such disease or condition”.

EFFECTIVE DATE OF 1985 AMENDMENT

Pub. L. 99-91, §8, Aug. 15, 1985, 99 Stat. 392, provided that:

“(a) GENERAL RULE.—Except as provided in subsection (b), this Act and the amendments made by this Act [amending this section, sections 360bb, 360cc, and 360ee of this title, and sections 295g-1 and 6022 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under section 301 of this title and section 236 of Title 42] shall take effect October 1, 1985.

“(b) EXCEPTION.—The amendments made by sections 2, 3, and 6(a) [amending this section and sections 360bb and 360cc of this title] shall take effect on the date of the enactment of this Act [Aug. 15, 1985]. The amendment made by section 6(b) [amending section 6022 of Title 42] shall take effect October 19, 1984. The amendments made by section 7 [amending section 295g-1 of Title 42] shall take effect October 1, 1984 and shall cease to be in effect after September 30, 1985.”

REVIEW GROUPS ON RARE DISEASES AND NEGLECTED DISEASES OF THE DEVELOPING WORLD; REPORT; GUIDANCE; STANDARDS

Pub. L. 111-80, title VII, §740, Oct. 21, 2009, 123 Stat. 2127, provided that:

“(a) The Commissioner of Food and Drugs shall establish within the Food and Drug Administration a review group which shall recommend to the Commissioner of Food and Drugs appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment of rare diseases: *Provided*, That the Commissioner of Food and Drugs shall appoint individuals employed by the Food and Drug Administration to serve on the review group: *Provided further*, That members of the review group shall have specific expertise relating to the development of articles for use in the prevention, diagnosis, or treatment of rare diseases, including specific expertise in developing or carrying out clinical trials.

“(b) The Commissioner of Food and Drugs shall establish within the Food and Drug Administration a review group which shall recommend to the Commissioner of Food and Drugs appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment of neglected diseases of the developing world: *Provided*, That the Commissioner of Food and Drugs shall appoint individuals employed by the Food and Drug Administration to serve on the review group: *Provided further*, That members of the review group shall have specific expertise relating to the development of articles for use in the prevention, diagnosis, or treatment of neglected diseases of the developing world, including specific expertise in developing or carrying out clinical trials: *Provided further*, That for the purposes of this section the term ‘neglected disease of the developing world’ means a tropical disease, as defined in section 524(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360n(a)(3)).

“(c) The Commissioner of Food and Drugs shall—

“(1) submit, not later than 1 year after the date of the establishment of review groups under subsections (a) and (b), a report to Congress that describes both the findings and recommendations made by the review groups under subsections (a) and (b);

“(2) issue, not later than 180 days after submission of the report to Congress under paragraph (1), guidance based on such recommendations for articles for use in the prevention, diagnosis, and treatment of rare diseases and for such uses in neglected diseases of the developing world; and

“(3) develop, not later than 180 days after submission of the report to Congress under paragraph (1), in-