(3) not later than 18 months after the close of the public comment period for the draft guidance described in paragraph (2), issue revised draft guidance or final guidance.

(f) Rule of construction

(1) In general

Subject to paragraph (2), nothing in this section prohibits the Secretary from using real world evidence for purposes not specified in this section, provided the Secretary determines that sufficient basis exists for any such nonspecified use.

(2) Standards of evidence and Secretary's authority

This section shall not be construed to alter—

(A) the standards of evidence under—

(i) subsection (c) or (d) of section 355 of this title, including the substantial evidence standard in such subsection (d); or

(ii) section 262(a) of title 42; or

(B) the Secretary's authority to require postapproval studies or clinical trials, or the standards of evidence under which studies or trials are evaluated.

(June 25, 1938, ch. 675, § 505F, as added Pub. L. 114–255, div. A, title III, § 3022, Dec. 13, 2016, 130 Stat. 1096; amended Pub. L. 115–52, title IX, § 901(c), (d), Aug. 18, 2017, 131 Stat. 1076.)

Editorial Notes

AMENDMENTS

2017—Subsec. (b). Pub. L. 115–52, § 901(c), substituted ''traditional'' for ''randomized''.

Subsec. (d). Pub. L. 115–52, § 901(d), substituted ''3 years'' for ''2 years''.

§ 355h. Regulation of certain nonprescription drugs that are marketed without an approved drug application

(a) Nonprescription drugs marketed without an approved application

Nonprescription drugs marketed without an approved drug application under section 355 of this title, as of March 27, 2020, shall be treated in accordance with this subsection.

(1) Drugs subject to a final monograph; category I drugs subject to a tentative final monograph

A drug is deemed to be generally recognized as safe and effective under section 321(p)(1) of this title, not a new drug under section 321(p) of this title, and not subject to section 353(b)(1) of this title, if—

(A) the drug is—

(i) in conformity with the requirements for nonprescription use of a final monograph issued under part 330 of title 21, Code of Federal Regulations (except as provided in paragraph (2)), the general requirements for nonprescription drugs, and conditions or requirements under subsections (b), (c), and (k); and

(ii) except as permitted by an order issued under subsection (b) or, in the case of a minor change in the drug, in conformity with an order issued under subsection (c), in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title; or

(B) the drug is—

(i) classified in category I for safety and effectiveness under a tentative final monograph that is the most recently applicable proposal or determination issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with the proposed requirements for nonprescription use of such tentative final monograph, any applicable subsequent determination by the Secretary, the general requirements for nonprescription drugs, and conditions or requirements under subsections (b), (c), and (k); and

(iii) except as permitted by an order issued under subsection (b) or, in the case of a minor change in the drug, in conformity with an order issued under subsection (c), in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title.

(2) Treatment of sunscreen drugs

With respect to sunscreen drugs subject to this section, the applicable requirements in terms of conformity with a final monograph, for purposes of paragraph (1)(A)(i), shall be the requirements specified in part 352 of title 21, Code of Federal Regulations, as published on May 21, 1999, beginning on page 27687 of volume 64 of the Federal Register, except that the applicable requirements governing effectiveness and labeling shall be those specified in section 201.327 of title 21, Code of Federal Regulations.

(3) Category III drugs subject to a tentative final monograph; category I drugs subject to proposed monograph or advance notice of proposed rulemaking

A drug that is not described in paragraph (1), (2), or (4) is not required to be the subject of an application approved under section 355 of this title, and is not subject to section 353(b)(1) of this title, if—

(A) the drug is—

(i) classified in category III for safety or effectiveness in the preamble of a proposed rule establishing a tentative final monograph that is the most recently applicable proposal or determination for such drug issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with—

(I) the conditions of use, including indication and dosage strength, if any, described for such category III drug in such preamble or in an applicable subsequent proposed rule;

(II) the proposed requirements for drugs classified in such tentative final monograph in category I in the most recently proposed rule establishing requirements related to such tentative final monograph and in any final rule es-

tablishing requirements that are applicable to the drug; and

(III) the general requirements for nonprescription drugs and conditions or requirements under subsection (b) or (k); and

(iii) in a dosage form that, immediately prior to March 27, 2020, had been used to a material extent and for a material time under section 321(p)(2) of this title; or

(B) the drug is—

(i) classified in category I for safety and effectiveness under a proposed monograph or advance notice of proposed rulemaking that is the most recently applicable proposal or determination for such drug issued under part 330 of title 21, Code of Federal Regulations;

(ii) in conformity with the requirements for nonprescription use of such proposed monograph or advance notice of proposed rulemaking, any applicable subsequent determination by the Secretary, the general requirements for nonprescription drugs, and conditions or requirements under subsection (b) or (k); and

(iii) in a dosage form that, immediately prior to March 27, 2020, has been used to a material extent and for a material time under section 321(p)(2) of this title.

(4) Category II drugs deemed new drugs

A drug that is classified in category II for safety or effectiveness under a tentative final monograph or that is subject to a determination to be not generally recognized as safe and effective in a proposed rule that is the most recently applicable proposal issued under part 330 of title 21, Code of Federal Regulations, shall be deemed to be a new drug under section 321(p) of this title, misbranded under section 352(ee) of this title, and subject to the requirement for an approved new drug application under section 355 of this title beginning on the day that is 180 calendar days after March 27, 2020, unless, before such day, the Secretary determines that it is in the interest of public health to extend the period during which the drug may be marketed without such an approved new drug application.

(5) Drugs not GRASE deemed new drugs

A drug that the Secretary has determined not to be generally recognized as safe and effective under section 321(p)(1) of this title under a final determination issued under part 330 of title 21, Code of Federal Regulations, shall be deemed to be a new drug under section 321(p) of this title, misbranded under section 352(ee) of this title, and subject to the requirement for an approved new drug application under section 355 of this title.

(6) Other drugs deemed new drugs

Except as provided in subsection (m), a drug is deemed to be a new drug under section 321(p) of this title and misbranded under section 352(ee) of this title if the drug—

(A) is not subject to section 353(b)(1) of this title; and

(B) is not described in paragraph (1), (2), (3), (4), or (5), or subsection (b)(1)(B).

(b) Administrative orders

(1) In general

(A) Determination

The Secretary may, on the initiative of the Secretary or at the request of one or more requestors, issue an administrative order determining whether there are conditions under which a specific drug, a class of drugs, or a combination of drugs, is determined to be—

(i) not subject to section 353(b)(1) of this title; and

(ii) generally recognized as safe and effective under section 321(p)(1) of this title.

(B) Effect

A drug or combination of drugs shall be deemed to not require approval under section 355 of this title if such drug or combination of drugs—

(i) is determined by the Secretary to meet the conditions specified in clauses (i) and (ii) of subparagraph (A);

(ii) is marketed in conformity with an administrative order under this subsection;

(iii) meets the general requirements for nonprescription drugs; and

(iv) meets the requirements under subsections (c) and (k).

(C) Standard

The Secretary shall find that a drug is not generally recognized as safe and effective under section 321(p)(1) of this title if—

(i) the evidence shows that the drug is not generally recognized as safe and effective under section 321(p)(1) of this title; or

(ii) the evidence is inadequate to show that the drug is generally recognized as safe and effective under section 321(p)(1) of this title.

(2) Administrative orders initiated by the Secretary

(A) In general

In issuing an administrative order under paragraph (1) upon the Secretary's initiative, the Secretary shall—

(i) make reasonable efforts to notify informally, not later than 2 business days before the issuance of the proposed order, the sponsors of drugs who have a listing in effect under section 360(j) of this title for the drugs or combination of drugs that will be subject to the administrative order;

(ii) after any such reasonable efforts of notification—

(I) issue a proposed administrative order by publishing it on the website of the Food and Drug Administration and include in such order the reasons for the issuance of such order; and

(II) publish a notice of availability of such proposed order in the Federal Register;

(iii) except as provided in subparagraph (B), provide for a public comment period with respect to such proposed order of not less than 45 calendar days; and

(iv) if, after completion of the proceedings specified in clauses (i) through (iii), the Secretary determines that it is appropriate to issue a final administrative order—

(I) issue the final administrative order, together with a detailed statement of reasons, which order shall not take effect until the time for requesting judicial review under paragraph (3)(D)(ii) has expired;

(II) publish a notice of such final administrative order in the Federal Register;

(III) afford requestors of drugs that will be subject to such order the opportunity for formal dispute resolution up to the level of the Director of the Center for Drug Evaluation and Research, which initially must be requested within 45 calendar days of the issuance of the order, and, for subsequent levels of appeal, within 30 calendar days of the prior decision; and

(IV) except with respect to drugs described in paragraph (3)(B), upon completion of the formal dispute resolution procedure, inform the persons which sought such dispute resolution of their right to request a hearing.

(B) Exceptions

When issuing an administrative order under paragraph (1) on the Secretary's initiative proposing to determine that a drug described in subsection (a)(3) is not generally recognized as safe and effective under section 321(p)(1) of this title, the Secretary shall follow the procedures in subparagraph (A), except that—

(i) the proposed order shall include notice of—

(I) the general categories of data the Secretary has determined necessary to establish that the drug is generally recognized as safe and effective under section 321(p)(1) of this title; and

(II) the format for submissions by interested persons;

(ii) the Secretary shall provide for a public comment period of no less than 180 calendar days with respect to such proposed order, except when the Secretary determines, for good cause, that a shorter period is in the interest of public health; and

(iii) any person who submits data in such comment period shall include a certification that the person has submitted all evidence created, obtained, or received by that person that is both within the categories of data identified in the proposed order and relevant to a determination as to whether the drug is generally recognized as safe and effective under section 321(p)(1) of this title.

(3) Hearings; judicial review

(A) In general

Only a person who participated in each stage of formal dispute resolution under subclause (III) of paragraph (2)(A)(iv) of an administrative order with respect to a drug may request a hearing concerning a final administrative order issued under such paragraph with respect to such drug. If a hearing is sought, such person must submit a request for a hearing, which shall be based solely on information in the administrative record, to the Secretary not later than 30 calendar days after receiving notice of the final decision of the formal dispute resolution procedure.

(B) No hearing required with respect to orders relating to certain drugs

(i) In general

The Secretary shall not be required to provide notice and an opportunity for a hearing pursuant to paragraph (2)(A)(iv) if the final administrative order involved relates to a drug—

(I) that is described in subsection (a)(3)(A); and

(II) with respect to which no human or non-human data studies relevant to the safety or effectiveness of such drug have been submitted to the administrative record since the issuance of the most recent tentative final monograph relating to such drug.

(ii) Human data studies and non-human data defined

In this subparagraph:

(I) The term ''human data studies'' means clinical trials of safety or effectiveness (including actual use studies), pharmacokinetics studies, or bioavailability studies.

(II) The term ''non-human data'' means data from testing other than with human subjects which provides information concerning safety or effectiveness.

(C) Hearing procedures

(i) Denial of request for hearing

If the Secretary determines that information submitted in a request for a hearing under subparagraph (A) with respect to a final administrative order issued under paragraph (2)(A)(iv) does not identify the existence of a genuine and substantial question of material fact, the Secretary may deny such request. In making such a determination, the Secretary may consider only information and data that are based on relevant and reliable scientific principles and methodologies.

(ii) Single hearing for multiple related requests

If more than one request for a hearing is submitted with respect to the same administrative order under subparagraph (A), the Secretary may direct that a single hearing be conducted in which all persons whose hearing requests were granted may participate.

(iii) Presiding officer

The presiding officer of a hearing requested under subparagraph (A) shall—

(I) be designated by the Secretary;

(II) not be an employee of the Center for Drug Evaluation and Research; and

(III) not have been previously involved in the development of the administrative order involved or proceedings relating to that administrative order.

(iv) Rights of parties to hearing

The parties to a hearing requested under subparagraph (A) shall have the right to present testimony, including testimony of expert witnesses, and to cross-examine witnesses presented by other parties. Where appropriate, the presiding officer may require that cross-examination by parties representing substantially the same interests be consolidated to promote efficiency and avoid duplication.

(v) Final decision

(I) At the conclusion of a hearing requested under subparagraph (A), the presiding officer of the hearing shall issue a decision containing findings of fact and conclusions of law. The decision of the presiding officer shall be final.

(II) The final decision may not take effect until the period under subparagraph (D)(ii) for submitting a request for judicial review of such decision expires.

(D) Judicial review of final administrative order

(i) In general

The procedures described in section 355(h) of this title shall apply with respect to judicial review of final administrative orders issued under this subsection in the same manner and to the same extent as such section applies to an order described in such section except that the judicial review shall be taken by filing in an appropriate district court of the United States in lieu of the appellate courts specified in such section.

(ii) Period to submit a request for judicial review

A person eligible to request a hearing under this paragraph and seeking judicial review of a final administrative order issued under this subsection shall file such request for judicial review not later than 60 calendar days after the latest of—

(I) the date on which notice of such order is published;

(II) the date on which a hearing with respect to such order is denied under subparagraph (B) or (C)(i);

(III) the date on which a final decision is made following a hearing under subparagraph (C)(v); or

(IV) if no hearing is requested, the date on which the time for requesting a hearing expires.

(4) Expedited procedure with respect to administrative orders initiated by the Secretary

(A) Imminent hazard to the public health

(i) In general

In the case of a determination by the Secretary that a drug, class of drugs, or combination of drugs subject to this section poses an imminent hazard to the public health, the Secretary, after first making reasonable efforts to notify, not later than 48 hours before issuance of such order under this subparagraph, sponsors who have a listing in effect under section 360(j) of this title for such drug or combination of drugs—

(I) may issue an interim final administrative order for such drug, class of drugs, or combination of drugs under paragraph (1), together with a detailed statement of the reasons for such order;

(II) shall publish in the Federal Register a notice of availability of any such order; and

(III) shall provide for a public comment period of at least 45 calendar days with respect to such interim final order.

(ii) Nondelegation

The Secretary may not delegate the authority to issue an interim final administrative order under this subparagraph.

(B) Safety labeling changes

(i) In general

In the case of a determination by the Secretary that a change in the labeling of a drug, class of drugs, or combination of drugs subject to this section is reasonably expected to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug, the Secretary may—

(I) make reasonable efforts to notify informally, not later than 48 hours before the issuance of the interim final order, the sponsors of drugs who have a listing in effect under section 360(j) of this title for such drug or combination of drugs;

(II) after reasonable efforts of notification, issue an interim final administrative order in accordance with paragraph (1) to require such change, together with a detailed statement of the reasons for such order;

(III) publish in the Federal Register a notice of availability of such order; and

(IV) provide for a public comment period of at least 45 calendar days with respect to such interim final order.

(ii) Content of order

An interim final order issued under this subparagraph with respect to the labeling of a drug may provide for new warnings and other information required for safe use of the drug.

(C) Effective date

An order under subparagraph (A) or (B) shall take effect on a date specified by the Secretary.

(D) Final order

After the completion of the proceedings in subparagraph (A) or (B), the Secretary shall—

(i) issue a final order in accordance with paragraph (1);

(ii) publish a notice of availability of such final administrative order in the Federal Register; and

(iii) afford sponsors of such drugs that will be subject to such an order the opportunity for formal dispute resolution up to the level of the Director of the Center for Drug Evaluation and Research, which must initially be within 45 calendar days of the issuance of the order, and for subsequent levels of appeal, within 30 calendar days of the prior decision.

(E) Hearings

A sponsor of a drug subject to a final order issued under subparagraph (D) and that participated in each stage of formal dispute resolution under clause (iii) of such subparagraph may request a hearing on such order. The provisions of subparagraphs (A), (B), and (C) of paragraph (3), other than paragraph (3)(C)(v)(II), shall apply with respect to a hearing on such order in the same manner and to the same extent as such provisions apply with respect to a hearing on an administrative order issued under paragraph (2)(A)(iv).

(F) Timing

(i) Final order and hearing

The Secretary shall—

(I) not later than 6 months after the date on which the comment period closes under subparagraph (A) or (B), issue a final order in accordance with paragraph (1); and

(II) not later than 12 months after the date on which such final order is issued, complete any hearing under subparagraph (E).

(ii) Dispute resolution request

The Secretary shall specify in an interim final order issued under subparagraph (A) or (B) such shorter periods for requesting dispute resolution under subparagraph (D)(iii) as are necessary to meet the requirements of this subparagraph.

(G) Judicial review

A final order issued pursuant to subparagraph (F) shall be subject to judicial review in accordance with paragraph (3)(D).

(5) Administrative order initiated at the request of a requestor

(A) In general

In issuing an administrative order under paragraph (1) at the request of a requestor with respect to certain drugs, classes of drugs, or combinations of drugs—

(i) the Secretary shall, after receiving a request under this subparagraph, determine whether the request is sufficiently complete and formatted to permit a substantive review;

(ii) if the Secretary determines that the request is sufficiently complete and formatted to permit a substantive review, the Secretary shall—

(I) file the request; and

(II) initiate proceedings with respect to issuing an administrative order in accordance with paragraphs (2) and (3); and

(iii) except as provided in paragraph (6), if the Secretary determines that a request does not meet the requirements for filing or is not sufficiently complete and formatted to permit a substantive review, the requestor may demand that the request be filed over protest, and the Secretary shall initiate proceedings to review the request in accordance with paragraph (2)(A).

(B) Request to initiate proceedings

(i) In general

A requestor seeking an administrative order under paragraph (1) with respect to certain drugs, classes of drugs, or combinations of drugs, shall submit to the Secretary a request to initiate proceedings for such order in the form and manner as specified by the Secretary. Such requestor may submit a request under this subparagraph for the issuance of an administrative order—

(I) determining whether a drug is generally recognized as safe and effective under section 321(p)(1) of this title, exempt from section 353(b)(1) of this title, and not required to be the subject of an approved application under section 355 of this title; or

(II) determining whether a change to a condition of use of a drug is generally recognized as safe and effective under section 321(p)(1) of this title, exempt from section 353(b)(1) of this title, and not required to be the subject of an approved application under section 355 of this title, if, absent such a changed condition of use, such drug is—

(aa) generally recognized as safe and effective under section 321(p)(1) of this title in accordance with subsection (a)(1), (a)(2), or an order under this subsection; or

(bb) subject to subsection (a)(3), but only if such requestor initiates such request in conjunction with a request for the Secretary to determine whether such drug is generally recognized as safe and effective under section 321(p)(1) of this title, which is filed by the Secretary under subparagraph (A)(ii).

(ii) Exception

The Secretary is not required to complete review of a request for a change described in clause (i)(II) if the Secretary determines that there is an inadequate basis to find the drug is generally recognized as safe and effective under section 321(p)(1) of this title under paragraph (1) and issues a final order announcing that determination.

(iii) Withdrawal

The requestor may withdraw a request under this paragraph, according to the procedures set forth pursuant to subsection (d)(2)(B). Notwithstanding any other provision of this section, if such request is withdrawn, the Secretary may cease proceedings under this subparagraph.

(C) Exclusivity

(i) In general

A final administrative order issued in response to a request under this section shall have the effect of authorizing solely the order requestor (or the licensees, assignees, or successors in interest of such requestor with respect to the subject of such order), for a period of 18 months following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order, to market drugs—

(I) incorporating changes described in clause (ii); and

(II) subject to the limitations under clause (iv).

(ii) Changes described

A change described in this clause is a change subject to an order specified in clause (i), which—

(I) provides for a drug to contain an active ingredient (including any ester or salt of the active ingredient) not previously incorporated in a drug described in clause (iii); or

(II) provides for a change in the conditions of use of a drug, for which new human data studies conducted or sponsored by the requestor (or for which the requestor has an exclusive right of reference) were essential to the issuance of such order.

(iii) Drugs described

The drugs described in this clause are drugs—

(I) specified in subsection (a)(1), (a)(2), or (a)(3);

(II) subject to a final order issued under this section;

(III) subject to a final sunscreen order (as defined in section 360fff(2)(A) of this title); or

(IV) described in subsection (m)(1), other than drugs subject to an active enforcement action under subchapter III of this chapter.

(iv) Limitations on exclusivity

(I) In general

Only one 18-month period under this subparagraph shall be granted, under each order described in clause (i), with respect to changes (to the drug subject to such order) which are either—

(aa) changes described in clause (ii)(I), relating to active ingredients; or

(bb) changes described in clause (ii)(II), relating to conditions of use.

(II) No exclusivity allowed

No exclusivity shall apply to changes to a drug which are—

(aa) the subject of a Tier 2 OTC monograph order request (as defined in section 379j–71 of this title);

(bb) safety-related changes, as defined by the Secretary, or any other changes the Secretary considers necessary to assure safe use; or

(cc) changes related to methods of testing safety or efficacy.

(v) New human data studies defined

In this subparagraph, the term ''new human data studies'' means clinical trials of safety or effectiveness (including actual use studies), pharmacokinetics studies, or bioavailability studies, the results of which—

(I) have not been relied on by the Secretary to support—

(aa) a proposed or final determination that a drug described in subclause (I), (II), or (III) of clause (iii) is generally recognized as safe and effective under section 321(p)(1) of this title; or

(bb) approval of a drug that was approved under section 355 of this title; and

(II) do not duplicate the results of another study that was relied on by the Secretary to support—

(aa) a proposed or final determination that a drug described in subclause (I), (II), or (III) of clause (iii) is generally recognized as safe and effective under section 321(p)(1) of this title; or

(bb) approval of a drug that was approved under section 355 of this title.

(vi) Notification of drug not available for sale

A requestor that is granted exclusivity with respect to a drug under this subparagraph shall notify the Secretary in writing within 1 year of the issuance of the final administrative order if the drug that is the subject of such order will not be available for sale within 1 year of the date of issuance of such order. The requestor shall include with such notice the—

(I) identity of the drug by established name and by proprietary name, if any;

(II) strength of the drug;

(III) date on which the drug will be available for sale, if known; and

(IV) reason for not marketing the drug after issuance of the order.

(6) Information regarding safe nonprescription marketing and use as condition for filing a generally recognized as safe and effective request

(A) In general

In response to a request under this section that a drug described in subparagraph (B) be generally recognized as safe and effective, the Secretary—

(i) may file such request, if the request includes information specified under subparagraph (C) with respect to safe nonprescription marketing and use of such drug; or

(ii) if the request fails to include information specified under subparagraph (C), shall refuse to file such request and require that nonprescription marketing of the drug be pursuant to a new drug application as described in subparagraph (D).

(B) Drug described

A drug described in this subparagraph is a nonprescription drug which contains an ac-

tive ingredient not previously incorporated in a drug—

(i) specified in subsection (a)(1), (a)(2), or (a)(3);

(ii) subject to a final order under this section; or

(iii) subject to a final sunscreen order (as defined in section 360fff(2)(A) of this title).

(C) Information demonstrating prima facie safe nonprescription marketing and use

Information specified in this subparagraph, with respect to a request described in subparagraph (A)(i), is—

(i) information sufficient for a prima facie demonstration that the drug subject to such request has a verifiable history of being marketed and safely used by consumers in the United States as a nonprescription drug under comparable conditions of use;

(ii) if the drug has not been previously marketed in the United States as a nonprescription drug, information sufficient for a prima facie demonstration that the drug was marketed and safely used under comparable conditions of marketing and use in a country listed in section 382(b)(1)(A) of this title or designated by the Secretary in accordance with section 382(b)(1)(B) of this title—

(I) for such period as needed to provide reasonable assurances concerning the safe nonprescription use of the drug; and

(II) during such time was subject to sufficient monitoring by a regulatory body considered acceptable by the Secretary for such monitoring purposes, including for adverse events associated with nonprescription use of the drug; or

(iii) if the Secretary determines that information described in clause (i) or (ii) is not needed to provide a prima facie demonstration that the drug can be safely marketed and used as a nonprescription drug, such other information the Secretary determines is sufficient for such purposes.

(D) Marketing pursuant to new drug application

In the case of a request described in subparagraph (A)(ii), the drug subject to such request may be resubmitted for filing only if—

(i) the drug is marketed as a nonprescription drug, under conditions of use comparable to the conditions specified in the request, for such period as the Secretary determines appropriate (not to exceed 5 consecutive years) pursuant to an application approved under section 355 of this title; and

(ii) during such period, 1,000,000 retail packages of the drug, or an equivalent quantity as determined by the Secretary, were distributed for retail sale, as determined in such manner as the Secretary finds appropriate.

(E) Rule of application

Except in the case of a request involving a drug described in section 360fff(9) of this title, as in effect on January 1, 2017, if the Secretary refuses to file a request under this paragraph, the requestor may not file such request over protest under paragraph (5)(A)(iii).

(7) Packaging

An administrative order issued under paragraph (2), (4)(A), or (5) may include requirements for the packaging of a drug to encourage use in accordance with labeling. Such requirements may include unit dose packaging, requirements for products intended for use by pediatric populations, requirements to reduce risk of harm from unsupervised ingestion, and other appropriate requirements. This paragraph does not authorize the Food and Drug Administration to require standards or testing procedures as described in part 1700 of title 16, Code of Federal Regulations.

(8) Final and tentative final monographs for category I drugs deemed final administrative orders

(A) In general

A final monograph or tentative final monograph described in subparagraph (B) shall be deemed to be a final administrative order under this subsection and may be amended, revoked, or otherwise modified in accordance with the procedures of this subsection.

(B) Monographs described

For purposes of subparagraph (A), a final monograph or tentative final monograph is described in this subparagraph if it—

(i) establishes conditions of use for a drug described in paragraph (1) or (2) of subsection (a); and

(ii) represents the most recently promulgated version of such conditions, including as modified, in whole or in part, by any proposed or final rule.

(C) Deemed orders include harmonizing technical amendments

The deemed establishment of a final administrative order under subparagraph (A) shall be construed to include any technical amendments to such order as the Secretary determines necessary to ensure that such order is appropriately harmonized, in terms of terminology or cross-references, with the applicable provisions of this chapter (and regulations thereunder) and any other orders issued under this section.

(c) Procedure for minor changes

(1) In general

Minor changes in the dosage form of a drug that is described in paragraph (1) or (2) of subsection (a) or the subject of an order issued under subsection (b) may be made by a requestor without the issuance of an order under subsection (b) if—

(A) the requestor maintains such information as is necessary to demonstrate that the change—

(i) will not affect the safety or effectiveness of the drug; and

(ii) will not materially affect the extent of absorption or other exposure to the ac-

tive ingredient in comparison to a suitable reference product; and

(B) the change is in conformity with the requirements of an applicable administrative order issued by the Secretary under paragraph (3).

(2) Additional information

(A) Access to records

A sponsor shall submit records requested by the Secretary relating to such a minor change under section 374(a)(4) of this title, within 15 business days of receiving such a request, or such longer period as the Secretary may provide.

(B) Insufficient information

If the Secretary determines that the information contained in such records is not sufficient to demonstrate that the change does not affect the safety or effectiveness of the drug or materially affect the extent of absorption or other exposure to the active ingredient, the Secretary—

(i) may so inform the sponsor of the drug in writing; and

(ii) if the Secretary so informs the sponsor, shall provide the sponsor of the drug with a reasonable opportunity to provide additional information.

(C) Failure to submit sufficient information

If the sponsor fails to provide such additional information within a time prescribed by the Secretary, or if the Secretary determines that such additional information does not demonstrate that the change does not—

(i) affect the safety or effectiveness of the drug; or

(ii) materially affect the extent of absorption or other exposure to the active ingredient in comparison to a suitable reference product,

the drug as modified is a new drug under section 321(p) of this title and shall be deemed to be misbranded under section 352(ee) of this title.

(3) Determining whether a change will affect safety or effectiveness

(A) In general

The Secretary shall issue one or more administrative orders specifying requirements for determining whether a minor change made by a sponsor pursuant to this subsection will affect the safety or effectiveness of a drug or materially affect the extent of absorption or other exposure to an active ingredient in the drug in comparison to a suitable reference product, together with guidance for applying those orders to specific dosage forms.

(B) Standard practices

The orders and guidance issued by the Secretary under subparagraph (A) shall take into account relevant public standards and standard practices for evaluating the quality of drugs, and may take into account the special needs of populations, including children.

(d) Confidentiality of information submitted to the Secretary

(1) In general

Subject to paragraph (2), any information, including reports of testing conducted on the drug or drugs involved, that is submitted by a requestor in connection with proceedings on an order under this section (including any minor change under subsection (c)) and is a trade secret or confidential information subject to section 552(b)(4) of title 5 or section 1905 of title 18 shall not be disclosed to the public unless the requestor consents to that disclosure.

(2) Public availability

(A) In general

Except as provided in subparagraph (B), the Secretary shall—

(i) make any information submitted by a requestor in support of a request under subsection (b)(5)(A) available to the public not later than the date on which the proposed order is issued; and

(ii) make any information submitted by any other person with respect to an order requested (or initiated by the Secretary) under subsection (b), available to the public upon such submission.

(B) Limitations on public availability

Information described in subparagraph (A) shall not be made public if—

(i) the information pertains to pharmaceutical quality information, unless such information is necessary to establish standards under which a drug is generally recognized as safe and effective under section 321(p)(1) of this title;

(ii) the information is submitted in a requestor-initiated request, but the requestor withdraws such request, in accordance with withdrawal procedures established by the Secretary, before the Secretary issues the proposed order;

(iii) the Secretary requests and obtains the information under subsection (c) and such information is not submitted in relation to an order under subsection (b); or

(iv) the information is of the type contained in raw datasets.

(e) Updates to drug listing information

A sponsor who makes a change to a drug subject to this section shall submit updated drug listing information for the drug in accordance with section 360(j) of this title within 30 calendar days of the date when the drug is first commercially marketed, except that a sponsor who was the order requestor with respect to an order subject to subsection (b)(5)(C) (or a licensee, assignee, or successor in interest of such requestor) shall submit updated drug listing information on or before the date when the drug is first commercially marketed.

(f) Approvals under section 355 of this title

The provisions of this section shall not be construed to preclude a person from seeking or maintaining the approval of an application for a drug under sections 355(b)(1), 355(b)(2), and 355(j)

of this title. A determination under this section that a drug is not subject to section 353(b)(1) of this title, is generally recognized as safe and effective under section 321(p)(1) of this title, and is not a new drug under section 321(p) of this title shall constitute a finding that the drug is safe and effective that may be relied upon for purposes of an application under section 355(b)(2) of this title, so that the applicant shall be required to submit for purposes of such application only information needed to support any modification of the drug that is not covered by such determination under this section.

(g) Public availability of administrative orders

The Secretary shall establish, maintain, update (as determined necessary by the Secretary but no less frequently than annually), and make publicly available, with respect to orders issued under this section—

(1) a repository of each final order and interim final order in effect, including the complete text of the order; and

(2) a listing of all orders proposed and under development under subsection (b)(2), including—

(A) a brief description of each such order; and

(B) the Secretary's expectations, if resources permit, for issuance of proposed orders over a 3-year period.

(h) Development advice to sponsors or requestors

The Secretary shall establish procedures under which sponsors or requestors may meet with appropriate officials of the Food and Drug Administration to obtain advice on the studies and other information necessary to support submissions under this section and other matters relevant to the regulation of nonprescription drugs and the development of new nonprescription drugs under this section.

(i) Participation of multiple sponsors or requestors

The Secretary shall establish procedures to facilitate efficient participation by multiple sponsors or requestors in proceedings under this section, including provision for joint meetings with multiple sponsors or requestors or with organizations nominated by sponsors or requestors to represent their interests in a proceeding.

(j) Electronic format

All submissions under this section shall be in electronic format.

(k) Effect on existing regulations governing nonprescription drugs

(1) Regulations of general applicability to nonprescription drugs

Except as provided in this subsection, nothing in this section supersedes regulations establishing general requirements for nonprescription drugs, including regulations of general applicability contained in parts 201, 250, and 330 of title 21, Code of Federal Regulations, or any successor regulations. The Secretary shall establish or modify such regulations by means of rulemaking in accordance with section 553 of title 5.

(2) Regulations establishing requirements for specific nonprescription drugs

(A) The provisions of section 310.545 of title 21, Code of Federal Regulations, as in effect on the day before March 27, 2020, shall be deemed to be a final order under subsection (b).

(B) Regulations in effect on the day before March 27, 2020, establishing requirements for specific nonprescription drugs marketed pursuant to this section (including such requirements in parts 201 and 250 of title 21, Code of Federal Regulations), shall be deemed to be final orders under subsection (b), only as they apply to drugs—

(i) subject to paragraph (1), (2), (3), or (4) of subsection (a); or

(ii) otherwise subject to an order under this section.

(3) Withdrawal of regulations

The Secretary shall withdraw regulations establishing final monographs and the procedures governing the over-the-counter drug review under part 330 and other relevant parts of title 21, Code of Federal Regulations (as in effect on the day before March 27, 2020), or make technical changes to such regulations to ensure conformity with appropriate terminology and cross references. Notwithstanding subchapter II of chapter 5 of title 5, any such withdrawal or technical changes shall be made without public notice and comment and shall be effective upon publication through notice in the Federal Register (or upon such date as specified in such notice).

***(l)* Guidance**

The Secretary shall issue guidance that specifies—

(1) the procedures and principles for formal meetings between the Secretary and sponsors or requestors for drugs subject to this section;

(2) the format and content of data submissions to the Secretary under this section;

(3) the format of electronic submissions to the Secretary under this section;

(4) consolidated proceedings for appeal and the procedures for such proceedings where appropriate; and

(5) for minor changes in drugs, recommendations on how to comply with the requirements in orders issued under subsection (c)(3).

(m) Rule of construction

(1) In general

This section shall not affect the treatment or status of a nonprescription drug—

(A) that is marketed without an application approved under section 355 of this title as of March 27, 2020;

(B) that is not subject to an order issued under this section; and

(C) to which paragraph (1), (2), (3), (4), or (5) of subsection (a) do not apply.

(2) Treatment of products previously found to be subject to time and extent requirements

(A) Notwithstanding subsection (a), a drug described in subparagraph (B) may only be lawfully marketed, without an application approved under section 355 of this title, pursuant to an order issued under this section.

(B) A drug described in this subparagraph is a drug which, prior to March 27, 2020, the Secretary determined in a proposed or final rule to be ineligible for review under the OTC drug review (as such phrase ''OTC drug review'' was used in section 330.14 of title 21, Code of Federal Regulations, as in effect on the day before March 27, 2020).

(3) Preservation of authority

(A) Nothing in paragraph (1) shall be construed to preclude or limit the applicability of any provision of this chapter other than this section.

(B) Nothing in subsection (a) shall be construed to prohibit the Secretary from issuing an order under this section finding a drug to be not generally recognized as safe and effective under section 321(p)(1) of this title, as the Secretary determines appropriate.

(n) Investigational new drugs

A drug is not subject to this section if an exemption for investigational use under section 355(i) of this title is in effect for such drug.

***(o)* Inapplicability of Paperwork Reduction Act**

Chapter 35 of title 44 shall not apply to collections of information made under this section.

(p) Inapplicability of notice and comment rulemaking and other requirements

The requirements of subsection (b) shall apply with respect to orders issued under this section instead of the requirements of subchapter II of chapter 5 of title 5.

(q) Definitions

In this section:

(1) The term ''nonprescription drug'' refers to a drug not subject to the requirements of section 353(b)(1) of this title.

(2) The term ''sponsor'' refers to any person marketing, manufacturing, or processing a drug that—

(A) is listed pursuant to section 360(j) of this title; and

(B) is or will be subject to an administrative order under this section of the Food and Drug Administration.

(3) The term ''requestor'' refers to any person or group of persons marketing, manufacturing, processing, or developing a drug.

(June 25, 1938, ch. 675, §505G, as added Pub. L. 116–136, div. A, title III, §3851(a), Mar. 27, 2020, 134 Stat. 435.)

Statutory Notes and Related Subsidiaries

DRUGS EXCLUDED FROM THE OVER-THE-COUNTER DRUG REVIEW

Pub. L. 116–136, div. A, title III, §3853, Mar. 27, 2020, 134 Stat. 454, provided that:

''(a) IN GENERAL.—Nothing in this Act [probably should be ''this subtitle'', meaning subtitle F (§§3851–3862) of title III of div. A of Pub. L. 116–136, enacting this section, section 360fff–8 of this title, and subpart 10 of part C of subchapter VII of this chapter, amending sections 352, 360fff–3, 379j–52, 379r, and 381 of this title, repealing section 360fff–5 of this title, and enacting provisions set out as notes under this section and sections 360fff–3, 360fff–6, 379j–52, and 379j–71 of this title] (or the amendments made by this Act) shall apply to any nonprescription drug (as defined in section 505G(q) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(q)], as added by section 3851 of this subtitle) which was excluded by the Food and Drug Administration from the Over-the-Counter Drug Review in accordance with the paragraph numbered 25 on page 9466 of volume 37 of the Federal Register, published on May 11, 1972.

''(b) RULE OF CONSTRUCTION.—Nothing in this section shall be construed to preclude or limit the applicability of any other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).''

TREATMENT OF AUTHORITY REGARDING FINALIZATION OF SUNSCREEN MONOGRAPH

Pub. L. 116–136, div. A, title III, §3854(c), Mar. 27, 2020, 134 Stat. 456, provided that:

''(1) IN GENERAL.—

''(A) REVISION OF FINAL SUNSCREEN ORDER.—The Secretary of Health and Human Services (referred to in this subsection as the 'Secretary') shall amend and revise the final administrative order concerning nonprescription sunscreen (referred to in this subsection as the 'sunscreen order') for which the content, prior to the date of enactment of this Act [Mar. 27, 2020], was represented by the final monograph for sunscreen drug products set forth in part 352 of title 21, Code of Federal Regulations (as in effect on May 21, 1999).

''(B) ISSUANCE OF REVISED SUNSCREEN ORDER; EFFECTIVE DATE.—A revised sunscreen order described in subparagraph (A) shall be—

''(i) issued in accordance with the procedures described in section 505G(b)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(b)(2)];

''(ii) issued in proposed form not later than 18 months after the date of enactment of this Act; and

''(iii) issued by the Secretary at least 1 year prior to the effective date of the revised order.

''(2) REPORTS.—If a revised sunscreen order issued under paragraph (1) does not include provisions related to the effectiveness of various sun protection factor levels, and does not address all dosage forms known to the Secretary to be used in sunscreens marketed in the United States without a new drug application approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), the Secretary shall submit a report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate on the rationale for omission of such provisions from such order, and a plan and timeline to compile any information necessary to address such provisions through such order.''

ANNUAL UPDATE TO CONGRESS ON APPROPRIATE PEDIATRIC INDICATION FOR CERTAIN OTC COUGH AND COLD DRUGS

Pub. L. 116–136, div. A, title III, §3855, Mar. 27, 2020, 134 Stat. 457, provided that:

''(a) IN GENERAL.—Subject to subsection (c), the Secretary of Health and Human Services shall, beginning not later than 1 year after the date of enactment of this Act [Mar. 27, 2020], annually 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 letter describing the progress of the Food and Drug Administration—

''(1) in evaluating the cough and cold monograph described in subsection (b) with respect to children under age 6; and

''(2) as appropriate, revising such cough and cold monograph to address such children through the order process under section 505G(b) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355h(b)], as added by section 3851 of this subtitle.

''(b) COUGH AND COLD MONOGRAPH DESCRIBED.—The cough and cold monograph described in this subsection consists of the conditions under which nonprescription drugs containing antitussive, expectorant, nasal decon-

gestant, or antihistamine active ingredients (or combinations thereof) are generally recognized as safe and effective, as specified in part 341 of title 21, Code of Federal Regulations (as in effect immediately prior to the date of enactment of this Act), and included in an order deemed to be established under section 505G(b) of the Federal Food, Drug, and Cosmetic Act, as added by section 3851 of this subtitle.

''(c) DURATION OF AUTHORITY.—The requirement under subsection (a) shall terminate as of the date of a letter submitted by the Secretary of Health and Human Services pursuant to such subsection in which the Secretary indicates that the Food and Drug Administration has completed its evaluation and revised, in a final order, as applicable, the cough and cold monograph as described in subsection (a)(2).''

§ 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 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(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 351(a)(3) of the Public Health Service Act [42 U.S.C. 262(a)(3)].

(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 351(a) of the Public Health Service Act [42 U.S.C. 262(a)] upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a