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 505A[1] 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 subcommittee[2] 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.

(Pub. L. 107–109, §17, Jan. 4, 2002, 115 Stat. 1422; Pub. L. 108–155, §3(b)(5), Dec. 3, 2003, 117 Stat. 1942.)

[1] So in original. Probably should be preceded by ''section''.

[2] So in original. Probably should be ''Committee''.

Editorial Notes

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, 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''.

Statutory Notes and Related Subsidiaries

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) General requirements

Except with respect to an application for which subparagraph (B) applies, a person that submits, on or after September 27, 2007, an application (or supplement to an application) for a drug—

(i) 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

(ii) 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).

(B) Certain molecularly targeted cancer indications

A person that submits, on or after the date that is 3 years after August 18, 2017, an original application for a new active ingredient under section 355 of this title or section 262 of title 42, shall submit with the application reports on the investigation described in paragraph (3) if the drug or biological product that is the subject of the application is—

(i) intended for the treatment of an adult cancer; and

(ii) directed at a molecular target that the Secretary determines to be substantially relevant to the growth or progression of a pediatric cancer.

(2) Assessments

(A) In general

The assessments referred to in paragraph (1)(A) 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) Molecularly targeted pediatric cancer investigation

(A) In general

With respect to a drug or biological product described in paragraph (1)(B), the investigation described in this paragraph is a molecularly targeted pediatric cancer investigation, which shall be designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each age group for which the study is required, regarding dosing, safety, and preliminary efficacy to inform potential pediatric labeling.

(B) Extrapolation of data

Paragraph (2)(B) shall apply to investigations described in this paragraph to the same extent and in the same manner as paragraph (2)(B) applies with respect to the assessments required under paragraph (1)(A).

(C) Deferrals and waivers

Deferrals and waivers under paragraphs (4) and (5) shall apply to investigations described in this paragraph to the same extent and in the same manner as such deferrals and waivers apply with respect to the assessments under paragraph (2)(B).

(4) 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)(A) or reports on the investigation required under paragraph (1)(B) 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 or reports on the investigation;

(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)(A) or reports on the investigation required under paragraph (1)(B) 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)(A) or reports on the investigation under paragraph (1)(B) 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 or investigation;

(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.

(5) 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 or reports on the investigation 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 example, 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 or reports on the investigation 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 and reports on the investigation

If a person fails to submit a required assessment described in subsection (a)(2) or the investigation described in subsection (a)(3), fails to meet the applicable requirements in subsection (a)(4), 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. The Secretary shall inform the Pediatric Advisory Committee of letters issued under this paragraph and responses to such letters.

(2) The drug or biological product that is the subject of an assessment described in subsection (a)(2) or the investigation described in subsection (a)(3), applicable requirements in subsection (a)(4), or request for approval of a pediatric formulation, may be considered misbranded 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) or the investigation described in subsection (a)(3).

(2) Timing; content; meetings

(A) Timing

An applicant shall submit the initial pediatric study plan under paragraph (1)—

(i) before the date on which the applicant submits the assessments under subsection (a)(2) or the investigation described in subsection (a)(3); 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 study plan earlier than the date otherwise applicable under this subparagraph.

(B) Content of initial pediatric study 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) Meetings

The Secretary—

(i) shall meet with the applicant—

(I) if requested by the applicant with respect to a drug or biological product that is intended to treat a serious or life-threatening disease or condition, to discuss preparation of the initial pediatric study plan, not later than the end-of-Phase 1 meeting (as such term is used in section 312.82(b) of title 21, Code of Federal Regulations, or successor regulations) or within 30 calendar days of receipt of such request, whichever is later;

(II) 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); and

(III) to discuss the bases for the deferral under subsection (a)(4) or a full or partial waiver under subsection (a)(5);

(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 under clause (i)(II) is necessary; and

(iii) if the Secretary determines that no meeting under clause (i)(II) 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)(II) 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 agreed initial pediatric study 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 study 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

any significant amendments to such 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)(4)(C); 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) Relation to orphan drugs

(1) In general; exemption for orphan indications

Unless the Secretary requires otherwise by regulation and except as provided in paragraph (2), this section does not apply to any drug or biological product for an indication for which orphan designation has been granted under section 360bb of this title.

(2) Applicability despite orphan designation of certain indications

This section shall apply with respect to a drug or biological product for which an indication has been granted orphan designation under 360bb[1] of this title if the investigation described in subsection (a)(3) applies to the drug or biological product as described in subsection (a)(1)(B).

(*l*) 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.

(m) List of primary molecular targets

(1) In general

Within one year of August 18, 2017, the Secretary shall establish and update regularly, and shall publish on the internet website of the Food and Drug Administration—

(A) a list of molecular targets considered, on the basis of data the Secretary determines to be adequate, to be substantially relevant to the growth and progression of a pediatric cancer, and that may trigger the requirements under this section; and

(B) a list of molecular targets of new cancer drugs and biological products in development for which pediatric cancer study requirements under this section will be automatically waived.

(2) Consultation

In establishing the lists described in paragraph (1), the Secretary shall consult the National Cancer Institute, members of the internal committee under section 355d of this title, and the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee, and shall take into account comments from the meeting under subsection (c).

(3) Rule of construction

Nothing in paragraph (1) shall be construed—

(A) to require the inclusion of a molecular target on the list published under such paragraph as a condition for triggering the requirements under subsection (a)(1)(B) with respect to a drug or biological product directed at such molecular target; or

(B) to authorize the disclosure of confidential commercial information, as prohibited under section 331(j) of this title or section 1905 of title 18.

[1] So in original. Probably should be preceded by ''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; Pub. L. 114–255, div. A, title III, §§ 3101(a)(2)(D), 3102(3), Dec. 13, 2016, 130 Stat. 1153, 1156; Pub. L. 115–52, title V, §§ 503–504(b), 505(e), Aug. 18, 2017, 131 Stat. 1038–1041, 1047; Pub. L. 117–328, div. FF, title II, § 2515(c), Dec. 29, 2022, 136 Stat. 5806.)

Editorial Notes

AMENDMENTS

2022—Subsec. (f)(6)(I). Pub. L. 117–328 substituted ''subsection (a)(4)(C)'' for ''subsection (a)(3)(B)''.

2017—Subsec. (a)(1). Pub. L. 115–52, § 504(a)(1)(A), designated existing provisions as subpar. (A) and inserted heading, substituted ''Except with respect to an application for which subparagraph (B) applies, a person'' for ''A person'', redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A) and realigned margins, substituted ''; or'' for '', or'' at end of subpar. (A)(i), and added subpar. (B).

Subsec. (a)(2)(A). Pub. L. 115–52, § 504(a)(1)(B), substituted ''paragraph (1)(A)'' for ''paragraph (1)'' in introductory provisions.

Subsec. (a)(3). Pub. L. 115–52, § 504(a)(1)(D), added par. (3). Former par. (3) redesignated (4).

Subsec. (a)(4). Pub. L. 115–52, § 504(a)(1)(C), redesignated par. (3) as (4). Former par. (4) redesignated (5).

Subsec. (a)(4)(A). Pub. L. 115–52, § 504(a)(1)(E)(i), substituted ''assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B)'' for ''assessments required under paragraph (1)'' in introductory provisions.

Subsec. (a)(4)(A)(ii)(I). Pub. L. 115–52, § 504(a)(1)(E)(ii), inserted ''or reports on the investigation'' after ''assessments''.

Subsec. (a)(4)(B)(i). Pub. L. 115–52, § 504(a)(1)(E)(i), substituted ''assessments required under paragraph (1)(A) or reports on the investigation required under paragraph (1)(B)'' for ''assessments required under paragraph (1)'' in introductory provisions.

Subsec. (a)(4)(B)(ii). Pub. L. 115–52, § 504(a)(1)(E)(iii), substituted ''assessment under paragraph (1)(A) or reports on the investigation under paragraph (1)(B)'' for ''assessment under paragraph (1)''.

Subsec. (a)(4)(C)(ii)(II). Pub. L. 115–52, § 504(a)(1)(E)(iv), inserted ''or investigation'' after ''assessment''.

Subsec. (a)(5). Pub. L. 115–52, § 504(a)(1)(C), redesignated par. (4) as (5).

Subsec. (a)(5)(A), (B). Pub. L. 115–52, § 504(a)(1)(F), inserted ''or reports on the investigation'' after ''assessments'' in introductory provisions.

Subsec. (d). Pub. L. 115–52, § 504(a)(2), inserted ''and reports on the investigation'' after ''Submission of assessments'' in heading and, in introductory provisions, inserted ''or the investigation described in subsection (a)(3)'' after ''assessment described in subsection (a)(2)'' and substituted ''subsection (a)(4)'' for ''subsection (a)(3)''.

Subsec. (d)(1). Pub. L. 115–52, § 505(e), inserted at end ''The Secretary shall inform the Pediatric Advisory Committee of letters issued under this paragraph and responses to such letters.''

Subsec. (d)(2). Pub. L. 115–52, § 504(a)(2)(A), (C), in introductory provisions, inserted ''or the investigation described in subsection (a)(3)'' after ''assessment described in subsection (a)(2)'' and substituted ''subsection (a)(4)'' for ''subsection (a)(3)''.

Subsec. (e)(1). Pub. L. 115–52, § 504(a)(3)(A), inserted ''or the investigation described in subsection (a)(3)'' after ''under subsection (a)(2)''.

Subsec. (e)(2). Pub. L. 115–52, § 503(b)(1), substituted ''meetings'' for ''meeting'' in heading.

Subsec. (e)(2)(A)(i). Pub. L. 115–52, § 504(a)(3)(B), inserted ''or the investigation described in subsection (a)(3)'' after ''under subsection (a)(2)''.

Subsec. (e)(2)(C). Pub. L. 115–52, § 503(b)(2), substituted ''Meetings'' for ''Meeting'' in heading.

Subsec. (e)(2)(C)(i). Pub. L. 115–52, § 503(a), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: ''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);''.

Subsec. (e)(2)(C)(ii), (iii). Pub. L. 115–52, § 503(b)(3), substituted ''no meeting under clause (i)(II)'' for ''no meeting''.

Subsec. (e)(3). Pub. L. 115–52, § 503(b)(4), substituted ''meeting under paragraph (2)(C)(i)(II)'' for ''meeting under paragraph (2)(C)(i)''.

Subsec. (k). Pub. L. 115–52, § 504(b), amended subsec. (k) generally. Prior to amendment, text read as follows: ''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.''

Subsec. (m). Pub. L. 115–52, § 504(a)(4), added subsec. (m).

2016—Subsec. (e)(2)(A). Pub. L. 114–255, § 3101(a)(2)(D)(i)(I)(aa), inserted ''study'' after ''initial pediatric'' in introductory and concluding provisions.

Subsec. (e)(2)(B). Pub. L. 114–255, § 3101(a)(2)(D)(i)(I)(bb), substituted ''Content of initial pediatric study plan'' for ''Content of initial plan'' in heading.

Subsec. (e)(5). Pub. L. 114–255, § 3101(a)(2)(D)(i)(II), inserted ''agreed initial pediatric study'' before ''plan'' in heading.

Subsec. (e)(6). Pub. L. 114–255, § 3101(a)(2)(D)(i)(III), substituted ''agreed initial pediatric study plan'' for ''agreed initial pediatric plan''.

Subsec. (f)(1). Pub. L. 114–255, § 3101(a)(2)(D)(ii), inserted ''and any significant amendments to such plans,'' after ''agreed initial pediatric study plans,''.

Subsecs. (*l*), (m). Pub. L. 114–255, § 3102(3), redesignated subsec. (m) as (*l*) and struck out former subsec. (*l*) which related to Institute of Medicine study.

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, appli-

cation to orphan drugs, and integration with other pediatric studies.

Statutory Notes and Related Subsidiaries

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.''

RULE OF CONSTRUCTION

Pub. L. 115–52, title V, § 504(e), Aug. 18, 2017, 131 Stat. 1045, provided that: ''Nothing in this section [amending this section and section 355c–1 of this title and enacting provisions set out as a note below], including the amendments made by this section, shall limit the authority of the Secretary of Health and Human Services to issue written requests under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) or section 351(m) of the Public Health Service Act (42 U.S.C. 262(m)), or to negotiate or implement amendments to such requests proposed by the an [sic] applicant.''

MEETING, CONSULTATION, AND GUIDANCE

Pub. L. 115–52, title V, § 504(c), Aug. 18, 2017, 131 Stat. 1041, provided that:

''(1) MEETING.—The Secretary of Health and Human Services (referred to in this subsection as the 'Secretary'), acting through the Commissioner of Food and Drugs and in collaboration with the Director of the National Cancer Institute, shall convene a public meeting not later than 1 year after the date of enactment of this Act [Aug. 18, 2017] to solicit feedback from physicians and researchers (including pediatric oncologists and rare disease specialists), patients, and other stakeholders to provide input on development of the guidance under paragraph (2) and the list under subsection (m) of section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c), as added by subsection (a). The Secretary shall seek input at such meeting on—

''(A) the data necessary to determine that there is scientific evidence that a drug or biological product is directed at a molecular target that is considered to be substantially relevant to the growth or progression of a pediatric cancer;

''(B) the data necessary to determine that there is scientific evidence that a molecular target is considered to be substantially relevant to the growth or progression of a pediatric cancer;

''(C) the data needed to meet the requirement of conducting an investigation described in section 505B(a)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(3)], as amended by subsection (a);

''(D) considerations when developing the list under section 505B(m) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(m)] that contains molecular targets shared between different tumor types;

''(E) the process the Secretary shall utilize to update regularly a list of molecular targets that may trigger a pediatric study under section 505B of the Federal Food, Drug, and Cosmetic Act, as so amended, and how often such updates shall occur;

''(F) how to overcome the challenges related to pediatric cancer drug and biological product development, including issues related to the ethical, practical, and other barriers to conducting clinical trials in pediatric cancer with small patient populations;

''(G) scientific or operational challenges associated with performing an investigation described in section 505B(a)(1)(B) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c(a)(1)(B)], including the effect on pediatric studies currently underway in a pediatric patient population, treatment of a pediatric patient population, and the ability to complete adult clinical trials;

''(H) the advantages and disadvantages of innovative clinical trial designs in addressing the development of cancer drugs or biological products directed at molecular targets in pediatric cancer patients;

''(I) the ways in which the Secretary can improve the current process outlined under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c) to encourage additional research and development of pediatric cancer treatments;

''(J) the ways in which the Secretary might streamline and improve the written request process, including when studies contained in a request under such section 505A are not feasible due to the ethical, practical, or other barriers to conducting clinical trials in pediatric cancer populations;

''(K) how the Secretary will facilitate collaboration among pediatric networks, academic centers and experts in pediatric cancer to conduct an investigation described in such section 505B(a)(3);

''(L) how the Secretary may facilitate collaboration among sponsors of same-in-class drugs and biological products that would be subject to the requirements for an investigation under such section 505B based on shared molecular targets; and

''(M) the ways in which the Secretary will help to mitigate the risks, if any, of discouraging the research and development of orphan drugs when implementing such section 505B as amended.

''(2) GUIDANCE.—Not later than 2 years after the date of enactment of this Act [Aug. 18, 2017], the Secretary, acting through the Commissioner of Food and Drugs, shall issue final guidance on implementation of the amendments to section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) regarding molecularly targeted cancer drugs made by this section, including—

''(A) the scientific criteria, types of data, and regulatory considerations for determining whether a molecular target is substantially relevant to the growth or progression of a pediatric cancer and would trigger an investigation under section 505B of the Federal Food, Drug, and Cosmetic Act, as amended;

''(B) the process by which the Secretary will engage with sponsors to discuss determinations, investigation requirements, deferrals, waivers, and any other issues that need to be resolved to ensure that any required investigation based on a molecular target can be reasonably conducted;

''(C) the scientific or operational challenges for which the Secretary may issue deferrals or waivers for an investigation described in subsection (a)(3) of such section 505B, including adverse impacts on current pediatric studies underway in a pediatric patient population, studies involving drugs designated as orphan drugs, treatment of a pediatric patient population, or the ability to complete adult clinical trials;

''(D) how the Secretary and sponsors will facilitate collaboration among pediatric networks, academic centers, and experts in pediatric cancer to conduct an investigation described in subsection (a)(3) of such section 505B;

''(E) scientific and regulatory considerations for study designs, including the applicability of innovative clinical trial designs for pediatric cancer drug and biological product developments under sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, 355c);

''(F) approaches to streamline and improve the amendment process, including when studies contained in a request under such section 505A are not feasible due to the ethical, practical, or other barriers to conducting clinical trials in pediatric cancer populations;

''(G) the process for submission of an initial pediatric study plan for the investigation described in section 505B(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(a)(3)), including the process for a sponsor to meet and reach agreement with the Secretary on the initial pediatric study plan; and

''(H) considerations for implementation of such section 505B, as so amended, and waivers of the requirements of such section 505B with regard to molecular targets for which several drugs or biological products may be under investigation.''

§ 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 popu-