new drug application and the listed drug shall use a single, shared system under subsection (f). The Secretary may waive the requirement under the preceding sentence for a drug that is the subject of an abbreviated new drug application, and permit the applicant to use a different, comparable aspect of the elements to assure safe use, if the Secretary determines that—

(i) the burden of creating a single, shared system outweighs the benefit of a single, system,[1] taking into consideration the impact on health care providers, patients, the applicant for the abbreviated new drug application, and the holder of the reference drug product; or

(ii) an aspect of the elements to assure safe use for the applicable listed drug is claimed by a patent that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the abbreviated new drug application certifies that it has sought a license for use of an aspect of the elements to assure safe use for the applicable listed drug and that it was unable to obtain a license.

A certification under clause (ii) shall include a description of the efforts made by the applicant for the abbreviated new drug application to obtain a license. In a case described in clause (ii), the Secretary may seek to negotiate a voluntary agreement with the owner of the patent, method, or process for a license under which the applicant for such abbreviated new drug application may use an aspect of the elements to assure safe use, if required under subsection (f) for the applicable listed drug, that is claimed by a patent that has not expired or is a method or process that as a trade secret is entitled to protection.

(2) Action by Secretary

For an applicable listed drug for which a drug is approved under section 355(j) of this title, the Secretary—

(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug; and

(B) shall inform the responsible person for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

(j) Drug Safety Oversight Board

(1) In general

There is established a Drug Safety Oversight Board.

(2) Composition; meetings

The Drug Safety Oversight Board shall—

(A) be composed of scientists and health care practitioners appointed by the Secretary, each of whom is an employee of the Federal Government;

(B) include representatives from offices throughout the Food and Drug Administration, including the offices responsible for postapproval safety of drugs;

(C) include at least 1 representative each from the National Institutes of Health and the Department of Health and Human Services (other than the Food and Drug Administration);

(D) include such representatives as the Secretary shall designate from other appropriate agencies that wish to provide representatives; and

(E) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.

(June 25, 1938, ch. 675, § 505–1, as added Pub. L. 110–85, title IX, § 901(b), Sept. 27, 2007, 121 Stat. 926.)

REFERENCES IN TEXT

For the effective date of this section, referred to in subsec. (a)(2)(A), see Effective Date note below.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (h)(4), (5)(C)(i), is section 101(c) of Pub. L. 110–85, which is set out as a note under section 379g of this title.

EFFECTIVE DATE

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

§ 355a. Pediatric studies of drugs

(a) Definitions

As used in this section, the term ''pediatric studies'' or ''studies'' means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used, and, at the discretion of the Secretary, may include preclinical studies.

(b) Market exclusivity for new drugs

(1) In general

Except as provided in paragraph (2), if, prior to approval of an application that is submitted under section 355(b)(1) of this title, the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

[1] So in original. Probably should be ''single, shared system,''.

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(c) Market exclusivity for already-marketed drugs

(1) In general

Except as provided in paragraph (2), if the Secretary determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under section 355(b)(1) of this title for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3)—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 355 of this title, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 360bb of this title for a rare disease or condition, the period referred to in section 360cc(a) of this title is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title,

the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B)(ii) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) Exception

The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination made under subsection (d)(3) is made later than 9 months prior to the expiration of such period.

(d) Conduct of pediatric studies

(1) Request for studies

(A) In general

The Secretary may, after consultation with the sponsor of an application for an investigational new drug under section 355(i) of this title, the sponsor of an application for a new drug under section 355(b)(1) of this title, or the holder of an approved application for a drug under section 355(b)(1) of this title, issue to the sponsor or holder a written

request for the conduct of pediatric studies for such drug. In issuing such request, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Such request to conduct pediatric studies shall be in writing and shall include a timeframe for such studies and a request to the sponsor or holder to propose pediatric labeling resulting from such studies.

(B) Single written request

A single written request—

(i) may relate to more than one use of a drug; and

(ii) may include uses that are both approved and unapproved.

(2) Written request for pediatric studies

(A) Request and response

(i) In general

If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (b) or (c), the applicant or holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the applicant or holder to act on the request by—

(I) indicating when the pediatric studies will be initiated, if the applicant or holder agrees to the request; or

(II) indicating that the applicant or holder does not agree to the request and stating the reasons for declining the request.

(ii) Disagree with request

If, on or after September 27, 2007, the applicant or holder does not agree to the request on the grounds that it is not possible to develop the appropriate pediatric formulation, the applicant or holder shall submit to the Secretary the reasons such pediatric formulation cannot be developed.

(B) Adverse event reports

An applicant or holder that, on or after September 27, 2007, agrees to the request for such studies shall provide the Secretary, at the same time as the submission of the reports of such studies, with all postmarket adverse event reports regarding the drug that is the subject of such studies and are available prior to submission of such reports.

(3) Meeting the studies requirement

Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

(4) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(e) Notice of determinations on studies requirement

(1) In general

The Secretary shall publish a notice of any determination, made on or after September 27, 2007, that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 355 of this title for a drug will be subject to the provisions of this section. Such notice shall be published not later than 30 days after the date of the Secretary's determination regarding market exclusivity and shall include a copy of the written request made under subsection (b) or (c).

(2) Identification of certain drugs

The Secretary shall publish a notice identifying any drug for which, on or after September 27, 2007, a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population (or specified subpopulation) if the pediatric formulation for such drug is not introduced onto the market within one year after the date that the Secretary publishes the notice described in paragraph (1). Such notice identifying such drug shall be published not later than 30 days after the date of the expiration of such one year period.

(f) Internal review of written requests and pediatric studies

(1) Internal review

The Secretary shall utilize the internal review committee established under section 355d of this title to review all written requests issued on or after September 27, 2007, in accordance with paragraph (2).

(2) Review of written requests

The committee referred to in paragraph (1) shall review all written requests issued pursuant to this section prior to being issued.

(3) Review of pediatric studies

The committee referred to in paragraph (1) may review studies conducted pursuant to this section to make a recommendation to the Secretary whether to accept or reject such reports under subsection (d)(3).

(4) Activity by committee

The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(5) Documentation of committee action

For each drug, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (2) or (3), which members of the committee participated in such activity.

(6) Tracking pediatric studies and labeling changes

The Secretary, in consultation with the committee referred to in paragraph (1), shall track and make available to the public, in an easily accessible manner, including through posting on the Web site of the Food and Drug Administration—

(A) the number of studies conducted under this section and under section 284m of title 42;

(B) the specific drugs and drug uses, including labeled and off-labeled indications, studied under such sections;

(C) the types of studies conducted under such sections, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons such formulations were not developed;

(E) the labeling changes made as a result of studies conducted under such sections;

(F) an annual summary of labeling changes made as a result of studies conducted under such sections for distribution pursuant to subsection (k)(2); and

(G) information regarding reports submitted on or after September 27, 2007.

(g) Limitations

Notwithstanding subsection (c)(2), a drug to which the six-month period under subsection (b) or (c) has already been applied—

(1) may receive an additional six-month period under subsection (c)(1)(A)(i)(II) for a supplemental application if all other requirements under this section are satisfied, except that such drug may not receive any additional such period under subsection (c)(1)(B); and

(2) may not receive any additional such period under subsection (c)(1)(A)(ii).

(h) Relationship to pediatric research requirements

Notwithstanding any other provision of law, if any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

(i) Labeling changes

(1) Priority status for pediatric applications and supplements

Any application or supplement to an application under section 355 of this title proposing a labeling change as a result of any pediatric study conducted pursuant to this section—

(A) shall be considered to be a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) Dispute resolution

(A) Request for labeling change and failure to agree

If, on or after September 27, 2007, the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor of the application does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) Action by the Pediatric Advisory Committee

Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) Consideration of recommendations

The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate.

(D) Misbranding

If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

(E) No effect on authority

Nothing in this subsection limits the authority of the United States to bring an enforcement action under this chapter when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(j) Other labeling changes

If, on or after September 27, 2007, the Secretary determines that a pediatric study conducted under this section does or does not demonstrate that the drug that is the subject of the study is safe and effective, including whether such study results are inconclusive, in pediatric populations or subpopulations, the Secretary shall order the labeling of such product to include information about the results of the study and a statement of the Secretary's determination.

(k) Dissemination of pediatric information

(1) In general

Not later than 210 days after the date of submission of a report on a pediatric study under this section, the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of pediatric studies conducted under subsection (b) or (c).

(2) Dissemination of information regarding labeling changes

Beginning on September 27, 2007, the Secretary shall include as a requirement of a written request that the sponsors of the studies that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(3)(F) distribute, at least annually (or more frequently if the Secretary determines that it would be beneficial to the public health), such information to physicians and other health care providers.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(*l*) Adverse event reporting

(1) Reporting in year one

Beginning on September 27, 2007, during the one-year period beginning on the date a labeling change is approved pursuant to subsection (i), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics established under section 393a of this title. In considering the reports, the Director of such Office shall provide for the review of the reports by the Pediatric Advisory Committee, including obtaining any recommendations of such Committee regarding whether the Secretary should take action under this chapter in response to such reports.

(2) Reporting in subsequent years

Following the one-year 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) Effect

The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(m) Clarification of interaction of market exclusivity under this section and market exclusivity awarded to an applicant for approval of a drug under section 355(j) of this title

If a 180-day period under section 355(j)(5)(B)(iv) of this title overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 355(j) of this title entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

(n) Referral if pediatric studies not completed

(1) In general

Beginning on September 27, 2007, if pediatric studies of a drug have not been completed under subsection (d) and if the Secretary, through the committee established under section 355d of this title, determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall carry out the following:

(A) For a drug for which a listed patent has not expired, make a determination regarding whether an assessment shall be required to be submitted under section 355c(b) of this title. Prior to making such a determination, the Secretary may not take more than 30 days to certify whether the Foundation for the National Institutes of Health has sufficient funding at the time of such certification to initiate and fund all of the studies in the written request in their entirety within the timeframes specified within the written request. Only if the Secretary makes such certification in the affirmative, the Secretary shall refer all pediatric studies in the written request to the Foundation for the National Institutes of Health for the conduct of such studies, and such Foundation shall fund such studies. If no certification has been made at the end of the 30-day period, or if the Secretary certifies that funds are not sufficient to initiate and fund all the studies in their entirety, the Secretary shall consider whether assessments shall be required under section 355c(b) of this title for such drug.

(B) For a drug that has no listed patents or has 1 or more listed patents that have expired, the Secretary shall refer the drug for inclusion on the list established under section 284m of title 42 for the conduct of studies.

(2) Public notice

The Secretary shall give the public notice of a decision under paragraph (1)(A) not to require an assessment under section 355c of this title and the basis for such decision.

(3) Effect of subsection

Nothing in this subsection alters or amends section 331(j) of this title or section 552 of title 5 or section 1905 of title 18.

(*o*) Prompt approval of drugs under section 355(j) when pediatric information is added to labeling

(1) General rule

A drug for which an application has been submitted or approved under section 355(j) of this title shall not be considered ineligible for approval under that section or misbranded under section 352 of this title on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertain-

ing to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title.

(2) Labeling

Notwithstanding clauses (iii) and (iv) of section 355(j)(5)(F) of this title, the Secretary may require that the labeling of a drug approved under section 355(j) of this title that omits a pediatric indication or other aspect of labeling as described in paragraph (1) include—

(A) a statement that, because of marketing exclusivity for a manufacturer—

(i) the drug is not labeled for pediatric use; or

(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

(B) a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary.

(3) Preservation of pediatric exclusivity and other provisions

This subsection does not affect—

(A) the availability or scope of exclusivity under this section;

(B) the availability or scope of exclusivity under section 355 of this title for pediatric formulations;

(C) the question of the eligibility for approval of any application under section 355(j) of this title that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 355(j)(5)(F) of this title; or

(D) except as expressly provided in paragraphs (1) and (2), the operation of section 355 of this title.

(p) Institute of Medicine study

Not later than 3 years after September 27, 2007, the Secretary shall enter into a contract with the Institute of Medicine to conduct a study and report to Congress regarding the written requests made and the studies conducted pursuant to this section. The Institute of Medicine may devise an appropriate mechanism to review a representative sample of requests made and studies conducted pursuant to this section in order to conduct such study. Such study shall—

(1) review such representative written requests issued by the Secretary since 1997 under subsections (b) and (c);

(2) review and assess such representative pediatric studies conducted under subsections (b) and (c) since 1997 and labeling changes made as a result of such studies;

(3) review the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, and ethical issues in pediatric clinical trials;

(4) review and assess the pediatric studies of biological products as required under subsections (a) and (b) of section 355c of this title; and

(5) make recommendations regarding appropriate incentives for encouraging pediatric studies of biologics.

(q) Sunset

A drug may not receive any 6-month period under subsection (b) or (c) unless—

(1) on or before October 1, 2012, the Secretary makes a written request for pediatric studies of the drug;

(2) on or before October 1, 2012, an application for the drug is accepted for filing under section 355(b) of this title; and

(3) all requirements of this section are met.

(June 25, 1938, ch. 675, § 505A, as added Pub. L. 105–115, title I, § 111, Nov. 21, 1997, 111 Stat. 2305; amended Pub. L. 107–109, §§ 2, 4, 5(b)(2), 7–11(a), 18(a), 19, Jan. 4, 2002, 115 Stat. 1408, 1411, 1413–1415, 1423, 1424; Pub. L. 108–155, §§ 2(b)(2), 3(a), (b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108–173, title XI, § 1104, Dec. 8, 2003, 117 Stat. 2461; Pub. L. 110–85, title V, § 502(a)(1), Sept. 27, 2007, 121 Stat. 876.)

AMENDMENTS

2007—Pub. L. 110–85 amended section generally. Prior to amendment, text consisted of subsecs. (a) to (n) relating to pediatric studies of drugs, including market exclusivity, conduct of pediatric studies, delay of effective date for certain applications, notice of determinations on studies requirement, limitations, research requirements, labeling supplements, dissemination of information, prompt approval of drugs, report to Congress not later than Jan. 1, 2001, and sunset provisions.

2003—Subsec. (b)(1)(A)(i). Pub. L. 108–173, § 1104(1), substituted ''(j)(5)(F)(ii)'' for ''(j)(5)(D)(ii)'' in two places.

Subsec. (b)(1)(A)(ii). Pub. L. 108–173, § 1104(2), substituted ''(j)(5)(F)'' for ''(j)(5)(D)''.

Subsec. (b)(2). Pub. L. 108–155, § 3(a), substituted ''355(j)(5)(B)'' for ''355(j)(4)(B)'' in two places.

Subsec. (c)(1)(A)(i). Pub. L. 108–173, § 1104(1), substituted ''(j)(5)(F)(ii)'' for ''(j)(5)(D)(ii)'' in two places.

Subsec. (c)(1)(A)(ii). Pub. L. 108–173, § 1104(2), substituted ''(j)(5)(F)'' for ''(j)(5)(D)''.

Subsec. (c)(2). Pub. L. 108–155, § 3(a), substituted ''355(j)(5)(B)'' for ''355(j)(4)(B)'' in two places.

Subsec. (e). Pub. L. 108–173, § 1104(3), substituted ''355(j)(5)(F)'' for ''355(j)(5)(D)''.

Subsec. (h). Pub. L. 108–155, § 2(b)(2), substituted ''pediatric research requirements'' for ''regulations'' in heading and ''by a provision of law (including a regulation) other than this section'' for ''pursuant to regulations promulgated by the Secretary'' in text.

Subsec. (i)(2). Pub. L. 108–155, § 3(b)(1), struck out ''Advisory Subcommittee of the Anti-Infective Drugs'' before ''Advisory Committee'' wherever appearing.

Subsec. (*l*). Pub. L. 108–173, § 1104(3), substituted ''355(j)(5)(F)'' for ''355(j)(5)(D)'' wherever appearing.

2002—Subsec. (a). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (g) as (a). Former subsec. (a) redesignated (b).

Subsec. (a)(1)(A). Pub. L. 107–109, § 19(1)(A), (B), substituted ''(j)(5)(D)(ii)'' for ''(j)(4)(D)(ii)'' in two places in cl. (i) and ''(j)(5)(D)'' for ''(j)(4)(D)'' in cl. (ii).

Subsec. (b). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (a) as (b).

Pub. L. 107–109, § 2(1), struck out heading and text of subsec. (b). Text read as follows: ''Not later than 180 days after November 21, 1997, the Secretary, after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.''

Subsec. (c). Pub. L. 107–109, § 2(2), in introductory provisions, inserted ''determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and'' after ''the Secretary'' and struck out ''concerning a drug identified in the list described in subsection (b) of this section'' after ''such studies)''.

Subsec. (c)(1)(A). Pub. L. 107–109, § 19(1)(A), (B), substituted ''(j)(5)(D)(ii)'' for ''(j)(4)(D)(ii)'' in two places in cl. (i) and ''(j)(5)(D)'' for ''(j)(4)(D)'' in cl. (ii).

Subsec. (d)(1). Pub. L. 107–109, § 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)'' in introductory provisions.

Subsec. (d)(2). Pub. L. 107–109, §§ 18(a), 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)'' and inserted ''In reaching an agreement regarding written protocols, the Secretary shall take into account adequate representation of children of ethnic and racial minorities.'' after first sentence.

Subsec. (d)(3). Pub. L. 107–109, § 19(4), substituted ''subsection (b) or (c)'' for ''subsection (a) or (c)''.

Subsec. (d)(4). Pub. L. 107–109, § 4, added par. (4).

Subsec. (e). Pub. L. 107–109, § 19(1)(C), (4), substituted ''section 355(j)(5)(D)'' for ''section 355(j)(4)(D)'' and ''subsection (b) or (c)'' for ''subsection (a) or (c)''.

Subsec. (g). Pub. L. 107–109, § 19(2), (3), (5), redesignated subsec. (h) as (g) and substituted ''subsection (b) or (c)'' for ''subsection (a) or (b)'' in introductory provisions. Former subsec. (g) redesignated (a).

Pub. L. 107–109, § 7, inserted ''(including neonates in appropriate cases)'' after ''pediatric age groups''.

Subsec. (h). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (i) as (h). Former subsec. (h) redesignated (g).

Subsec. (i). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*l*) as (i). Former subsec. (i) redesignated (h).

Subsec. (j). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (m) as (j). Former subsec. (j) redesignated (n).

Pub. L. 107–109, § 8, added subsec. (j) and struck out heading and text of former subsec. (j). Text read as follows: ''A drug may not receive any six-month period under subsection (a) or (c) of this section unless the application for the drug under section 355(b)(1) of this title is submitted on or before January 1, 2002. After January 1, 2002, a drug shall receive a six-month period under subsection (c) of this section if—

''(1) the drug was in commercial distribution as of November 21, 1997;

''(2) the drug was included by the Secretary on the list under subsection (b) of this section as of January 1, 2002;

''(3) the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population and that the drug may provide health benefits in that population; and

''(4) all requirements of this section are met.''

Subsec. (k). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (n) as (k). Former subsec. (k) redesignated (m).

Subsec. (*l*). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*o*) as (*l*). Former subsec. (*l*) redesignated (i).

Pub. L. 107–109, § 5(b)(2), added subsec. (*l*).

Subsec. (m). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (k) as (m). Former subsec. (m) redesignated (j).

Pub. L. 107–109, § 9, added subsec. (m).

Subsec. (n). Pub. L. 107–109, § 19(4), which directed substitution of ''subsection (b) or (c)'' for ''subsection (a) or (c)'' in subsec. (m), was executed by making the substitution in introductory provisions of subsec. (n), to reflect the probable intent of Congress.

Pub. L. 107–109, § 19(2), (3), redesignated subsec. (j) as (n). Former subsec. (n) redesignated (k).

Pub. L. 107–109, § 10, added subsec. (n).

Subsec. (*o*). Pub. L. 107–109, § 19(2), (3), redesignated subsec. (*o*) as (*l*).

Pub. L. 107–109, § 11(a), added subsec. (*o*).

EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110–85, title V, § 502(a)(2), Sept. 27, 2007, 121 Stat. 885, provided that:

''(A) IN GENERAL.—The amendment made by this subsection [amending this section] shall apply to written requests under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a) issued on or after the date of the enactment of this Act [Sept. 27, 2007].

''(B) CERTAIN WRITTEN REQUESTS.—A written request issued under section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on the day before the date of the enactment of this Act, which has been accepted and for which no determination under subsection (d)(2) of such section has been made before such date of enactment, shall be subject to such section 505A, except that such written requests shall be subject to subsections (d)(2)(A)(ii), (e)(1) and (2), (f), (i)(2)(A), (j), (k)(1), (*l*)(1), and (n) of section 505A of the Federal Food, Drug, and Cosmetic Act, as in effect on or after the date of the enactment of this Act.''

EFFECTIVE DATE OF 2003 AMENDMENT

Amendment by Pub. L. 108–155 effective Dec. 3, 2003, except as otherwise provided, see section 4 of Pub. L. 108–155, set out as an Effective Date note under section 355c of this title.

EFFECTIVE DATE OF 2002 AMENDMENT

Pub. L. 107–109, § 11(b), Jan. 4, 2002, 115 Stat. 1416, provided that: ''The amendment made by subsection (a) [amending this section] takes effect on the date of enactment of this Act [Jan. 4, 2002], including with respect to applications under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) that are approved or pending on that date.''

CONSTRUCTION OF 2007 AMENDMENTS ON PEDIATRIC STUDIES

Pub. L. 110–85, title IX, § 901(e), Sept. 27, 2007, 121 Stat. 942, provided that: ''This title [enacting sections 353b, 355–1, 355e, 360a, and 360bbb–6 of this title, amending sections 331, 333, 334, 352, 355, and 381 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under sections 331, 352, and 355 of this title] and the amendments made by this title may not be construed as affecting the authority of the Secretary of Health and Human Services to request pediatric studies under section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a] or to require such studies under section 505B of such Act [21 U.S.C. 355c].''

REPORT ON PEDIATRIC EXCLUSIVITY PROGRAM

Pub. L. 107–109, § 16, Jan. 4, 2002, 115 Stat. 1421, as amended by Pub. L. 108–155, § 3(b)(4), Dec. 3, 2003, 117 Stat. 1942, required the Comptroller General, not later than Oct. 1, 2006, and in consultation with the Secretary of Health and Human Services, to submit to Congress a report on specified issues concerning the effectiveness of the pediatric exclusivity program.

STUDY BY GENERAL ACCOUNTING OFFICE

Pub. L. 107–109, § 18(b), Jan. 4, 2002, 115 Stat. 1423, required the Comptroller General, not later than Jan. 10, 2003, to conduct a study relating to the representation of children of ethnic and racial minorities in studies under section 355a of this title and to submit a report to Congress describing the findings of the study.

§ 355b. Adverse-event reporting

(a) Toll-free number in labeling

Not later than one year after January 4, 2002, the Secretary of Health and Human Services shall promulgate a final rule requiring that the labeling of each drug for which an application is approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] (regardless of the date on which approved) include the toll-free number maintained by the Secretary for the purpose of receiving reports of adverse events regarding drugs and a statement that such number is to be used for reporting purposes only, not to receive medical advice. With respect to the final rule:

(1) The rule shall provide for the implementation of such labeling requirement in a manner that the Secretary considers to be most