

(B) the number of times the Secretary entered into discussions concerning a disagreement with an application holder or holders and a summary of the decision regarding a labeling change, if any; and

(2) includes any recommendations of the Secretary for modifying the program under this section.

(June 25, 1938, ch. 675, §503D, as added Pub. L. 116-260, div. BB, title III, §324, Dec. 27, 2020, 134 Stat. 2933.)

#### § 354. Veterinary feed directive drugs

##### (a) Lawful veterinary feed directive requirement

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

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

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

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

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

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

(C) Any person who distributes animal feed bearing or containing a veterinary feed directive drug shall upon first engaging in such distribu-

tion notify the Secretary of that person's name and place of business. The failure to provide such notification shall be deemed to be an act which results in the drug being misbranded.

##### (b) Labeling and advertising

A veterinary feed directive drug and any feed bearing or containing a veterinary feed directive drug shall be deemed to be misbranded if their labeling fails to bear such cautionary statement and such other information as the Secretary may by general regulation or by order prescribe, or their advertising fails to conform to the conditions and indications for use published pursuant to section 360b(i) of this title, or the index listing pursuant to section 360ccc-1(e) of this title or fails to contain the general cautionary statement prescribed by the Secretary.

##### (c) Nonprescription status

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

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

#### Editorial Notes

##### PRIOR PROVISIONS

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

##### AMENDMENTS

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

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

#### § 355. New drugs

##### (a) Necessity of effective approval of application

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

##### (b) Filing application; contents

(1)(A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—

(i) full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use;

(ii) a full list of the articles used as components of such drug;

(iii) a full statement of the composition of such drug;

(iv) a full description of the methods used in, and the facilities and controls used for, the

manufacture, processing, and packing of such drug;

(v) such samples of such drug and of the articles used as components thereof as the Secretary may require;

(vi) specimens of the labeling proposed to be used for such drug;

(vii) any assessments required under section 355c of this title; and

(viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—

(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

(II) claims a method of using such drug for which approval is sought or has been granted in the application.

(B) If an application is filed under this subsection for a drug, and a patent of the type described in subparagraph (A)(viii) is issued after the filing date but before approval of the application, the applicant shall amend the application to include the patent number and expiration date.

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

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

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

(ii) that such patent has expired,

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

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

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

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

(A) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the appli-

cation a statement that the applicant will give notice as required by this paragraph.

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

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

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

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

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

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

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

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

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

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

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

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

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of

title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size—

(i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or

(II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or

(ii) with respect to an application for approval of a biological product under section 262(k) of title 42, of any necessary clinical study or studies.

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

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

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

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

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

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

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

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

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

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

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

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

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application. If the patent information described in subsection (b) could not be filed with the submission of an application under subsection (b) because the application was filed before the patent information was required under subsection (b) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii). If the holder of an approved application could not file patent information under subsection (b) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) because no patent of the type for which information is required to be submitted in subsection (b)(1)(A)(viii) had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall pub-

lish it. Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.

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

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

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

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

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

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

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

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

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

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

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

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

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

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

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

(D) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

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

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

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

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

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

is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

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

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

(bb) an approved method of using the drug.

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

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action

under clause (i) or a counterclaim under clause (ii).

(E)(i) Repealed. Pub. L. 117-9, §1(b)(1)(A), Apr. 23, 2021, 135 Stat. 258.

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under subsection (b) after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A). The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations

(other than bioavailability<sup>1</sup> studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

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

(5)(A) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under subsection (b), if such supplemental application complies with subparagraph (B).

(B) A supplemental application is eligible for review as described in subparagraph (A) only if—

(i) there is existing data available and acceptable to the Secretary demonstrating the safety of the drug; and

(ii) all data used to develop the qualified data summaries are submitted to the Secretary as part of the supplemental application.

(C) The Secretary shall post on the Internet website of the Food and Drug Administration and update annually—

(i) the number of applications reviewed solely under subparagraph (A) or section 262(a)(2)(E) of title 42;

(ii) the average time for completion of review under subparagraph (A) or section 262(a)(2)(E) of title 42;

(iii) the average time for review of supplemental applications where the Secretary did not use review flexibility under subparagraph (A) or section 262(a)(2)(E) of title 42; and

(iv) the number of applications reviewed under subparagraph (A) or section 262(a)(2)(E) of title 42 for which the Secretary made use of full data sets in addition to the qualified data summary.

(D) In this paragraph—

(i) the term “qualified indication” means an indication for a drug that the Secretary determines to be appropriate for summary level review under this paragraph; and

(ii) the term “qualified data summary” means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication.

**(d) Grounds for refusing application; approval of application; “substantial evidence” defined**

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term “substantial evidence” means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of

<sup>1</sup> So in original. Probably should be “bioavailability”.

use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decision-making, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

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

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for

maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.

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

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

**(g) Service of orders**

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

**(h) Appeal from order**

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and

file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

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

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

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

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

(C) the establishment and maintenance of such records, and the making of such reports

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

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

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

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

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

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

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

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

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

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

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or



any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.

**(j) Abbreviated new drug applications**

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

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

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

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

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

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

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

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

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

(vi) the items specified in clauses (ii) through (vi) of subsection (b)(1)(A);

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

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

(II) that such patent has expired,

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

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

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

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

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

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

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

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

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the

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

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

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

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

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

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

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

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(B) information submitted with the application is insufficient to show that each of the

proposed conditions of use have been previously approved for the listed drug referred to in the application;

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

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

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

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

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

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

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

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

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

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

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required be-

cause of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

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

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

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

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

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

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

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

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

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month

period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

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

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

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

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

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

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

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

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

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

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

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

(iv) 180-DAY EXCLUSIVITY PERIOD.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the

application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) DEFINITIONS.—In this paragraph:

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

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

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

(dd) TENTATIVE APPROVAL.—

(AA) IN GENERAL.—The term “tentative approval” means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

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

(v) 180-DAY EXCLUSIVITY PERIOD FOR COMPETITIVE GENERIC THERAPIES.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.

(II) LIMITATION.—The exclusivity period under subclause (I) shall not apply with respect to a competitive generic therapy that has previously received an exclusivity period under subclause (I).

(III) DEFINITIONS.—In this clause and subparagraph (D)(iv):

(aa) The term “competitive generic therapy” means a drug—

(AA) that is designated as a competitive generic therapy under section 356h of this title; and

(BB) for which there are no unexpired patents or exclusivities on the list of products described in section 355(j)(7)(A) of this title at the time of submission.

(bb) The term “first approved applicant” means any applicant that has submitted an application that—

(AA) is for a competitive generic therapy that is approved on the first day on which any application for such competitive generic therapy is approved;

(BB) is not eligible for a 180-day exclusivity period under clause (iv) for the drug that is the subject of the application for the competitive generic therapy; and

(CC) is not for a drug for which all drug versions have forfeited eligibility for a 180-day exclusivity period under clause (iv) pursuant to subparagraph (D).

(C) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

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

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

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

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

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

applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

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

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

(bb) an approved method of using the drug.

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

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

(D) FORFEITURE OF 180-DAY EXCLUSIVITY PERIOD.—

(i) DEFINITION OF FORFEITURE EVENT.—In this subparagraph, the term “forfeiture event”, with respect to an application under this subsection, means the occurrence of any of the following:

(I) FAILURE TO MARKET.—The first applicant fails to market the drug by the later of—

(aa) the earlier of the date that is—

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) WITHDRAWAL OF APPLICATION.—The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) AMENDMENT OF CERTIFICATION.—The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) FAILURE TO OBTAIN TENTATIVE APPROVAL.—The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER.—The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of title 15, except that the term includes section 45 of title 15 to the extent that that section applies to unfair methods of competition).

(VI) EXPIRATION OF ALL PATENTS.—All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) FORFEITURE.—The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) SUBSEQUENT APPLICANT.—If all first applicants forfeit the 180-day exclusivity period under clause (ii)—

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(iv) SPECIAL FORFEITURE RULE FOR COMPETITIVE GENERIC THERAPY.—The 180-day exclusivity period described in subparagraph (B)(v) shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) Repealed. Pub. L. 117-9, §1(b)(1)(B), Apr. 23, 2021, 135 Stat. 258.

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any

other application under subsection (b), is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (c) respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(iv) For each drug included on the list, the Secretary shall specify any exclusivity period that is applicable, for which the Secretary has determined the expiration date, and for which such period has not yet expired, under—

(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E);

(II) clause (iv) or (v) of paragraph (5)(B);

(III) clause (ii), (iii), or (iv) of paragraph (5)(F);

(IV) section 355a of this title;

(V) section 355f of this title;

(VI) section 360cc(a) of this title; or

(VII) subsection (u).

(v)(I) With respect to an application submitted pursuant to subsection (b)(2) for a drug that is subject to section 353(b) of this title for which the sole difference from a listed drug relied upon in the application is a difference in inactive ingredients not permitted under clause (iii) or (iv) of section 314.94(a)(9) of title 21, Code of Federal Regulations (or any successor regulations), the Secretary shall make an evaluation with respect to whether such drug is a therapeutic equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regula-

tions)) to another approved drug product in the prescription drug product section of the list under this paragraph as follows:

(aa) With respect to such an application submitted after December 29, 2022, the evaluation shall be made with respect to a listed drug relied upon in the application pursuant to subsection (b)(2) that is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug in the application pursuant to subsection (b)(2) at the time of approval of such application or not later than 180 days after the date of such approval, provided that the request for such an evaluation is made in the original application (or in a resubmission to a complete response letter), and all necessary data and information are submitted in the original application (or in a resubmission in response to a complete response letter) for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(bb) With respect to such an application approved prior to or on December 29, 2022, the evaluation shall be made not later than 180 days after receipt of a request for a therapeutic equivalence evaluation submitted as part of a supplement to such application; or with respect to an application that was submitted prior to December 29, 2022, but not approved as of December 29, 2022, the evaluation shall be made not later than 180 days after the date of approval of such application if a request for such evaluation is submitted as an amendment to the application, provided that—

(AA) such request for a therapeutic equivalence evaluation is being sought with respect to a listed drug relied upon in the application, and the relied upon listed drug is in the prescription drug product section of the list under this paragraph and is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug for which a therapeutic equivalence evaluation is sought; and

(BB) the amendment or supplement, as applicable, containing such request, or the relevant application, includes all necessary data and information for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(II) When the Secretary makes an evaluation under subclause (I), the Secretary shall, in revisions made to the list pursuant to clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph (6) or if the Secretary

determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(D) In the case of a listed drug for which the list under subparagraph (A)(i) includes a patent for such drug, and any claim of the patent has been cancelled or invalidated pursuant to a final decision issued by the Patent Trial and Appeal Board of the United States Patent and Trademark Office or by a court, from which no appeal has been, or can be, taken, if the holder of the applicable application approved under subsection (c) determines that a patent for such drug, or any patent information for such drug, no longer meets the listing requirements under this section—

(i) the holder of such approved application shall notify the Secretary, in writing, within 14 days of such decision of such cancellation or invalidation and request that such patent or patent information, as applicable, be amended or withdrawn in accordance with the decision issued by the Patent Trial and Appeal Board or a court;

(ii) the holder of such approved application shall include in any notification under clause (i) information related to such patent cancellation or invalidation decision and submit such information, including a copy of such decision, to the Secretary; and

(iii) the Secretary shall, in response to a notification under clause (i), amend or remove patent or patent information in accordance with the relevant decision from the Patent Trial and Appeals Board or court, as applicable, except that the Secretary shall not remove from the list any patent or patent information before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV).

(8) For purposes of this subsection:

(A)(i) The term “bioavailability” means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—



(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if—

(i) a revision to the labeling of the listed drug has been approved by the Secretary within 90 days of when the application is otherwise eligible for approval under this subsection;

(ii) the sponsor of the application agrees to submit revised labeling for the drug that is the subject of the application not later than 60 days after approval under this subsection of the application;

(iii) the labeling revision described under clause (i) does not include a change to the "Warnings" section of the labeling; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines

that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(11)(A) Subject to subparagraph (B), the Secretary shall prioritize the review of, and act within 8 months of the date of the submission of, an original abbreviated new drug application submitted for review under this subsection that is for a drug—

(i) for which there are not more than 3 approved drug products listed under paragraph (7) and for which there are no blocking patents and exclusivities; or

(ii) that has been included on the list under section 356e of this title.

(B) To qualify for priority review under this paragraph, not later than 60 days prior to the submission of an application described in subparagraph (A) or that the Secretary may prioritize pursuant to subparagraph (D), the applicant shall provide complete, accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application, including facilities in corresponding Type II active pharmaceutical ingredients drug master files referenced in an application and sites or organizations involved in bioequivalence and clinical studies used to support the application, to enable the Secretary to make a determination regarding whether an inspection of a facility is necessary. Such information shall include the relevant (as determined by the Secretary) sections of such application, which shall be unchanged relative to the date of the submission of such application, except to the extent that a change is made to such information to exclude a facility that was not used to generate data to meet any application requirements for such submission and that is not the only facility intended to conduct one or more unit operations in commercial production. Information provided by an applicant under this subparagraph shall not be considered the submission of an application under this subsection.

(C) The Secretary may expedite an inspection or reinspection under section 374 of this title of an establishment that proposes to manufacture a drug described in subparagraph (A).

(D) Nothing in this paragraph shall prevent the Secretary from prioritizing the review of other applications as the Secretary determines appropriate.

(12) The Secretary shall publish on the internet website of the Food and Drug Administration, and update at least once every 6 months, a list of all drugs approved under subsection (c) for which all patents and periods of exclusivity under this chapter have expired and for which no application has been approved under this subsection.

(13) Upon the request of an applicant regarding one or more specified pending applications under this subsection, the Secretary shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.

**(k) Records and reports; required information; regulations and orders; access to records**

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e). Regulations and orders issued under this subsection and under subsection (i) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

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

**(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—**

(A) DEFINITION.—In this paragraph, the term “data” refers to information with respect to a drug approved under this section or under section 262 of title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities—

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

(i) IN GENERAL.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355-1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) TIMELINESS OF REPORTING.—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) PRIVATE SECTOR RESOURCES.—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) **COMPLEMENTARY APPROACHES.**—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) **AUTHORITY FOR CONTRACTS.**—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) **ADVANCED ANALYSIS OF DRUG SAFETY DATA.**—

(A) **PURPOSE.**—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b-1 of title 42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) **PRIVACY.**—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) **PUBLIC PROCESS FOR PRIORITY QUESTIONS.**—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through—

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

(D) **PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.**—

(i) **IN GENERAL.**—Not later than 180 days after the date of the establishment of the active postmarket risk identification and anal-

ysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including—

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drug,<sup>2</sup> safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) **REQUEST FOR SPECIFIC METHODOLOGY.**—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) **USE OF ANALYSES.**—The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

(F) **QUALIFIED ENTITIES.**—

(i) **IN GENERAL.**—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) **QUALIFICATION.**—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic

<sup>2</sup> So in original. Probably should be “drug.”

data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) **CONTRACT REQUIREMENTS.**—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) **ENSURING PRIVACY.**—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) **COMPONENT OF ANOTHER ORGANIZATION.**—If a qualified entity is a component of another organization—

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) **TERMINATION OR NONRENEWAL.**—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) **CONFIDENTIALITY AND PRIVACY PROTECTIONS.**—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) **DISPOSITION OF DATA.**—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) **COMPETITIVE PROCEDURES.**—The Secretary shall use competitive procedures (as defined in section 132 of title 41) to enter into contracts under subparagraph (G).

(I) **REVIEW OF CONTRACT IN THE EVENT OF A MERGER OR ACQUISITION.**—The Secretary shall review the contract with a qualified entity

under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) **COORDINATION.**—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall—

(A) conduct regular screenings of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse<sup>3</sup> Event Reporting System within the last quarter; and<sup>4</sup>

(B) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments; and

(C) make available on the Internet website of the Food and Drug Administration—

(i) guidelines, developed with input from experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that detail best practices for drug safety surveillance using the Adverse Event Reporting System; and

(ii) criteria for public posting of adverse event signals.

**(I) Public disclosure of safety and effectiveness data and action package**

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

(2) **ACTION PACKAGE FOR APPROVAL.**—

(A) **ACTION PACKAGE.**—The Secretary shall publish the action package for approval of an

<sup>3</sup> So in original. Probably should be preceded by “the”.

<sup>4</sup> So in original. The word “and” probably should not appear.

application under subsection (b) or section 262 of title 42 on the Internet Web site of the Food and Drug Administration—

(i) not later than 30 days after the date of approval of such applications—

(I) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(II) for a biological product, no active ingredient of which has been approved in any other application under section 262 of title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5 for any other drug or biological product.

(B) IMMEDIATE PUBLICATION OF SUMMARY REVIEW.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) CONTENTS.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes—

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) REVIEW.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) CONFIDENTIAL INFORMATION.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or finan-

cial information, or other matter listed in section 552(b) of title 5.

**(m) "Patent" defined**

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

**(n) Scientific advisory panels**

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule.

While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

**(o) Postmarket studies and clinical trials; labeling**

**(1) In general**

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

**(2) Definitions**

For purposes of this subsection:

**(A) Responsible person**

The term “responsible person” means a person who—

- (i) has submitted to the Secretary a covered application that is pending; or
- (ii) is the holder of an approved covered application.

**(B) Covered application**

The term “covered application” means—

- (i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and
- (ii) an application under section 262 of title 42.

**(C) New safety information; serious risk**

The terms “new safety information”, “serious risk”, and “signal of a serious risk” have the meanings given such terms in section 355-1(b) of this title.

**(3) Studies and clinical trials**

**(A) In general**

For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

**(B) Purposes of study or clinical trial**

The purposes referred to in this subparagraph with respect to a postapproval study

or postapproval clinical trial are the following:

- (i) To assess a known serious risk related to the use of the drug involved.
- (ii) To assess signals of serious risk related to the use of the drug.
- (iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

**(C) Establishment of requirement after approval of covered application**

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

**(D) Determination by Secretary**

**(i) Postapproval studies**

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

**(ii) Postapproval clinical trials**

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

**(E) Notification; timetables; periodic reports**

**(i) Notification**

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

**(ii) Timetable; periodic reports**

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted

under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

**(F) Dispute resolution**

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

**(4) Safety labeling changes requested by Secretary**

**(A) New safety or new effectiveness information**

If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

**(B) Response to notification**

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions, or new effectiveness information; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

**(C) Review**

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to

reach agreement on whether the labeling for the drug should be modified to reflect the new safety or new effectiveness information, and if so, the contents of such labeling changes.

**(D) Discussions**

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

**(E) Order**

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety or new effectiveness information. Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

**(F) Dispute resolution**

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

**(G) Violation**

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

**(H) Public health threat**

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

**(I) Rule of construction**

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

**(5) Non-delegation**

Determinations by the Secretary under this subsection for a drug shall be made by individ-

uals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

**(p) Risk evaluation and mitigation strategy**

**(1) In general**

A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355-1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355-1 of this title, including requirements regarding assessments of approved strategies.

**(2) Certain postmarket studies**

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

**(q) Petitions and civil actions regarding approval of certain applications**

**(1) In general**

**(A) Determination**

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 262(k) of title 42 because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

**(B) Notification**

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

**(C) Format**

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

(i) a document; or

(ii) a meeting with the applicant involved.

**(D) Public disclosure**

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

**(E) Denial based on intent to delay**

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

**(F) Final agency action**

The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

**(G) Extension of 30-month period**

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

**(H) Certification**

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: “I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any rep-



representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: \_\_\_\_\_ . If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons \_\_\_\_\_ or \_\_\_\_\_ organizations: \_\_\_\_\_ . I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.”, with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

**(I) Verification**

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: “I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about \_\_\_\_\_. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: \_\_\_\_\_. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.”, with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

**(2) Exhaustion of administrative remedies**

**(A) Final agency action within 150 days**

The Secretary shall be considered to have taken final agency action on a petition if—

(i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

**(B) Dismissal of certain civil actions**

If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

**(C) Administrative record**

For purposes of judicial review related to the approval of an application for which a

petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

(i) the petition filed under paragraph (1) and any supplements and comments there-to;

(ii) the Secretary’s response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary’s determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

**(3) Annual report on delays in approvals per petitions**

The Secretary shall annually submit to the Congress a report that specifies—

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

**(4) Exceptions**

(A) This subsection does not apply to—

(i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an application submitted pursuant to section 262(k) of title 42.

**(5) Definitions**

**(A) Application**

For purposes of this subsection, the term “application” means an application submitted under subsection (b)(2) or (j) of this section or section 262(k) of title 42.

**(B) Petition**

For purposes of this subsection, other than paragraph (1)(A)(i), the term “petition” means a request described in paragraph (1)(A)(i).

**(r) Postmarket drug safety information for patients and providers**

**(1) Establishment**

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of title 42; and  
 (B) improves communication of drug safety information to patients and providers.

**(2) Internet Web site**

The Secretary shall carry out paragraph (1) by—

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of title 42;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

**(3) Posting of drug labeling**

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

**(4) Private sector resources**

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

**(5) Authority for contracts**

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

**(6) Review**

The Advisory Committee on Risk Communication under section 360bbb-6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

**(s) Referral to advisory committee**

The Secretary shall—

(1) refer a drug or biological product to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee prior to the approval of such drug or biological if it is—

(A) a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(B) a biological product, no active ingredient of which has been approved in any other application under section 262 of title 42; or

(2) if the Secretary does not refer a drug or biological product described in paragraph (1) to a Food and Drug Administration advisory committee prior to such approval, provide in the action letter on the application for the drug or biological product a summary of the reasons why the Secretary did not refer the drug or biological product to an advisory committee prior to approval.

**(t) Database for authorized generic drugs**

**(1) In general**

**(A) Publication**

The Commissioner shall—

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

**(B) Notification**

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

**(2) Inclusion**

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

**(3) Authorized generic drug**

In this section, the term “authorized generic drug” means a listed drug (as that term is used in subsection (j)) that—

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

**(u) Certain drugs containing single enantiomers**

**(1) In general**

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active moiety as that contained in the approved racemic drug, if—

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug—

(I) includes full reports of new clinical investigations (other than bioavailability studies)—

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations (other than bioavailability studies) that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use—

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

**(2) Limitation**

**(A) No approval in certain therapeutic categories**

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

**(B) Labeling**

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

**(3) Definition**

**(A) In general**

For purposes of this subsection, the term “therapeutic category” means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w-104(b)(3)(C)(ii) of title 42 and as in effect on September 27, 2007.

**(B) Publication by Secretary**

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

**(4) Availability**

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2027.

**(v) Antibiotic drugs submitted before November 21, 1997**

**(1) Antibiotic drugs approved before November 21, 1997**

**(A) In general**

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the

3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

**(B) Application; antibiotic drug described**

**(i) Application**

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

**(ii) Antibiotic drug**

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

**(2) Antibiotic drugs submitted before November 21, 1997, but not approved**

**(A) In general**

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug—

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of title 35, subject to the requirements of such section.

**(B) Application; antibiotic drug described**

**(i) Application**

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

**(ii) Antibiotic drug**

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

**(3) Limitations**

**(A) Exclusivities and extensions**

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs<sup>5</sup> (1)(B)(i) or (2)(B)(i), as appli-

cable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

**(B) Conditions of use**

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

**(4) Application of certain provisions**

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

**(w) Deadline for determination on certain petitions**

The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

**(x) Date of approval in the case of recommended controls under the CSA**

**(1) In general**

In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

**(2) Date of approval**

For purposes of this section, with respect to an application described in paragraph (1), the term “date of approval” shall mean the later of—

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

**(y) Contrast agents intended for use with applicable medical imaging devices**

**(1) In general**

The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 360j(p)(1) of this title.

**(2) Review of supplement**

In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may—

<sup>5</sup> So in original. Probably should be “subparagraph”.

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 360e, 360(k), or 360c(f)(2) of this title so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

**(3) Definitions**

For purposes of this subsection—

(A) the term “new use” means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 360j(p) of this title, but that is not described in the approved labeling of the contrast agent; and

(B) the terms “applicable medical imaging device” and “contrast agent” have the meanings given such terms in section 360j(p) of this title.

**(z)<sup>6</sup> Nonclinical test defined**

For purposes of this section, the term “non-clinical test” means a test conducted in vitro, in silico, or in chemico, or a nonhuman in vivo test, that occurs before or during the clinical trial phase of the investigation of the safety and effectiveness of a drug. Such test may include the following:

(1) Cell-based assays.

(2) Organ chips and microphysiological systems.

(3) Computer modeling.

(4) Other nonhuman or human biology-based test methods, such as bioprinting.

(5) Animal tests.

**(z)<sup>6</sup> Diversity action plan for clinical studies<sup>7</sup>**

(1) With respect to a clinical investigation of a new drug that is a phase 3 study, as defined in section 312.21(c) of title 21, Code of Federal Regulations (or successor regulations), or, as appropriate, another pivotal study of a new drug (other than bioavailability or bioequivalence studies), the sponsor of such drug shall submit to the Secretary a diversity action plan.

(2) Such diversity action plan shall include—

(A) the sponsor’s goals for enrollment in such clinical study;

(B) the sponsor’s rationale for such goals; and

(C) an explanation of how the sponsor intends to meet such goals.

(3) The sponsor shall submit to the Secretary such diversity action plan, in the form and manner specified by the Secretary in guidance, as soon as practicable but not later than the date on which the sponsor submits the protocol to the Secretary for such a phase 3 study or other pivotal study of the drug. The sponsor may submit modifications to the diversity action plan. Any such modifications shall be in the form and manner specified by the Secretary in guidance.

(4)(A) On the initiative of the Secretary or at the request of a sponsor, the Secretary may waive any requirement in paragraph (1), (2), or

(3) if the Secretary determines that a waiver is necessary based on what is known or what can be determined about the prevalence or incidence of the disease or condition for which the new drug is under investigation (including in terms of the patient population that may use the drug), if conducting a clinical investigation in accordance with a diversity action plan would otherwise be impracticable, or if such waiver is necessary to protect public health during a public health emergency.

(B) The Secretary shall issue a written response granting or denying a request from a sponsor for a waiver within 60 days of receiving such request.

(5) No diversity action plan shall be required for a submission described in section 360bbb of this title.

(June 25, 1938, ch. 675, §505, 52 Stat. 1052; Pub. L. 86–507, §1(18), June 11, 1960, 74 Stat. 201; Pub. L. 87–781, title I, §§102(b)–(d), 103(a), (b), 104(a)–(d)(2), Oct. 10, 1962, 76 Stat. 781–783, 784, 785; Pub. L. 92–387, §4(d), Aug. 16, 1972, 86 Stat. 562; Pub. L. 98–417, title I, §§101, 102(a)–(b)(5), 103, 104, Sept. 24, 1984, 98 Stat. 1585, 1592, 1593, 1597; Pub. L. 102–282, §5, May 13, 1992, 106 Stat. 161; Pub. L. 103–80, §3(n), Aug. 13, 1993, 107 Stat. 777; Pub. L. 105–115, title I, §§115, 117, 119, 120, 124(a), Nov. 21, 1997, 111 Stat. 2313, 2315, 2316, 2318, 2324; Pub. L. 106–113, div. B, §1000(a)(9) [title IV, §4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A–584; Pub. L. 107–109, §15(c)(1), Jan. 4, 2002, 115 Stat. 1420; Pub. L. 108–155, §2(b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub. L. 108–173, title XI, §§1101(a), (b), 1102(a), 1103(a), Dec. 8, 2003, 117 Stat. 2448, 2452, 2457, 2460; Pub. L. 110–85, title VII, §701(b), title VIII, §801(b)(3)(A), (B), title IX, §§901(a), 903, 905(a), 914(a), 915, 916, 918, 921, title XI, §1113, Sept. 27, 2007, 121 Stat. 903, 921, 922, 943, 944, 953, 957, 958, 960–962, 976; Pub. L. 110–316, title III, §301, Aug. 14, 2008, 122 Stat. 3524; Pub. L. 110–379, §4(a), Oct. 8, 2008, 122 Stat. 4076; Pub. L. 111–31, div. A, title I, §103(e), June 22, 2009, 123 Stat. 1837; Pub. L. 111–148, title VII, §7002(d)(1), title X, §10609, Mar. 23, 2010, 124 Stat. 816, 1014; Pub. L. 112–144, title IX, §905, title XI, §§1101, 1134(a), 1135, July 9, 2012, 126 Stat. 1092, 1108, 1123; Pub. L. 113–5, title III, §301, Mar. 13, 2013, 127 Stat. 179; Pub. L. 114–89, §2(a)(1), Nov. 25, 2015, 129 Stat. 698; Pub. L. 114–255, div. A, title III, §§3024(b), 3031(a), 3075(a), (b), 3101(a)(2)(B), 3102(1), Dec. 13, 2016, 130 Stat. 1099, 1138, 1152, 1156; Pub. L. 115–52, title VI, §601, title VII, §706(b), title VIII, §§801, 802, 808, title IX, §901(a), Aug. 18, 2017, 131 Stat. 1048, 1059, 1068, 1069, 1074, 1076; Pub. L. 115–271, title III, §3041(b), Oct. 24, 2018, 132 Stat. 3942; Pub. L. 116–290, §2(a)–(d)(1), (g), Jan. 5, 2021, 134 Stat. 4889–4892; Pub. L. 117–9, §1(a)(1), (b)(1), Apr. 23, 2021, 135 Stat. 256, 258; Pub. L. 117–180, div. F, title V, §5004, Sept. 30, 2022, 136 Stat. 2167; Pub. L. 117–229, div. C, title III, §305, Dec. 16, 2022, 136 Stat. 2312; Pub. L. 117–328, div. FF, title III, §§3105, 3209(a), 3222, 3224, 3601(a), Dec. 29, 2022, 136 Stat. 5807, 5821, 5829, 5831, 5860.)

**DELAYED APPLICABILITY OF AMENDMENT**

*For delayed applicability of subsection (z) of this section as added by section 3601(a) of Pub. L. 117–328, see Effective Date of 2022 Amendment note below.*

<sup>6</sup> So in original. Two subsecs. (z) have been enacted.

<sup>7</sup> See Delayed Applicability of Amendment note below.

## Editorial Notes

## REFERENCES IN TEXT

Section 264(c) of the Health Insurance Portability and Accountability Act of 1996, referred to in subsec. (k)(3)(C)(i)(I), (4)(G)(i)(I), is section 264(c) of Pub. L. 104-191, which is set out as a note under section 1320d-2 of Title 42, The Public Health and Welfare.

The General Schedule, referred to in subsec. (n)(5), is set out under section 5332 of Title 5, Government Organization and Employees.

Section 101(c) of the Food and Drug Administration Amendments Act of 2007, referred to in subsec. (o)(3)(E)(i), is section 101(c) of Pub. L. 110-85, which is set out as a note under section 379g of this title.

The Food and Drug Administration Modernization Act of 1997, referred to in subsec. (v)(1)(A), (2)(A), (4), is Pub. L. 105-115, Nov. 21, 1997, 111 Stat. 2296. Section 125 of the Act amended sections 321, 331, 335a, 352, 360, 360j, 360aa to 360cc, 360ee, 374, 379g, 381, and 382 of this title, section 45C of Title 26, Internal Revenue Code, section 156 of Title 35, Patents, and section 8126 of Title 38, Veterans' Benefits, repealed sections 356 and 357 of this title, and enacted provisions set out as a note under this section. For complete classification of this Act to the Code, see Short Title of 1997 Amendment note set out under section 301 of this title and Tables.

The Drug Price Competition and Patent Term Restoration Act of 1984, referred to in subsec. (v)(4), is Pub. L. 98-417, Sept. 24, 1984, 98 Stat. 1585. For complete classification of this Act to the Code, see Short Title of 1984 Amendment note set out under section 301 of this title and Tables.

The Controlled Substances Act, referred to in subsec. (x)(1), is title II of Pub. L. 91-513, Oct. 27, 1970, 84 Stat. 1242, which is classified principally to subchapter I (§ 801 et seq.) of chapter 13 of this title. For complete classification of this Act to the Code, see Short Title note set out under section 801 of this title and Tables.

## CODIFICATION

In subsec. (k)(4)(H), “section 132 of title 41” substituted for “section 4(5) of the Federal Procurement Policy Act” on authority of Pub. L. 111-350, § 6(c), Jan. 4, 2011, 124 Stat. 3854, which Act enacted Title 41, Public Contracts.

## AMENDMENTS

2022—Subsec. (i)(1)(A). Pub. L. 117-328, § 3209(a)(1)(A), substituted “nonclinical tests” for “preclinical tests (including tests on animals)”.

Subsec. (i)(2)(B). Pub. L. 117-328, § 3209(a)(1)(B), substituted “nonclinical tests” for “animal”.

Subsec. (j)(7)(A)(v). Pub. L. 117-328, § 3222, added cl. (v).

Subsec. (j)(10)(A)(i) to (iii). Pub. L. 117-328, § 3224, added cls. (i) to (iii) and struck out former cls. (i) to (iii) which read as follows:

“(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the listed drug has been approved by the Secretary within 60 days of such expiration;

“(ii) the labeling revision described under clause (i) does not include a change to the ‘Warnings’ section of the labeling;

“(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and”.

Subsec. (u)(1)(A)(ii)(II). Pub. L. 117-328, § 3105(1), inserted “(other than bioavailability studies)” after “any clinical investigations”.

Subsec. (u)(4). Pub. L. 117-328, § 3105(2), substituted “October 1, 2027” for “December 24, 2022”.

Pub. L. 117-229 substituted “December 24, 2022” for “December 17, 2022”.

Pub. L. 117-180 substituted “December 17” for “October 1”.

Subsec. (z). Pub. L. 117-328, § 3601(a), added subsec. (z) relating to diversity action plan for clinical studies.

Pub. L. 117-328, § 3209(a)(2), added subsec. (z) defining nonclinical test.

2021—Subsec. (b)(1). Pub. L. 116-290, § 2(a)(1), amended par. (1) generally. Prior to amendment, par. (1) related to requirements for filing an application with respect to any drug subject to the provisions of subsec. (a).

Subsec. (c)(2). Pub. L. 116-290, § 2(b)(1), inserted at beginning “Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application.”; substituted “described in subsection (b)(1)(A)(viii).” for “which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.”; inserted “of the type for which information is required to be submitted in subsection (b)(1)(A)(viii)” after “could not file patent information under subsection (b) because no patent”; and inserted at end “Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.”

Subsec. (c)(3)(E). Pub. L. 117-9, § 1(a)(1)(A), substituted “active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))” for “active ingredient (including any ester or salt of the active ingredient)” wherever appearing.

Pub. L. 116-290, § 2(g)(1), substituted “subsection (b)(1)(A)(i)” for “clause (A) of subsection (b)(1)” wherever appearing.

Subsec. (c)(3)(E)(i). Pub. L. 117-9, § 1(b)(1)(A), struck out cl. (i) which read as follows: “If an application (other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b).”

Subsec. (j)(2)(A)(vi). Pub. L. 116-290, § 2(g)(2), substituted “clauses (ii) through (vi) of subsection (b)(1)(A)” for “clauses (B) through (F) of subsection (b)(1)”.

Subsec. (j)(5)(F). Pub. L. 117-9, § 1(a)(1)(B), substituted “active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))” for “active ingredient (including any ester or salt of the active ingredient)” wherever appearing.

Subsec. (j)(5)(F)(i). Pub. L. 117-9, § 1(b)(1)(B), struck out cl. (i) which read as follows: “If an application

(other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b)."

Subsec. (j)(7)(A)(iii). Pub. L. 116-290, §2(b)(2), struck out "(b) or" before "(c)".

Subsec. (j)(7)(A)(iv). Pub. L. 116-290, §2(c), added cl. (iv).

Subsec. (j)(7)(D). Pub. L. 116-290, §2(d)(1), added subpar. (D).

Subsec. (l)(2)(A)(i). Pub. L. 117-9, §1(a)(1)(C)(i), amended cl. (i) generally. Prior to amendment, cl. (i) read as follows: "not later than 30 days after the date of approval of such application for a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42; and".

Subsec. (l)(2)(A)(ii). Pub. L. 117-9, §1(a)(1)(C)(ii), inserted "or biological product" before period at end.

Subsec. (s). Pub. L. 117-9, §1(a)(1)(D), amended subsec. (s) generally. Prior to amendment, text read as follows: "Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42, the Secretary shall—

"(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

"(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval."

Subsec. (u)(1). Pub. L. 117-9, §1(a)(1)(E), in introductory provisions, substituted "active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))" for "active ingredient (including any ester or salt of the active ingredient)" and "same active moiety" for "same active ingredient".

2018—Subsec. (o)(4)(A). Pub. L. 115-271, §3041(b)(1), substituted "safety or new effectiveness information" for "safety information" in heading and "If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug" for "If the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug" in text. Amendment to heading was executed to reflect the probable intent of Congress, notwithstanding error in text directed to be stricken.

Subsec. (o)(4)(B)(i). Pub. L. 115-271, §3041(b)(2), inserted ", or new effectiveness information" after "adverse reactions".

Subsec. (o)(4)(C). Pub. L. 115-271, §3041(b)(3), substituted "safety or new effectiveness information" for "safety information".

Subsec. (o)(4)(E). Pub. L. 115-271, §3041(b)(4), substituted "safety or new effectiveness information" for "safety information".

2017—Subsec. (j)(5)(B)(v). Pub. L. 115-52, §808(1), added cl. (v).

Subsec. (j)(5)(D)(iv). Pub. L. 115-52, §808(2), added cl. (iv).

Subsec. (j)(11), (12). Pub. L. 115-52, §801, added pars. (11) and (12).

Subsec. (j)(13). Pub. L. 115-52, §802, added par. (13).

Subsec. (k)(5). Pub. L. 115-52, §901(a), made technical amendments to directory language of Pub. L. 114-255, §3075(a). See 2016 Amendment notes below.

Subsec. (u)(4). Pub. L. 115-52, §601, substituted "2022" for "2017".

Subsec. (y). Pub. L. 115-52, §706(b), added subsec. (y). 2016—Subsec. (c)(5). Pub. L. 114-255, §3031(a), added par. (5).

Subsec. (d). Pub. L. 114-255, §3101(a)(2)(B)(i), substituted "marketing approval" for "premarket approval" in last sentence.

Subsec. (i)(4). Pub. L. 114-255, §3024(b), substituted "except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings" for "except where it is not feasible or it is contrary to the best interests of such human beings".

Subsec. (k)(5)(A). Pub. L. 114-255, §3075(a)(1), as amended by Pub. L. 115-52, §901(a)(1), substituted "screenings" for "bi-weekly screening".

Pub. L. 114-255, §3102(1)(A), inserted "and" after the semicolon.

Subsec. (k)(5)(B). Pub. L. 114-255, §3075(a)(2), as amended by Pub. L. 115-52, §901(a), substituted "and" for period at end.

Pub. L. 114-255, §3102(1)(B), (C), redesignated subpar. (C) as (B) and struck out former subpar. (B) which read as follows: "report to Congress not later than 2 year after September 27, 2007, on procedures and processes of the Food and Drug Administration for addressing ongoing post market safety issues identified by the Office of Surveillance and Epidemiology and how recommendations of the Office of Surveillance and Epidemiology are handled within the agency; and".

Subsec. (k)(5)(C). Pub. L. 114-255, §3075(a)(3), as amended by Pub. L. 115-52, §901(a)(1), added subpar. (C).

Pub. L. 114-255, §3102(1)(C), redesignated subpar. (C) as (B).

Subsec. (q)(5)(A). Pub. L. 114-255, §3101(a)(2)(B)(ii), substituted "subsection (b)(2) or (j) of this section or section 262(k) of title 42" for "subsection (b)(2) or (j) of the Act or 262(k) of title 42".

Subsec. (r)(2)(D). Pub. L. 114-255, §3075(b), substituted "and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of title 42" for "by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports received for the drug, including identification of any new risks not previously identified, potential new risks, or known risks reported in unusual number;"

2015—Subsec. (x). Pub. L. 114-89 added subsec. (x).

2013—Subsec. (b)(5)(B). Pub. L. 113-5 substituted "size—" for "size of clinical trials intended to form the primary basis of an effectiveness claim or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies.", added cls. (i) and (ii), and designated last two sentences as concluding provisions.

2012—Subsec. (d). Pub. L. 112-144, §905, inserted at end "The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for premarket approval of a drug."

Subsec. (q)(1)(A). Pub. L. 112-144, §1135(1)(A), substituted "subsection (b)(2) or (j) of this section or section 262(k) of title 42" for "subsection (b)(2) or (j)" in introductory provisions.

Subsec. (q)(1)(F). Pub. L. 112-144, §1135(1)(B), substituted "150 days" for "180 days" in introductory provisions.

Subsec. (q)(2)(A). Pub. L. 112-144, §1135(2)(A), substituted "150" for "180" in heading.

Subsec. (q)(2)(A)(i). Pub. L. 112-144, §1135(2)(B), substituted “150-day” for “180-day”.

Subsec. (q)(4). Pub. L. 112-144, §1135(3), designated existing provisions as subpar. (A), redesignated former subpars. (A) and (B) as cls. (i) and (ii), respectively, of subpar. (A), and added subpar. (B).

Subsec. (q)(5)(A). Pub. L. 112-144, §1135(4), substituted “subsection (b)(2) or (j) of the Act or 262(k) of title 42” for “subsection (b)(2) or (j)”.

Subsec. (u)(1)(A)(ii)(II). Pub. L. 112-144, §1101(b), inserted “clinical” after “any”.

Subsec. (u)(4). Pub. L. 112-144, §1101(a), substituted “2017” for “2012”.

Subsec. (w). Pub. L. 112-144, §1134(a), added subsec. (w).

2010—Subsec. (b)(5)(B). Pub. L. 111-148, §7002(d)(1), inserted “or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies” before period at end of first sentence.

Subsec. (j)(10). Pub. L. 111-148, §10609, added par. (10).  
2009—Subsec. (n)(2). Pub. L. 111-31 made technical amendment to reference in original act which appears in text as reference to section 394 of this title.

2008—Subsec. (q)(1)(A). Pub. L. 110-316, §301, inserted concluding provisions.

Subsec. (v). Pub. L. 110-379 added subsec. (v).

2007—Subsec. (b)(6). Pub. L. 110-85, §801(b)(3)(B), added par. (6).

Subsec. (e). Pub. L. 110-85, §903, inserted at end “The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.”

Subsec. (i)(4). Pub. L. 110-85, §801(b)(3)(A), inserted at end “The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.”

Subsec. (k)(3), (4). Pub. L. 110-85, §905(a), added pars. (3) and (4).

Subsec. (k)(5). Pub. L. 110-85, §921, added par. (5).

Subsec. (l). Pub. L. 110-85, §916, designated existing provisions as par. (1), redesignated former pars. (1) to (5) as subpars. (A) to (E), respectively, of par. (1), and added par. (2).

Subsec. (n)(4) to (8). Pub. L. 110-85, §701(b), redesignated pars. (5) to (8) as (4) to (7), respectively, and struck out former par. (4) which read as follows: “Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member’s own scientific work is involved.”

Subsecs. (o), (p). Pub. L. 110-85, §901(a), added subsecs. (o) and (p).

Subsec. (q). Pub. L. 110-85, §914(a), added subsec. (q).

Subsec. (r). Pub. L. 110-85, §915, added subsec. (r).

Subsec. (s). Pub. L. 110-85, §918, added subsec. (s).

Subsec. (t). Pub. L. 110-85, §920, added subsec. (t).

Subsec. (u). Pub. L. 110-85, §1113, added subsec. (u).

2003—Subsec. (b)(1). Pub. L. 108-155, in second sentence, substituted “(F)” for “and (F)” and inserted “, and (G) any assessments required under section 355c of this title” before period at end.

Subsec. (b)(3). Pub. L. 108-173, §1101(b)(1)(A), added par. (3) and struck out former par. (3) which, in subpar. (A), required an applicant making a certification under

par. (2)(A)(iv) to include statement that applicant will give notice to each owner of the patent which is the subject of the certification and to the holder of the approved application, in subpar. (B), directed that notice state that an application has been submitted and include a detailed statement of the applicant’s opinion that the patent is not valid or will not be infringed, and, in subpar. (C), provided that if an application is amended, notice shall be given when the amended application is submitted.

Subsec. (b)(4), (5). Pub. L. 108-173, §1101(b)(1)(B), added par. (4) and redesignated former par. (4) as (5).

Subsec. (c)(3). Pub. L. 108-173, §1101(b)(2)(A), substituted “by applying the following to each certification made under subsection (b)(2)(A)” for “under the following” in introductory provisions.

Subsec. (c)(3)(C). Pub. L. 108-173, §1101(b)(2)(B)(iii), which directed the substitution of “subsection (b)(3)” for “paragraph (3)(B)” in third sentence, could not be executed because such words do not appear. See note below.

Pub. L. 108-173, §1101(b)(2)(B)(ii)(VI), in concluding provisions, struck out “Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.” after “expediting the action.”

Pub. L. 108-173, §1101(b)(2)(B)(i), (ii)(I), in first sentence of introductory provisions, substituted “unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted” for “unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received” and, in second sentence of introductory provisions, substituted “subsection (b)(3)” for “paragraph (3)(B)”.

Subsec. (c)(3)(C)(i). Pub. L. 108-173, §1101(b)(2)(B)(ii)(II), added cl. (i) and struck out former cl. (i) which read as follows: “if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision.”

Subsec. (c)(3)(C)(ii). Pub. L. 108-173, §1101(b)(2)(B)(ii)(III), added cl. (ii) and struck out former cl. (ii) which read as follows: “if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or”.

Subsec. (c)(3)(C)(iii). Pub. L. 108-173, §1101(b)(2)(B)(ii)(IV), substituted “as provided in clause (i); or” for “on the date of such court decision.”

Subsec. (c)(3)(C)(iv). Pub. L. 108-173, §1101(b)(2)(B)(ii)(V), added cl. (iv).

Subsec. (c)(3)(D), (E). Pub. L. 108-173, §1101(b)(2)(C), (D), added subpar. (D) and redesignated former subpar. (D) as (E).

Subsec. (j)(2)(B). Pub. L. 108-173, §1101(a)(1)(A), added subpar. (B) and struck out former subpar. (B) which, in cl. (i), required that an applicant making a certification under subpar. (A)(vii)(IV) include in the application a statement that notice would be given to each owner of the patent and the holder of the approved application, in cl. (ii), required that notice would state that an application had been submitted and that it would include a detailed statement of the basis of the applicant’s opinion, and, in cl. (iii), directed that notice of an amended application be given when the amended application had been submitted.



Subsec. (j)(2)(D). Pub. L. 108-173, § 1101(a)(1)(B), added subpar. (D).

Subsec. (j)(5)(B). Pub. L. 108-173, § 1101(a)(2)(A)(i), substituted “by applying the following to each certification made under paragraph (2)(A)(vii)” for “under the following” in introductory provisions.

Subsec. (j)(5)(B)(iii). Pub. L. 108-173, § 1101(a)(2)(A)(ii)(II)(ee), which directed amendment of the second sentence of subsec. (j)(5)(B)(iii) by striking “Until the expiration” and all that follows in the matter after and below subclause (IV), was executed by striking “Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.” after “expediting the action.” in concluding provisions, to reflect the probable intent of Congress.

Pub. L. 108-173, § 1101(a)(2)(A)(ii)(I), in introductory provisions, substituted “unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted” for “unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received”.

Subsec. (j)(5)(B)(iii)(I). Pub. L. 108-173, § 1101(a)(2)(A)(ii)(II)(aa), added subcl. (I) and struck out former subcl. (I) which read as follows: “if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision.”

Subsec. (j)(5)(B)(iii)(II). Pub. L. 108-173, § 1101(a)(2)(A)(ii)(II)(bb), added subcl. (II) and struck out former subcl. (II) which read as follows: “if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or”.

Subsec. (j)(5)(B)(iii)(III). Pub. L. 108-173, § 1101(a)(2)(A)(ii)(II)(cc), substituted “as provided in subclause (I); or” for “on the date of such court decision.”

Subsec. (j)(5)(B)(iii)(IV). Pub. L. 108-173, § 1101(a)(2)(A)(ii)(II)(dd), added subcl. (IV).

Subsec. (j)(5)(B)(iv). Pub. L. 108-173, § 1102(a)(1), added cl. (iv) and struck out former cl. (iv) which read as follows: “If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

“(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

“(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.”

Subsec. (j)(5)(C). Pub. L. 108-173, § 1101(a)(2)(B), (C), added subpar. (C). Former subpar. (C) redesignated (E).

Subsec. (j)(5)(D). Pub. L. 108-173, § 1102(a)(2), added subpar. (D).

Pub. L. 108-173, § 1101(a)(2)(B), redesignated subpar. (D) as (F).

Subsec. (j)(5)(E), (F). Pub. L. 108-173, § 1101(a)(2)(B), redesignated subpars. (C) and (D) as (E) and (F), respectively.

Subsec. (j)(8)(A). Pub. L. 108-173, § 1103(a)(1), added subpar. (A) and struck out former subpar. (A) which read as follows: “The term ‘bioavailability’ means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.”

Subsec. (j)(8)(C). Pub. L. 108-173, § 1103(a)(2), added subpar. (C).

2002—Subsec. (i)(1)(D). Pub. L. 107-109 added subpar. (D).

1999—Subsec. (m). Pub. L. 106-113 substituted “United States Patent and Trademark Office” for “Patent and Trademark Office of the Department of Commerce”.

1997—Subsec. (b)(1). Pub. L. 105-115, § 115(b), inserted at end “The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).”

Subsec. (b)(4). Pub. L. 105-115, § 119(a), added par. (4).

Subsec. (c)(4). Pub. L. 105-115, § 124(a), added par. (4).

Subsec. (d). Pub. L. 105-115, § 115(a), inserted at end “If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.”

Subsec. (i). Pub. L. 105-115, § 117, inserted “(1)” after “(i)”, redesignated former pars. (1) to (3) as subpars. (A) to (C), respectively, of par. (1), added pars. (2) to (4), and struck out closing provisions which read as follows: “Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.”

Subsec. (j)(2)(A)(i). Pub. L. 105-115, § 119(b)(2)(A), substituted “paragraph (7)” for “paragraph (6)”.

Subsec. (j)(3). Pub. L. 105-115, § 119(b)(1)(B), added par. (3). Former par. (3) redesignated (4).

Subsec. (j)(4). Pub. L. 105-115, § 119(b)(1)(A), (2)(B), redesignated par. (3) as (4) and in introductory provisions substituted “paragraph (5)” for “paragraph (4)”. Former par. (4) redesignated (5).

Subsec. (j)(4)(I). Pub. L. 105-115, § 119(b)(2)(C), substituted “paragraph (6)” for “paragraph (5)”.

Subsec. (j)(5), (6). Pub. L. 105-115, § 119(b)(1)(A), redesignated pars. (4) and (5) as (5) and (6), respectively. Former par. (6) redesignated (7).

Subsec. (j)(7). Pub. L. 105-115, § 119(b)(1)(A), (2)(D), redesignated par. (6) as (7) and in subpar. (C) substituted “paragraph (6)” for “paragraph (5)” in two places. Former par. (7) redesignated (8).

Subsec. (j)(8), (9). Pub. L. 105-115, § 119(b)(1)(A), redesignated pars. (7) and (8) as (8) and (9), respectively.

Subsec. (n). Pub. L. 105-115, § 120, added subsec. (n).

1993—Subsec. (j)(6)(A)(ii). Pub. L. 103-80, § 3(n)(1)(A), substituted “Secretary” for “Secretary”.

Subsec. (j)(6)(A)(iii). Pub. L. 103-80, § 3(n)(1)(B), inserted comma after “published by the Secretary”.

Subsec. (k)(1). Pub. L. 103-80, § 3(n)(2), substituted “section. Regulations” for “section: *Provided, however, That regulations*”.

1992—Subsec. (j)(8). Pub. L. 102-282 added par. (8).

1984—Subsec. (a). Pub. L. 98-417, § 102(b)(1), inserted “or (j)” after “subsection (b)”.

Subsec. (b). Pub. L. 98-417, §§102(a)(1), 103(a), designated existing provisions of subsec. (b) as par. (1) thereof and redesignated existing cls. (1) through (6) of such par. (1) as cls. (A) through (F) thereof, respectively, inserted requirement that the applicant file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, that the applicant amend the application to include such information if an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, and that upon approval of the application, the Secretary publish the information submitted, and added pars. (2) and (3).

Subsec. (c). Pub. L. 98-417, §§102(a)(2), (b)(2), 103(b), designated existing provisions of subsec. (c) as par. (1) thereof and in par. (1) as so designated substituted "subsection (b)" for "this subsection" and redesignated former pars. (1) and (2) as subpars. (A) and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(6), (7). Pub. L. 98-417, §102(a)(3)(A), added cl. (6) relating to the failure of the application to contain the patent information prescribed by subsec. (b) of this section, and redesignated former cl. (6) as (7).

Subsec. (e). Pub. L. 98-417, §102(a)(3)(B), in first sentence, added a new cl. (4) relating to the failure to file the patent information prescribed by subsec. (c) of this section within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information, and redesignated former cl. (4) as (5).

Pub. L. 98-417, §102(b)(3), (4), in second sentence, inserted in provisions preceding cl. (1) "submitted under subsection (b) or (j)" and in cl. (1) substituted "under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title" for "under subsection (j) or to comply with the notice requirements of section 360(j)(2) of this title".

Subsecs. (j), (k). Pub. L. 98-417, §101, added subsec. (j) and redesignated former subsec. (j) as (k).

Subsec. (k)(1). Pub. L. 98-417, §102(b)(5), substituted "under subsection (b) or (j)" for "pursuant to this section".

Subsecs. (l), (m). Pub. L. 98-417, §104, added subsecs. (l) and (m).

1972—Subsec. (e). Pub. L. 92-387 inserted "or to comply with the notice requirements of section 360(j)(2) of this title" in cl. (1) of second sentence relating to the maintenance of records.

1962—Subsec. (a). Pub. L. 87-781, §104(a), inserted "an approval of" before "an application".

Subsec. (b). Pub. L. 87-781, §102(b), inserted "and whether such drug is effective in use" after "is safe for use".

Subsec. (c). Pub. L. 87-781, §104(b), substituted provisions requiring the Secretary, within 180 days after filing an application, or such additional period as the Secretary and the applicant agree upon, to either approve the application, if meeting the requirements of subsec. (d) of this section, or give notice of opportunity for hearing on question of whether such application is approvable, and providing that if applicant requests hearing in writing within 30 days, the hearing shall begin within 90 days after expiration of said 30 days, unless the Secretary and applicant agree otherwise, that such hearing shall be expedited, and that the Secretary's order shall be issued within 90 days after date for filing final briefs, for provisions which had an application become effective on the sixtieth day after filing thereof unless prior thereto the Secretary postponed the date by written notice to such time, but not more than 180 days after filing, as the Secretary deemed necessary to study and investigate the application.

Subsec. (d). Pub. L. 87-781, §102(c), inserted references to subsec. (c), added cls. (5) and (6), provided that if after notice and opportunity for hearing, the Secretary

finds that cls. (1) to (6) do not apply, he shall approve the application, and defined "substantial evidence" as used in this subsection and subsec. (e) of this section.

Subsec. (e). Pub. L. 87-781, §102(d), amended subsec. (e) generally, and among other changes, directed the Secretary to withdraw approval of an application if by tests, other scientific data or experience, or new evidence of clinical experience not contained in the application or available at the time of its approval, the drug is shown to be unsafe, or on the basis of new information, there is shown a lack of substantial evidence that the drug has the effect it is represented to have, and provided that if the Secretary, or acting Secretary, finds there is an imminent hazard to the public health, he may suspend approval immediately, notify the applicant, and give him opportunity for an expedited hearing, that the Secretary may withdraw approval if the applicant fails to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain records and make reports, or has refused access to, or copying or verification of such records, or if the Secretary finds on new evidence that the methods, facilities and controls in the manufacturing, processing, and packing are inadequate to assure and preserve the drugs' identity, strength, quality and purity, and were not made adequate within a reasonable time after receipt of written notice thereof, or finds on new evidence, that the labeling is false or misleading and was not corrected within a reasonable time after receipt of written notice thereof.

Subsec. (f). Pub. L. 87-781, §104(c), substituted provisions requiring the Secretary to revoke any previous order under subsecs. (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and to approve such application or reinstate such approval, for provisions which required him to revoke an order refusing effectiveness to an application.

Subsec. (h). Pub. L. 87-781, §104(d)(1), (2), inserted "as provided in section 2112 of title 28", and "except that until the filing of the record the Secretary may modify or set aside his order", substituted "or withdrawing approval of an application under this section" for "to permit the application to become effective, or suspending the effectiveness of the application", "United States court of appeals for the circuit" for "district court of the United States within any district", "Court of Appeals for the District of Columbia Circuit" for "District Court for the District of Columbia", "transmitted by the clerk of the court to" for "served upon", and "by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28" for "as provided in sections 225, 346, and 347 of title 28, as amended, and in section 7, as amended, of the Act entitled 'An Act to establish a Court of Appeals for the District of Columbia', approved February 9, 1893", and eliminated "upon" before "any officer designated", "a transcript of" before "the record" and "and decree" before "of the court affirming".

Subsec. (i). Pub. L. 87-781, §103(b), inserted "the foregoing subsections of" after "operation of", and "and effectiveness" after "safety", and provided that the regulations may condition exemptions upon the submission of reports of preclinical tests to justify the proposed clinical testing, upon the obtaining by the manufacturer or sponsor of the investigation of a new drug of a signed agreement from each of the investigators that patients to whom the drug is administered will be under his supervision or under investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings, or upon the establishment and maintenance of records and reports of data obtained by the investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug, and provided that the regulations shall condition an exemption upon the manufacturer or sponsor of the investigation requiring that experts using such drugs certify that they will inform humans to whom such drugs or any controls connected therewith are administered, or their representatives, and

will obtain the consent of such people where feasible and not contrary to the best interests of such people, and that reports on the investigational use of drugs are not required to be submitted directly to the Secretary.

Subsec. (j). Pub. L. 87-781, §103(a), added subsec. (j).

1960—Subsec. (g). Pub. L. 86-507 inserted “or by certified mail” after “registered mail”.

#### Statutory Notes and Related Subsidiaries

##### EFFECTIVE DATE OF 2022 AMENDMENT

Pub. L. 117-328, div. FF, title III, §3602(c), Dec. 29, 2022, 136 Stat. 5863, provided that: “Sections 505(z) and 520(g)(9) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z), 360j(g)(9)], as added by section 3601, shall apply only with respect to clinical investigations for which enrollment commences after the date that is 180 days after the publication of final guidance required under this section [see section 3602(a), (b) of Pub. L. 117-328, set out below].”

##### EFFECTIVE DATE OF 2021 AMENDMENT

Pub. L. 116-290, §2(d)(2), Jan. 5, 2021, 134 Stat. 4891, provided that: “Subparagraph (D) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), as added by paragraph (1), applies only with respect to a decision described in such subparagraph that is issued on or after the date of enactment of this Act [Jan. 5, 2021].”

##### EFFECTIVE DATE OF 2012 AMENDMENT

Pub. L. 112-144, title XI, §1134(b), July 9, 2012, 126 Stat. 1123, provided that: “The amendment made by subsection (a) [amending this section] shall apply to any petition that is submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), on or after the date of enactment of this Act [July 9, 2012].”

##### EFFECTIVE DATE OF 2007 AMENDMENT

Pub. L. 110-85, title VII, §701(c), Sept. 27, 2007, 121 Stat. 904, provided that: “The amendments made by this section [enacting section 379d-1 of this title and amending this section] shall take effect on October 1, 2007.”

Amendment by sections 901(a), 903, and 905(a) of Pub. L. 110-85 effective 180 days after Sept. 27, 2007, see section 909 of Pub. L. 110-85, set out as a note under section 331 of this title.

##### EFFECTIVE DATE OF 2003 AMENDMENTS

Pub. L. 108-173, title XI, §1101(c), Dec. 8, 2003, 117 Stat. 2456, provided that:

“(1) IN GENERAL.—Except as provided in paragraphs (2) and (3), the amendments made by subsections (a) and (b) [amending this section] apply to any proceeding under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) that is pending on or after the date of the enactment of this Act [Dec. 8, 2003] regardless of the date on which the proceeding was commenced or is commenced.

“(2) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—The amendments made by subsections (a)(1) and (b)(1) apply with respect to any certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) submitted on or after August 18, 2003, in an application filed under subsection (b) or (j) of that section or in an amendment or supplement to an application filed under subsection (b) or (j) of that section.

“(3) EFFECTIVE DATE OF APPROVAL.—The amendments made by subsections (a)(2)(A)(ii)(I) and (b)(2)(B)(i) apply with respect to any patent information submitted under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) on or after August 18, 2003.”

Pub. L. 108-173, title XI, §1102(b), Dec. 8, 2003, 117 Stat. 2460, provided that:

“(1) IN GENERAL.—Except as provided in paragraph (2), the amendment made by subsection (a) [amending this section] shall be effective only with respect to an application filed under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which no certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act.

“(2) COLLUSIVE AGREEMENTS.—If a forfeiture event described in section 505(j)(5)(D)(i)(V) of that Act occurs in the case of an applicant, the applicant shall forfeit the 180-day period under section 505(j)(5)(B)(iv) of that Act without regard to when the first certification under section 505(j)(2)(A)(vii)(IV) of that Act for the listed drug was made.

“(3) DECISION OF A COURT WHEN THE 180-DAY EXCLUSIVITY PERIOD HAS NOT BEEN TRIGGERED.—With respect to an application filed before, on, or after the date of the enactment of this Act [Dec. 8, 2003] for a listed drug for which a certification under section 505(j)(2)(A)(vii)(IV) of that Act was made before the date of the enactment of this Act and for which neither of the events described in subclause (I) or (II) of section 505(j)(5)(B)(iv) of that Act (as in effect on the day before the date of the enactment of this Act) has occurred on or before the date of the enactment of this Act, the term ‘decision of a court’ as used in clause (iv) of section 505(j)(5)(B) of that Act means a final decision of a court from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken.”

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

##### EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106-113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, §4731] of Pub. L. 106-113, set out as a note under section 1 of Title 35, Patents.

##### EFFECTIVE DATE OF 1997 AMENDMENT

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

##### EFFECTIVE DATE OF 1984 AMENDMENT

Pub. L. 98-417, title I, §105, Sept. 24, 1984, 98 Stat. 1597, provided that:

“(a) The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 505 of the Federal Food, Drug, and Cosmetic Act [this section], as amended by sections 101, 102, and 103 of this Act, within one year of the date of enactment of this Act [Sept. 24, 1984].

“(b) During the period beginning sixty days after the date of the enactment of this Act [Sept. 24, 1984], and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new drug applications may be submitted in accordance with the provisions of section 314.2 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 505(c) of the Federal Food, Drug, and Cosmetic Act [subsec. (c) of this section] before the date of the enactment of this Act. If any such provision is inconsistent with the requirements of section 505(j) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall consider the application under the applicable requirements of such section. The Secretary of Health and Human Services may not approve such an abbreviated new drug application which is filed for a drug which is described in sections 505(c)(3)(D) and 505(j)(4)(D) of the Federal Food, Drug, and Cosmetic Act, except in accordance with such section.”

## EFFECTIVE DATE OF 1972 AMENDMENT

Amendment by Pub. L. 92-387 effective on first day of sixth month beginning after Aug. 16, 1972, see section 5 of Pub. L. 92-387, set out as a note under section 360 of this title.

## EFFECTIVE DATE OF 1962 AMENDMENT

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

## CONSTRUCTION OF AMENDMENT BY PUB. L. 110-85

Pub. L. 110-85, title IX, §905(b), Sept. 27, 2007, 121 Stat. 949, provided that: “Nothing in this section [amending this section] or the amendment made by this section shall be construed to prohibit the lawful disclosure or use of data or information by an entity other than as described in paragraph (4)(B) or (4)(G) of section 505(k) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(k)], as added by subsection (a).”

## CONSTRUCTION OF AMENDMENTS BY PUB. L. 102-282

Amendment by Pub. L. 102-282 not to preclude any other civil, criminal, or administrative remedy provided under Federal or State law, including any private right of action against any person for the same action subject to any action or civil penalty under an amendment made by Pub. L. 102-282, see section 7 of Pub. L. 102-282, set out as a note under section 335a of this title.

## EXTENDING EXPIRATION DATES FOR CERTAIN DRUGS

Pub. L. 117-328, div. FF, title II, §2512(a), Dec. 29, 2022, 136 Stat. 5804, provided that: “Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary of Health and Human Services (referred to in this section as the ‘Secretary’) shall issue draft guidance, or revise existing guidance, to address recommendations for sponsors of applications submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) regarding—

“(1) the submission of stability testing data in such applications, including considerations for data requirements that could be streamlined or reduced to facilitate faster review of longer proposed expiration dates;

“(2) establishing in the labeling of drugs the longest feasible expiration date scientifically supported by such data, taking into consideration how extended expiration dates may—

“(A) help prevent or mitigate drug shortages; and  
“(B) affect product quality; and

“(3) the use of innovative approaches for drug and combination product stability modeling to support initial product expiration dates and expiration date extensions.”

## ANTIFUNGAL RESEARCH AND DEVELOPMENT

Pub. L. 117-328, div. FF, title III, §3211, Dec. 29, 2022, 136 Stat. 5825, provided that:

“(a) DRAFT GUIDANCE.—Not later than 3 years after the date of enactment of this Act [Dec. 29, 2022], the Secretary [of Health and Human Services], acting through the Commissioner of Food and Drugs, shall issue draft guidance for industry for the purposes of assisting entities seeking approval under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or licensure under section 351 of the Public Health Service Act (42 U.S.C. 262) of antifungal therapies designed to treat coccidioidomycosis (commonly known as Valley Fever).

“(b) FINAL GUIDANCE.—Not later than 18 months after the close of the public comment period on the draft guidance issued pursuant to subsection (a), the Secretary, acting through the Commissioner of Food and Drugs, shall finalize the draft guidance.

“(c) WORKSHOP.—To assist entities developing preventive vaccines for fungal infections and coccidioidomycosis, the Secretary shall hold a public workshop.”

## GUIDANCE ON DIVERSITY ACTION PLANS FOR CLINICAL STUDIES

Pub. L. 117-328, div. FF, title III, §3602(a), (b), Dec. 29, 2022, 136 Stat. 5861, 5862, provided that:

“(a) IN GENERAL.—The Secretary [of Health and Human Services] shall update or issue guidance relating to—

“(1) the format and content of the diversity action plans required by sections 505(z) and 520(g)(9) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(z); 360j(g)(9)) (as amended by section 3601) pertaining to the sponsor’s goals for clinical study enrollment, disaggregated by age group, sex, and racial and ethnic demographic characteristics of clinically relevant study populations, and may include characteristics such as geographic location and socioeconomic status, including with respect to—

“(A) the rationale for the sponsor’s enrollment goals, which may include—

“(i) the estimated prevalence or incidence in the United States of the disease or condition for which the drug or device is being investigated in the relevant clinical trial, if such estimated prevalence or incidence is known or can be determined based on available data;

“(ii) what is known about the disease or condition for which the drug or device is being investigated;

“(iii) any relevant pharmacokinetic or pharmacogenomic data;

“(iv) what is known about the patient population for such disease or condition, including, to the extent data is available—

“(I) demographic information, which may include age group, sex, race, geographic location, socioeconomic status, and ethnicity;

“(II) non-demographic factors, including comorbidities affecting the patient population; and

“(III) potential barriers to enrolling diverse participants, such as patient population size, geographic location, and socioeconomic status; and

“(v) any other data or information relevant to selecting appropriate enrollment goals, disaggregated by demographic subgroup, such as the inclusion of pregnant and lactating women; and

“(B) an explanation for how the sponsor intends to meet such goals, including demographic-specific outreach and enrollment strategies, study-site selection, clinical study inclusion and exclusion practices, and any diversity training for study personnel;

“(2) submission of any modifications to the diversity action plan;

“(3) considerations for the public posting by a sponsor of key information from the diversity action plan that would be useful to patients and providers on the sponsor’s website, as appropriate;

“(4) criteria that the Secretary will consider in assessing whether to grant a sponsor’s request to waive the requirement to submit a diversity action plan under section 505(z)(4) or 520(g)(9)(C) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z)(4), 360j(g)(9)(C)] (as amended by section 3601); and

“(5) how sponsors may include in regular reports otherwise required by the Secretary—

“(A) the sponsor’s progress in meeting the goals referred to in paragraph (1)(A); and

“(B) any updates needed to be made to a diversity action plan referred to in paragraph (1) to help meet goals referred to in paragraph (1)(A); and

“(C) if the sponsor does not expect to meet goals referred to in paragraph (1)(A), the sponsor’s reasons for why the sponsor does not expect to meet such goals.

“(b) ISSUANCE.—The Secretary shall—

“(1) not later than 12 months after the date of enactment of this Act [Dec. 29, 2022], issue new draft

guidance or update existing draft guidance described in subsection (a); and

“(2) not later than 9 months after closing the comment period on such draft guidance, finalize such guidance.”

#### ANNUAL SUMMARY REPORT ON PROGRESS TO INCREASE DIVERSITY IN CLINICAL STUDIES

Pub. L. 117-328, div. FF, title III, §3604, Dec. 29, 2022, 136 Stat. 5864, provided that:

“(a) IN GENERAL.—Beginning not later than 2 years after the date of enactment of this Act [Dec. 29, 2022], and each year thereafter, the Secretary [of Health and Human Services] shall submit to the Congress, and publish on the public website of the Food and Drug Administration, a report that—

“(1) summarizes, in aggregate, the diversity action plans received pursuant to section 505(z) or 520(g)(9) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(z), 360j(g)(9)], as added by section 3601; and

“(2) contains information, in the aggregate, on—

“(A) for drugs, biological products, and devices approved, licensed, cleared, or classified under section 505, 515, 510(k), or 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355; 360e; 360(k); and 360(f)(2) [probably means “360c(f)(2)”]), or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)), whether the clinical studies conducted with respect to such applications met the demographic subgroup enrollment goals from the diversity action plan submitted for such applications; and

“(B) the reasons provided, if any, for why enrollment goals from submitted diversity action plans were not met.

“(b) CONFIDENTIALITY.—Nothing in this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code.”

#### FACILITATING THE USE OF REAL WORLD EVIDENCE

Pub. L. 117-328, div. FF, title III, §3629, Dec. 29, 2022, 136 Stat. 5891, provided that:

“(a) GUIDANCE.—Not later than 1 year after the date of enactment of this Act [Dec. 29, 2022], the Secretary [of Health and Human Services] shall issue or revise existing guidance on considerations for the use of real world data and real world evidence to support regulatory decision-making, as follows:

“(1) With respect to drugs, such guidance shall address the use of such data and evidence to support the approval of a drug application under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or a biological product application under section 351 of the Public Health Service Act (42 U.S.C. 262), and to support an investigational use exemption submission under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)). Such guidance shall include considerations for the inclusion, in such applications and submissions, of real world data and real world evidence obtained as a result of the use of drugs authorized for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-3), and considerations for standards and methodologies for collection and analysis of real world evidence included in such applications and submissions, as appropriate.

“(2) With respect to devices, such guidance shall address the use of such data and evidence to support the approval, clearance, or classification of a device pursuant to an application or submission submitted under section 510(k), 513(f)(2), or 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(k), 360c(f)(2), 360e), to support an investigational use exemption submission under section 520(g) of such Act (21 U.S.C. 360j(g)), and to support a determination by

the Secretary for purposes of section 353 of the Public Health Service Act (42 U.S.C. 263a) (including the category described under subsection (d)(3) of such section). Such guidance shall include considerations for the inclusion, in such applications and submissions, of real world data and real world evidence obtained as a result of the use of devices authorized for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-3), including considerations related to a determination under section 353(d)(3) of the Public Health Service Act (42 U.S.C. 263a(d)(3)), and considerations for standards and methodologies for collection and analysis of real world evidence included in such applications, submissions, or determinations, as appropriate.

“(b) REPORT TO CONGRESS.—Not later than 2 years after the end of the public health emergency declared by the Secretary under section 319 of the Public Health Service Act (42 U.S.C. 247d) on January 31, 2020, with respect to COVID-19, the Secretary shall submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives on—

“(1) the number of applications, submissions, or requests submitted for clearance, approval, or authorization under section 505, 510(k), 513(f)(2), or 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 360(k), 360c(f)(2), 360e) or section 351 of the Public Health Service Act (42 U.S.C. 262), for which an authorization under section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-3) was previously granted;

“(2) of the number of applications so submitted, the number of such applications—

“(A) for which real world evidence was submitted and used to support a regulatory decision; and

“(B) for which real world evidence was submitted and determined to be insufficient to support a regulatory decision; and

“(3) a summary explanation of why, in the case of applications described in paragraph (2)(B), real world evidence could not be used to support regulatory decisions.

“(c) INFORMATION DISCLOSURE.—Nothing in this section shall be construed to authorize the disclosure of information that is prohibited from disclosure under section 1905 of title 18, United States Code, or subject to withholding under subsection (b)(4) of section 552 of title 5, United States Code (commonly referred to as the ‘Freedom of Information Act’).”

#### CLARIFYING FDA REGULATION OF NON-ADDICTIVE PAIN PRODUCTS

Pub. L. 115-271, title III, §3001, Oct. 24, 2018, 132 Stat. 3932, provided that:

“(a) PUBLIC MEETINGS.—Not later than one year after the date of enactment of this Act [Oct. 24, 2018], the Secretary of Health and Human Services (referred to in this section as the ‘Secretary’), acting through the Commissioner of Food and Drugs, shall hold not less than one public meeting to address the challenges and barriers of developing non-addictive medical products intended to treat acute or chronic pain or addiction, which may include—

“(1) the manner by which the Secretary may incorporate the risks of misuse and abuse of a controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)) into the risk benefit assessments under subsections (d) and (e) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), section 510(k) of such Act (21 U.S.C. 360(k)), or section 515(c) of such Act (21 U.S.C. 360e(c)), as applicable;

“(2) the application of novel clinical trial designs (consistent with section 3021 of the 21st Century Cures Act (Public Law 114-255) [set out as a note below]), use of real world evidence (consistent with section 505F of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355g)), and use of patient experience data (consistent with section 569C of the Federal

Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–8c)) for the development of non-addictive medical products intended to treat pain or addiction;

“(3) the evidentiary standards and the development of opioid-sparing data for inclusion in the labeling of medical products intended to treat acute or chronic pain; and

“(4) the application of eligibility criteria under sections 506 and 515B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356, 360e–3) for non-addictive medical products intended to treat pain or addiction.

“(b) GUIDANCE.—Not less than one year after the public meetings are conducted under subsection (a) the Secretary shall issue one or more final guidance documents, or update existing guidance documents, to help address challenges to developing non-addictive medical products to treat pain or addiction. Such guidance documents shall include information regarding—

“(1) how the Food and Drug Administration may apply sections 506 and 515B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356, 360e–3) to non-addictive medical products intended to treat pain or addiction, including the circumstances under which the Secretary—

“(A) may apply the eligibility criteria under such sections 506 and 515B to non-addictive medical products intended to treat pain or addiction;

“(B) considers the risk of addiction of controlled substances approved to treat pain when establishing unmet medical need; and

“(C) considers pain, pain control, or pain management in assessing whether a disease or condition is a serious or life-threatening disease or condition;

“(2) the methods by which sponsors may evaluate acute and chronic pain, endpoints for non-addictive medical products intended to treat pain, the manner in which endpoints and evaluations of efficacy will be applied across and within review divisions, taking into consideration the etiology of the underlying disease, and the manner in which sponsors may use surrogate endpoints, intermediate endpoints, and real world evidence;

“(3) the manner in which the Food and Drug Administration will assess evidence to support the inclusion of opioid-sparing data in the labeling of non-addictive medical products intended to treat acute or chronic pain, including—

“(A) alternative data collection methodologies, including the use of novel clinical trial designs (consistent with section 3021 of the 21st Century Cures Act (Public Law 114–255) [set out as a note below]) and real world evidence (consistent with section 505F of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355g)), including patient registries and patient reported outcomes, as appropriate, to support product labeling;

“(B) ethical considerations of exposing subjects to controlled substances in clinical trials to develop opioid-sparing data and considerations on data collection methods that reduce harm, which may include the reduction of opioid use as a clinical benefit;

“(C) endpoints, including primary, secondary, and surrogate endpoints, to evaluate the reduction of opioid use;

“(D) best practices for communication between sponsors and the agency on the development of data collection methods, including the initiation of data collection; and

“(E) the appropriate format in which to submit such data results to the Secretary; and

“(4) the circumstances under which the Food and Drug Administration considers misuse and abuse of a controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)) in making the risk benefit assessment under paragraphs (2) and (4) of subsection (d) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and in finding that a drug is unsafe under paragraph (1) or (2) of subsection (e) of such section.

“(c) DEFINITIONS.—In this section—

“(1) the term ‘medical product’ means a drug (as defined in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(g)(1))), biological product (as defined in section 351(i) of the Public Health Service Act (42 U.S.C. 262(i))), or device (as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(h))); and

“(2) the term ‘opioid-sparing’ means reducing, replacing, or avoiding the use of opioids or other controlled substances intended to treat acute or chronic pain.”

#### GUIDANCE REGARDING REDUCTION IN DRUG EFFECTIVENESS

Pub. L. 115–271, title III, §3041(c), Oct. 24, 2018, 132 Stat. 3943, provided that: “Not less than one year after the date of enactment of this Act [Oct. 24, 2018], the Secretary of Health and Human Services shall issue guidance regarding the circumstances under which the Food and Drug Administration may require postmarket studies or clinical trials to assess the potential reduction in effectiveness of a drug and how such reduction in effectiveness could result in a change to the benefits of the drug and the risks to the patient. Such guidance shall also address how the Food and Drug Administration may apply this section [amending this section and section 355–1 of this title] and the amendments made thereby with respect to circumstances under which the Food and Drug Administration may require postmarket studies or clinical trials and safety labeling changes related to the use of controlled substances for acute or chronic pain.”

#### ANNUAL REPORT ON INSPECTIONS

Pub. L. 115–52, title IX, §902, Aug. 18, 2017, 131 Stat. 1077, as amended by Pub. L. 117–328, div. FF, title III, §3617, Dec. 29, 2022, 136 Stat. 5876, provided that: “Not later than 120 days after the end of each fiscal year, the Secretary of Health and Human Services shall post on the website of the Food and Drug Administration information related to inspections of facilities necessary for approval of a drug under subsection (c) or (j) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or approval of a device under section 515 of such Act (21 U.S.C. 360e) that were conducted during the previous fiscal year. Such information shall include the following:

“(1) The median time following a request from staff of the Food and Drug Administration reviewing an application or report to the beginning of the inspection, including—

“(A) the median time for drugs described in 505(j)(11)(A)(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(11)(A)(i));

“(B) the median time for drugs for which a notification has been submitted in accordance with section 506C(a) of such Act (21 U.S.C. 356c(a)) during the previous fiscal year; and

“(C) the median time for drugs on the drug shortage list in effect under section 506E of such Act (21 U.S.C. 356e) at the time of such request.

“(2) The median time from the issuance of a report pursuant to section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(b)) to the sending of a warning letter, issuance of an import alert, or holding of a regulatory meeting for inspections for which the Secretary concluded that regulatory or enforcement action was indicated, including the median time for each category of drugs listed in subparagraphs (A) through (C) of paragraph (1).

“(3) The median time from the sending of a warning letter, issuance of an import alert, or holding of a regulatory meeting related to conditions observed by the Secretary during an inspection, to the time at which the Secretary concludes that corrective actions to resolve such conditions have been taken.

“(4) The number of facilities that failed to implement adequate corrective or preventive actions fol-

lowing a report issued pursuant to such section 704(b), resulting in a withhold recommendation for an application under review, including the number of such facilities manufacturing each category of drugs listed in subparagraphs (A) through (C) of paragraph (1).”

#### REPORT ON PATIENT EXPERIENCE DRUG DEVELOPMENT

Pub. L. 114-255, div. A, title III, §3004, Dec. 13, 2016, 130 Stat. 1085, provided that: “Not later than June 1 of 2021, 2026, and 2031, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall prepare and publish on the Internet website of the Food and Drug Administration a report assessing the use of patient experience data in regulatory decisionmaking, in particular with respect to the review of patient experience data and information on patient-focused drug development tools as part of applications approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)).”

#### NOVEL CLINICAL TRIAL DESIGNS

Pub. L. 114-255, div. A, title III, §3021, Dec. 13, 2016, 130 Stat. 1095, provided that:

“(a) PROPOSALS FOR USE OF NOVEL CLINICAL TRIAL DESIGNS FOR DRUGS AND BIOLOGICAL PRODUCTS.—For purposes of assisting sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and biological products under section 351 of the Public Health Service Act (42 U.S.C. 262), the Secretary of Health and Human Services (referred to in this section as the ‘Secretary’) shall conduct a public meeting and issue guidance in accordance with subsection (b).

“(b) GUIDANCE ADDRESSING USE OF NOVEL CLINICAL TRIAL DESIGNS.—

“(1) IN GENERAL.—The Secretary, acting through the Commissioner of Food and Drugs, shall update or issue guidance addressing the use of complex adaptive and other novel trial design in the development and regulatory review and approval or licensure for drugs and biological products.

“(2) CONTENTS.—The guidance under paragraph (1) shall address—

“(A) the use of complex adaptive and other novel trial designs, including how such clinical trials proposed or submitted help to satisfy the substantial evidence standard under section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d));

“(B) how sponsors may obtain feedback from the Secretary on technical issues related to modeling and simulations prior to—

“(i) completion of such modeling or simulations; or

“(ii) the submission of resulting information to the Secretary;

“(C) the types of quantitative and qualitative information that should be submitted for review; and

“(D) recommended analysis methodologies.

“(3) PUBLIC MEETING.—Prior to updating or issuing the guidance required by paragraph (1), the Secretary shall consult with stakeholders, including representatives of regulated industry, academia, patient advocacy organizations, consumer groups, and disease research foundations, through a public meeting to be held not later than 18 months after the date of enactment of this Act [Dec. 13, 2016].

“(4) TIMING.—The Secretary shall update or issue a draft version of the guidance required by paragraph (1) not later than 18 months after the date of the public meeting required by paragraph (3) and finalize such guidance not later than 1 year after the date on which the public comment period for the draft guidance closes.”

#### VARIATIONS FROM CGMP STREAMLINED APPROACH

Pub. L. 114-255, div. A, title III, §3038(c), Dec. 13, 2016, 130 Stat. 1110, provided that: “Not later than 18 months after the date of enactment of this Act [Dec. 13, 2016], the Secretary of Health and Human Services (referred to in this subsection as the ‘Secretary’) shall identify types of combination products and manufacturing processes with respect to which the Secretary proposes that good manufacturing processes may be adopted that vary from the requirements set forth in section 4.4 of title 21, Code of Federal Regulations (or any successor regulations) or that the Secretary proposes can satisfy the requirements in section 4.4 through alternative or streamlined mechanisms. The Secretary shall identify such types, variations from such requirements, and such mechanisms, in a proposed list published in the Federal Register. After a public comment period regarding the appropriate good manufacturing practices for such types, the Secretary shall publish a final list in the Federal Register, notwithstanding section 553 of title 5, United States Code. The Secretary shall evaluate such types, variations, and mechanisms using a risk-based approach. The Secretary shall periodically review such final list.”

#### FDA OPIOID ACTION PLAN

Pub. L. 114-198, title I, §106(a), July 22, 2016, 130 Stat. 702, provided that:

“(1) NEW DRUG APPLICATION.—

“(A) IN GENERAL.—Subject to subparagraph (B), prior to the approval pursuant to an application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) of a new drug that is an opioid, the Secretary of Health and Human Services (referred to in this section [enacting provisions set out as notes under this section and section 355-1 of this title] as the ‘Secretary’) shall refer the application to an advisory committee of the Food and Drug Administration to seek recommendations from such advisory committee.

“(B) PUBLIC HEALTH EXEMPTION.—A referral to an advisory committee under subparagraph (A) is not required with respect to a new opioid drug or drugs if the Secretary—

“(i) finds that such a referral is not in the interest of protecting and promoting public health;

“(ii) finds that such a referral is not necessary based on a review of the relevant scientific information; and

“(iii) submits a notice containing the rationale for such findings to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives.

“(2) PEDIATRIC OPIOID LABELING.—The Secretary shall convene the Pediatric Advisory Committee of the Food and Drug Administration to seek recommendations from such Committee regarding a framework for the inclusion of information in the labeling of drugs that are opioids relating to the use of such drugs in pediatric populations before the Secretary approves any labeling or change to labeling for any drug that is an opioid intended for use in a pediatric population.

“(3) SUNSET.—The requirements of paragraphs (1) and (2) shall cease to be effective on October 1, 2022.”

#### GUIDANCE ON EVALUATING THE ABUSE DETERRENCE OF GENERIC SOLID ORAL OPIOID DRUG PRODUCTS

Pub. L. 114-198, title I, §106(c), July 22, 2016, 130 Stat. 703, provided that: “Not later than 18 months after the end of the period for public comment on the draft guidance entitled ‘General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products’ issued by the Center for Drug Evaluation and Research of the Food and Drug Administration in March 2016, the Commissioner of Food and Drugs shall publish in the Federal Register a final version of such guidance.”

## GUIDANCE ON PATHOGEN-FOCUSED ANTIBACTERIAL DRUG DEVELOPMENT

Pub. L. 112-144, title VIII, §806, July 9, 2012, 126 Stat. 1082, provided that:

“(a) DRAFT GUIDANCE.—Not later than June 30, 2013, in order to facilitate the development of antibacterial drugs for serious or life-threatening bacterial infections, particularly in areas of unmet need, the Secretary of Health and Human Services shall publish draft guidance that—

“(1) specifies how preclinical and clinical data can be utilized to inform an efficient and streamlined pathogen-focused antibacterial drug development program that meets the approval standards of the Food and Drug Administration; and

“(2) provides advice on approaches for the development of antibacterial drugs that target a more limited spectrum of pathogens.

“(b) FINAL GUIDANCE.—Not later than December 31, 2014, after notice and opportunity for public comment on the draft guidance under subsection (a), the Secretary of Health and Human Services shall publish final guidance consistent with this section.”

## GUIDANCE ON ABUSE-DETERRENT PRODUCTS

Pub. L. 112-144, title XI, §1122(c), July 9, 2012, 126 Stat. 1113, as amended by Pub. L. 114-255, div. A, title III, §3101(b)(3)(B), Dec. 13, 2016, 130 Stat. 1156, provided that: “Not later than 6 months after the date of enactment of this Act [July 9, 2012], the Secretary [of Health and Human Services] shall issue guidance on the development of abuse-deterrent drug products.”

## EXTENSION OF PERIOD FOR FIRST APPLICANT TO OBTAIN TENTATIVE APPROVAL WITHOUT FORFEITING 180-DAY-EXCLUSIVITY PERIOD

Pub. L. 112-144, title XI, §1133, July 9, 2012, 126 Stat. 1122, provided that:

“(a) EXTENSION.—

“(1) IN GENERAL.—If a first applicant files an application during the 30-month period ending on the date of enactment of this Act [July 9, 2012] and such application initially contains a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), or if a first applicant files an application and the application is amended during such period to first contain such a certification, the phrase ‘30 months’ in paragraph (5)(D)(i)(IV) of such section shall, with respect to such application, be read as meaning—

“(A) during the period beginning on the date of enactment of this Act, and ending on September 30, 2015, ‘40 months’; and

“(B) during the period beginning on October 1, 2015, and ending on September 30, 2016, ‘36 months’.

“(2) CONFORMING AMENDMENT.—In the case of an application to which an extended period under paragraph (1) applies, the reference to the 30-month period under section 505(q)(1)(G) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(q)(1)(G)) shall be read to be the applicable period under paragraph (1).

“(b) PERIOD FOR OBTAINING TENTATIVE APPROVAL OF CERTAIN APPLICATIONS.—If an application is filed on or before the date of enactment of this Act [July 9, 2012] and such application is amended during the period beginning on the day after the date of enactment of this Act and ending on September 30, 2017, to first contain a certification described in paragraph (2)(A)(vii)(IV) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)), the date of the filing of such amendment (rather than the date of the filing of such application) shall be treated as the beginning of the 30-month period described in paragraph (5)(D)(i)(IV) of such section 505(j).

“(c) DEFINITIONS.—For the purposes of this section, the terms ‘application’ and ‘first applicant’ mean application and first applicant, as such terms are used in section 505(j)(5)(D)(i)(IV) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(5)(D)(i)(IV)).”

## EFFECT OF AMENDMENTS BY PUB. L. 110-85 ON VETERINARY MEDICINE

Pub. L. 110-85, title IX, §907, Sept. 27, 2007, 121 Stat. 950, provided that: “This subtitle [subtitle A (§§901-909) of title IX of Pub. L. 110-85, enacting sections 353c and 355-1 of this title, amending this section and sections 331, 333, and 352 of this title and section 262 of Title 42, The Public Health and Welfare, and enacting provisions set out as notes under this section and sections 331, 352, and 355a of this title], and the amendments made by this subtitle, shall have no effect on the use of drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355] by, or on the lawful written or oral order of, a licensed veterinarian within the context of a veterinarian-client-patient relationship, as provided for under section 512(a)(5) of such Act [21 U.S.C. 360b(a)(5)].”

## EFFECT OF AMENDMENT BY PUB. L. 108-173 ON ABBREVIATED NEW DRUG APPLICATIONS

Pub. L. 108-173, title XI, §1103(b), Dec. 8, 2003, 117 Stat. 2461, provided that: “The amendment made by subsection (a) [amending this section] does not alter the standards for approval of drugs under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)).”

## FEDERAL TRADE COMMISSION REVIEW

Pub. L. 108-173, title XI, subtitle B, Dec. 8, 2003, 117 Stat. 2461, as amended by Pub. L. 115-263, §3, Oct. 10, 2018, 132 Stat. 3673; Pub. L. 115-271, title IV, §4004, Oct. 24, 2018, 132 Stat. 3960, provided that:

## “SEC. 1111. DEFINITIONS.

“In this subtitle:

“(1) ANDA.—The term ‘ANDA’ means an abbreviated drug application, as defined under section 201(aa) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(aa)].

“(2) ASSISTANT ATTORNEY GENERAL.—The term ‘Assistant Attorney General’ means the Assistant Attorney General in charge of the Antitrust Division of the Department of Justice.

“(3) BIOSIMILAR BIOLOGICAL PRODUCT.—The term ‘biosimilar biological product’ means a biological product for which a biosimilar biological product application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)] is approved.

“(4) BIOSIMILAR BIOLOGICAL PRODUCT APPLICANT.—The term ‘biosimilar biological product applicant’ means a person who has filed or received approval for a biosimilar biological product application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)].

“(5) BIOSIMILAR BIOLOGICAL PRODUCT APPLICATION.—The term ‘biosimilar biological product application’ means an application under section 351(k) of the Public Health Service Act [42 U.S.C. 262(k)] for licensure of a biological product as biosimilar to, or interchangeable with, a reference product.

“(6) BRAND NAME DRUG.—The term ‘brand name drug’ means a drug for which an application is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(c)], including an application referred to in section 505(b)(2) of such Act [21 U.S.C. 355(b)(2)], or a biological product for which an application is approved under section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)].

“(7) BRAND NAME DRUG COMPANY.—The term ‘brand name drug company’ means the party that holds the approved application referred to in paragraph (6) for a brand name drug that is a listed drug in an ANDA or a reference product in a biosimilar biological product application, or a party that is the owner of a patent for which information is submitted for such drug under subsection (b) or (c) of section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(b), (c)] or the owner, or exclusive licensee, of a patent included in a list provided under section 351(l)(3) of the Public Health Service Act [42 U.S.C. 262(l)(3)].



“(8) COMMISSION.—The term ‘Commission’ means the Federal Trade Commission.

“(9) GENERIC DRUG.—The term ‘generic drug’ means a drug for which an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)] is approved.

“(10) GENERIC DRUG APPLICANT.—The term ‘generic drug applicant’ means a person who has filed or received approval for an ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)].

“(11) LISTED DRUG.—The term ‘listed drug’ means a brand name drug that is listed under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(7)].

“(12) REFERENCE PRODUCT.—The term ‘reference product’ has the meaning given such term in section 351(i) of the Public Health Service Act [42 U.S.C. 262(i)].

“SEC. 1112. NOTIFICATION OF AGREEMENTS.

“(a) AGREEMENT WITH BRAND NAME DRUG COMPANY.—

“(1) REQUIREMENT.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] or a biosimilar biological product applicant who has submitted a biosimilar biological product application and a brand name drug company that enter into an agreement described in paragraph (2) shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of the generic drug that is the subject of the ANDA or the biosimilar biological product that is the subject of the biosimilar biological product application, as applicable.

“(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph between a generic drug applicant or a biosimilar biological product applicant and a brand name drug company is an agreement regarding—

“(A) the manufacture, marketing, or sale of the brand name drug that is the listed drug in the ANDA or the reference product in the biosimilar biological product application involved;

“(B) the manufacture, marketing, or sale of the generic drug for which the ANDA was submitted or of the biosimilar biological product for which the biosimilar biological product application was submitted; or

“(C) as applicable—

“(i) the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to such ANDA or to any other ANDA based on the same listed drug; or

“(ii) any of the time periods referred to in section 351(k)(6) of the Public Health Service Act [42 U.S.C. 262(k)(6)] as such period applies to such biosimilar biological product application or to any other biosimilar biological product application based on the same reference product.

“(b) AGREEMENT WITH ANOTHER GENERIC DRUG APPLICANT OR BIOSIMILAR BIOLOGICAL PRODUCT APPLICANT.—

“(1) REQUIREMENT.—

“(A) GENERIC DRUGS.—A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(2)(A)(vii)(IV)] with respect to a listed drug and another generic drug applicant that has submitted an ANDA containing such a certification for the same listed drug shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of either of the generic drugs for which such ANDAs were submitted.

“(B) BIOSIMILAR BIOLOGICAL PRODUCTS.—A biosimilar biological product applicant that has submitted a biosimilar biological product application

that references a reference product and another biosimilar biological product applicant that has submitted a biosimilar biological product application that references the same reference product shall each file the agreement in accordance with subsection (c). The agreement shall be filed prior to the date of the first commercial marketing of either of the biosimilar biological products for which such biosimilar biological product applications were submitted.

“(2) SUBJECT MATTER OF AGREEMENT.—An agreement described in this paragraph is, as applicable, an agreement between 2 or more generic drug applicants regarding the 180-day period referred to in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(j)(5)(B)(iv)] as it applies to the ANDAs with which the agreement is concerned, [sic] an agreement between 2 or more biosimilar biological product applicants regarding a time period referred to in section 351(k)(6) of the Public Health Service Act [42 U.S.C. 262(k)(6)] as it applies to the biosimilar biological product, or an agreement between 2 or more biosimilar biological product applicants regarding the manufacture, marketing, or sale of a biosimilar biological product.

“(c) FILING.—

“(1) AGREEMENT.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any such agreement, except that such parties are not required to file an agreement that solely concerns—

“(A) purchase orders for raw material supplies;

“(B) equipment and facility contracts;

“(C) employment or consulting contracts; or

“(D) packaging and labeling contracts.

“(2) OTHER AGREEMENTS.—The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any agreements between the parties that are not described in such subsections and are contingent upon, provide a contingent condition for, were entered into within 30 days of, or are otherwise related to an agreement that is required in subsection (a) or (b) to be filed in accordance with this subsection.

“(3) DESCRIPTION.—In the event that any agreement required in subsection (a) or (b) to be filed in accordance with this subsection has not been reduced to text, each of the parties involved shall file written descriptions of such agreement that are sufficient to disclose all the terms and conditions of the agreement.

“SEC. 1113. FILING DEADLINES.

“Any filing required under section 1112 shall be filed with the Assistant Attorney General and the Commission not later than 10 business days after the date the agreements are executed.

“SEC. 1114. DISCLOSURE EXEMPTION.

“Any information or documentary material filed with the Assistant Attorney General or the Commission pursuant to this subtitle shall be exempt from disclosure under section 552 of title 5, United States Code, and no such information or documentary material may be made public, except as may be relevant to any administrative or judicial action or proceeding. Nothing in this section is intended to prevent disclosure to either body of the Congress or to any duly authorized committee or subcommittee of the Congress.

“SEC. 1115. ENFORCEMENT.

“(a) CIVIL PENALTY.—Any brand name drug company, generic drug applicant, or biosimilar biological product applicant which fails to comply with any provision of this subtitle shall be liable for a civil penalty of not more than \$11,000, for each day during which such entity is in violation of this subtitle. Such penalty may be recovered in a civil action brought by the United States, or brought by the Commission in accordance

with the procedures established in section 16(a)(1) of the Federal Trade Commission Act (15 U.S.C. 56(a) [15 U.S.C. 56(a)(1)]).

“(b) COMPLIANCE AND EQUITABLE RELIEF.—If any brand name drug company, generic drug applicant, or biosimilar biological product applicant fails to comply with any provision of this subtitle, the United States district court may order compliance, and may grant such other equitable relief as the court in its discretion determines necessary or appropriate, upon application of the Assistant Attorney General or the Commission.

“SEC. 1116. RULEMAKING.

“The Commission, with the concurrence of the Assistant Attorney General and by rule in accordance with section 553 of title 5, United States Code, consistent with the purposes of this subtitle—

“(1) may define the terms used in this subtitle;

“(2) may exempt classes of persons or agreements from the requirements of this subtitle; and

“(3) may prescribe such other rules as may be necessary and appropriate to carry out the purposes of this subtitle.

“SEC. 1117. SAVINGS CLAUSE.

“Any action taken by the Assistant Attorney General or the Commission, or any failure of the Assistant Attorney General or the Commission to take action, under this subtitle shall not at any time bar any proceeding or any action with respect to any agreement between a brand name drug company and a generic drug applicant or a biosimilar biological product applicant, any agreement between generic drug applicants, or any agreement between biosimilar biological product applicants, under any other provision of law, nor shall any filing under this subtitle constitute or create a presumption of any violation of any competition laws.

“SEC. 1118. EFFECTIVE DATE.

“This subtitle shall—

“(1) take effect 30 days after the date of the enactment of this Act [Dec. 8, 2003]; and

“(2) shall apply to agreements described in section 1112 that are entered into 30 days after the date of the enactment of this Act.”

REPORT ON PATIENT ACCESS TO NEW THERAPEUTIC AGENTS FOR PEDIATRIC CANCER

Pub. L. 107–109, §15(d), Jan. 4, 2002, 115 Stat. 1421, provided that: “Not later than January 31, 2003, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs and in consultation with the Director of the National Institutes of Health, shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents.”

DATA REQUIREMENTS FOR DRUGS AND BIOLOGICS

Pub. L. 105–115, title I, §118, Nov. 21, 1997, 111 Stat. 2316, provided that: “Within 12 months after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue guidance that describes when abbreviated study reports may be submitted, in lieu of full reports, with a new drug application under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) and with a biologics license application under section 351 of the Public Health Service Act (42 U.S.C. 262) for certain types of studies. Such guidance shall describe the kinds of studies for which abbreviated reports are appropriate and the appropriate abbreviated report formats.”

REQUIREMENTS FOR REVIEW OF APPROVAL PROCEDURES AND CURRENT GOOD MANUFACTURING PRACTICES FOR POSITRON EMISSION TECHNOLOGY

Pub. L. 105–115, title I, §121(c), Nov. 21, 1997, 111 Stat. 2321, provided that:

“(1) PROCEDURES AND REQUIREMENTS.—

“(A) IN GENERAL.—In order to take account of the special characteristics of positron emission tomography drugs and the special techniques and processes required to produce these drugs, not later than 2 years after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services shall establish—

“(i) appropriate procedures for the approval of positron emission tomography drugs pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355); and

“(ii) appropriate current good manufacturing practice requirements for such drugs.

“(B) CONSIDERATIONS AND CONSULTATION.—In establishing the procedures and requirements required by subparagraph (A), the Secretary of Health and Human Services shall take due account of any relevant differences between not-for-profit institutions that compound the drugs for their patients and commercial manufacturers of the drugs. Prior to establishing the procedures and requirements, the Secretary of Health and Human Services shall consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists licensed to make or use positron emission tomography drugs.

“(2) SUBMISSION OF NEW DRUG APPLICATIONS AND ABREVIATED NEW DRUG APPLICATIONS.—

“(A) IN GENERAL.—Except as provided in subparagraph (B), the Secretary of Health and Human Services shall not require the submission of new drug applications or abbreviated new drug applications under subsection (b) or (j) of section 505 (21 U.S.C. 355), for compounded positron emission tomography drugs that are not adulterated drugs described in section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) (as amended by subsection (b)), for a period of 4 years after the date of enactment of this Act [Nov. 21, 1997], or for 2 years after the date on which the Secretary establishes procedures and requirements under paragraph (1), whichever is longer.

“(B) EXCEPTION.—Nothing in this Act [see Short Title of 1997 Amendment note set out under section 301 of this title] shall prohibit the voluntary submission of such applications or the review of such applications by the Secretary of Health and Human Services. Nothing in this Act shall constitute an exemption for a positron emission tomography drug from the requirements of regulations issued under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)).”

“COMPOUNDED POSITRON EMISSION TOPOGRAPHY DRUG” DEFINED

Pub. L. 105–115, title I, §121(e), Nov. 21, 1997, 111 Stat. 2322, provided that: “As used in this section [amending sections 321 and 351 of this title and enacting provisions set out as notes under this section and section 351 of this title], the term ‘compounded positron emission tomography drug’ has the meaning given the term in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321).”

REQUIREMENTS FOR RADIOPHARMACEUTICALS

Pub. L. 105–115, title I, §122, Nov. 21, 1997, 111 Stat. 2322, provided that:

“(a) REQUIREMENTS.—

“(1) REGULATIONS.—

“(A) PROPOSED REGULATIONS.—Not later than 180 days after the date of enactment of this Act [Nov. 21, 1997], the Secretary of Health and Human Services, after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, shall issue proposed regulations governing the approval of radiopharmaceuticals. The regulations shall provide that the determination of the safety

and effectiveness of such a radiopharmaceutical under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) shall include consideration of the proposed use of the radiopharmaceutical in the practice of medicine, the pharmacological and toxicological activity of the radiopharmaceutical (including any carrier or ligand component of the radiopharmaceutical), and the estimated absorbed radiation dose of the radiopharmaceutical.

“(B) FINAL REGULATIONS.—Not later than 18 months after the date of enactment of this Act, the Secretary shall promulgate final regulations governing the approval of the radiopharmaceuticals.

“(2) SPECIAL RULE.—In the case of a radiopharmaceutical, the indications for which such radiopharmaceutical is approved for marketing may, in appropriate cases, refer to manifestations of disease (such as biochemical, physiological, anatomic, or pathological processes) common to, or present in, one or more disease states.

“(b) DEFINITION.—In this section, the term ‘radiopharmaceutical’ means—

“(1) an article—

“(A) that is intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans; and

“(B) that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

“(2) any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of any such article.”

#### SPECIAL RULE

Pub. L. 105–115, title I, §123(f), Nov. 21, 1997, 111 Stat. 2324, provided that: “The Secretary of Health and Human Services shall take measures to minimize differences in the review and approval of products required to have approved biologics license applications under section 351 of the Public Health Service Act (42 U.S.C. 262) and products required to have approved new drug applications under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)).”

#### TRANSITION

Pub. L. 110–379, §4(b), Oct. 8, 2008, 122 Stat. 4077, provided that:

“(1) With respect to a patent issued on or before the date of the enactment of this Act [Oct. 8, 2008], any patent information required to be filed with the Secretary of Health and Human Services under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) to be listed on a drug to which subsection (v)(1) of such section 505 (as added by this section) applies shall be filed with the Secretary not later than 60 days after the date of the enactment of this Act.

“(2) With respect to any patent information referred to in paragraph (1) of this subsection that is filed with the Secretary within the 60-day period after the date of the enactment of this Act [Oct. 8, 2008], the Secretary shall publish such information in the electronic version of the list referred to at section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) as soon as it is received, but in no event later than the date that is 90 days after the enactment of this Act.

“(3) With respect to any patent information referred to in paragraph (1) that is filed with the Secretary within the 60-day period after the date of enactment of this Act [Oct. 8, 2008], each applicant that, not later than 120 days after the date of the enactment of this Act, amends an application that is, on or before the date of the enactment of this Act, a substantially complete application (as defined in paragraph (5)(B)(iv) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j))) to contain a certification described in paragraph (2)(A)(vii)(IV) of such section 505(j)

with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j)).”

Pub. L. 105–115, title I, §125(d), Nov. 21, 1997, 111 Stat. 2326, provided that:

“(1) IN GENERAL.—An application that was approved by the Secretary of Health and Human Services before the date of the enactment of this Act [Nov. 21, 1997] for the marketing of an antibiotic drug under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as in effect on the day before the date of the enactment of this Act, shall, on and after such date of enactment, be considered to be an application that was submitted and filed under section 505(b) of such Act (21 U.S.C. 355(b)) and approved for safety and effectiveness under section 505(c) of such Act (21 U.S.C. 355(c)), except that if such application for marketing was in the form of an abbreviated application, the application shall be considered to have been filed and approved under section 505(j) of such Act (21 U.S.C. 355(j)).

“(2) EXCEPTION.—The following subsections of section 505 (21 U.S.C. 355) shall not apply to any application for marketing in which the drug that is the subject of the application contains an antibiotic drug and the antibiotic drug was the subject of any application for marketing received by the Secretary of Health and Human Services under section 507 of such Act (21 U.S.C. 357) before the date of the enactment of this Act [Nov. 21, 1997]:

“(A)(i) Subsections (c)(2), (d)(6), (e)(4), (j)(2)(A)(vii), (j)(2)(A)(viii), (j)(2)(B), (j)(4)(B), and (j)(4)(D); and

“(ii) The third and fourth sentences of subsection (b)(1) (regarding the filing and publication of patent information); and

“(B) Subsections (b)(2)(A), (b)(2)(B), (b)(3), and (c)(3) if the investigations relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

“(3) PUBLICATION.—For purposes of this section, the Secretary is authorized to make available to the public the established name of each antibiotic drug that was the subject of any application for marketing received by the Secretary for Health and Human Services under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357) before the date of enactment of this Act [Nov. 21, 1997].”

#### TERMINATION OF ADVISORY PANELS

Advisory panels established after Jan. 5, 1973, to terminate not later than the expiration of the 2-year period beginning on the date of their establishment, unless, in the case of a panel established by the President or an officer of the Federal Government, such panel is renewed by appropriate action prior to the expiration of such 2-year period, or in the case of a panel established by Congress, its duration is otherwise provided for by law. See sections 1001(2) and 1013 of Title 5, Government Organization and Employees.

#### APPEALS TAKEN PRIOR TO OCTOBER 10, 1962

Pub. L. 87–781, title I, §104(d)(3), Oct. 10, 1962, 76 Stat. 785, made amendments to subsec. (h) of this section inapplicable to any appeal taken prior to Oct. 10, 1962.

#### Executive Documents

#### TRANSFER OF FUNCTIONS

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

**§ 355-1. Risk evaluation and mitigation strategies****(a) Submission of proposed strategy****(1) Initial approval**

If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

(A) The estimated size of the population likely to use the drug involved.

(B) The seriousness of the disease or condition that is to be treated with the drug.

(C) The expected benefit of the drug with respect to such disease or condition.

(D) The expected or actual duration of treatment with the drug.

(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(F) Whether the drug is a new molecular entity.

**(2) Postapproval requirement****(A) In general**

If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices described in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

**(B) Submission of proposed strategy**

Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

**(3) Abbreviated new drug applications**

The applicability of this section to an application under section 355(j) of this title is subject to subsection (i).

**(4) Non-delegation**

Determinations by the Secretary under this subsection for a drug shall be made by individ-

uals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

**(b) Definitions**

For purposes of this section:

**(1) Adverse drug experience**

The term “adverse drug experience” means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

(A) an adverse event occurring in the course of the use of the drug in professional practice;

(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

(C) an adverse event occurring from abuse of the drug;

(D) an adverse event occurring from withdrawal of the drug; and

(E) any failure of expected pharmacological action of the drug, which may include reduced effectiveness under the conditions of use prescribed in the labeling of such drug, but which may not include reduced effectiveness that is in accordance with such labeling.

**(2) Covered application**

The term “covered application” means an application referred to in section 355(p)(1)(A) of this title.

**(3) New safety information**

The term “new safety information”, with respect to a drug, means information derived from a clinical trial, an adverse event report, a postapproval study (including a study under section 355(o)(3) of this title), or peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system under section 355(k) of this title; or other scientific data deemed appropriate by the Secretary about—

(A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of (that may be based on a new analysis of existing information) since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

**(4) Serious adverse drug experience**

The term “serious adverse drug experience” is an adverse drug experience that—

(A) results in—

(i) death;

(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);

(iii) inpatient hospitalization or prolongation of existing hospitalization;