

PRIOR PROVISIONS

A prior section 360a, act June 25, 1938, ch. 675, §511, as added July 15, 1965, Pub. L. 89-74, §3(b), 79 Stat. 227; amended Oct. 24, 1968, Pub. L. 90-639, §2(a), 82 Stat. 1361, regulated the manufacture, compounding, and processing of depressant and stimulant drugs and their sale, delivery, disposal, possession, and recordkeeping activities connected therewith, prior to repeal by Pub. L. 91-513, title II, §§701(a), 704, Oct. 27, 1970, 84 Stat. 1281, 1284, effective on the first day of the seventh calendar month that began after Oct. 26, 1970.

§ 360a-1. Clinical trials**(a) Review and revision of guidance documents****(1) In general**

The Secretary of Health and Human Services (referred to in this section as the “Secretary”) shall review and, as appropriate, revise not fewer than 3 guidance documents per year, which shall include—

(A) reviewing the guidance documents of the Food and Drug Administration for the conduct of clinical trials with respect to antibacterial and antifungal drugs; and

(B) as appropriate, revising such guidance documents to reflect developments in scientific and medical information and technology and to ensure clarity regarding the procedures and requirements for approval of antibacterial and antifungal drugs under chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.).

(2) Issues for review

At a minimum, the review under paragraph (1) shall address the appropriate animal models of infection, in vitro techniques, valid microbiological surrogate markers, the use of noninferiority versus superiority trials, trial enrollment, data requirements, and appropriate delta values for noninferiority trials.

(3) Rule of construction

Except to the extent to which the Secretary makes revisions under paragraph (1)(B), nothing in this section shall be construed to repeal or otherwise effect the guidance documents of the Food and Drug Administration.

(b) Recommendations for investigations**(1) Request**

The sponsor of a drug intended to be designated as a qualified infectious disease product may request that the Secretary provide written recommendations for nonclinical and clinical investigations which the Secretary believes may be necessary to be conducted with the drug before such drug may be approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) for use in treating, detecting, preventing, or identifying a qualifying pathogen, as defined in section 505E of such Act [21 U.S.C. 355f].

(2) Recommendations

If the Secretary has reason to believe that a drug for which a request is made under this subsection is a qualified infectious disease product, the Secretary shall provide the person making the request written recommendations for the nonclinical and clinical investigations which the Secretary believes, on the

basis of information available to the Secretary at the time of the request, would be necessary for approval under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) of such drug for the use described in paragraph (1).

(c) Qualified infectious disease product

For purposes of this section, the term “qualified infectious disease product” has the meaning given such term in section 505E(g) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355f(g)], as added by section 801 of this Act.

(Pub. L. 112-144, title VIII, §804, July 9, 2012, 126 Stat. 1080.)

REFERENCES IN TEXT

The Federal Food, Drug, and Cosmetic Act, referred to in subsec. (a)(1)(B), is act June 25, 1938, ch. 675, 52 Stat. 1040, which is classified generally to this chapter. Chapter V of the Act is classified generally to this subchapter. For complete classification of this Act to the Code, see section 301 of this title and Tables.

This Act, referred to in subsec. (c), is Pub. L. 112-144, July 9, 2012, 126 Stat. 993, known as the Food and Drug Administration Safety and Innovation Act. For complete classification of this Act to the Code, see Tables.

CODIFICATION

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

§ 360b. New animal drugs**(a) Unsafe new animal drugs and animal feed containing such drugs; conditions of safety; exemption of drugs for research; import tolerances**

(1) A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for purposes of section 351(a)(5) of this title and section 342(a)(2)(C)(ii) of this title unless—

(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such approved application;

(B) there is in effect a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such use or intended use of such drug, and such drug, its labeling, and such use conform to such conditionally approved application; or

(C) there is in effect an index listing pursuant to section 360ccc-1 of this title with respect to such use or intended use of such drug in a minor species, and such drug, its labeling, and such use conform to such index listing.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal

feed, such consignee (i) holds a license issued under subsection (m) of this section and has in its possession current approved labeling for such drug in animal feed; or (ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of a license issued under subsection (m) of this section.

(2) An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed be deemed unsafe for purposes of section 351(a)(6) of this title unless—

(A) there is in effect—

(i) an approval of an application filed pursuant to subsection (b) of this section with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such approved application;

(ii) a conditional approval of an application filed pursuant to section 360ccc of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such conditionally approved application; or

(iii) an index listing pursuant to section 360ccc-1 of this title with respect to such drug, as used in such animal feed, and such animal feed and its labeling, distribution, holding, and use conform to such index listing; and

(B) such animal feed is manufactured at a site for which there is in effect a license issued pursuant to subsection (m)(1) of this section to manufacture such animal feed.

(3) A new animal drug or an animal feed bearing or containing a new animal drug shall not be deemed unsafe for the purposes of section 351(a)(5) or (6) of this title if such article is for investigational use and conforms to the terms of an exemption in effect with respect thereto under subsection (j) of this section.

(4)(A) Except as provided in subparagraph (B), if an approval of an application filed under subsection (b) of this section is in effect with respect to a particular use or intended use of a new animal drug, the drug shall not be deemed unsafe for the purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a different use or intended use of the drug, other than a use in or on animal feed, if such use or intended use—

(i) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(ii) is in compliance with regulations promulgated by the Secretary that establish the conditions for such different use or intended use.

The regulations promulgated by the Secretary under clause (ii) may prohibit particular uses of an animal drug and shall not permit such different use of an animal drug if the labeling of another animal drug that contains the same active ingredient and which is in the same dosage form and concentration provides for such different use.

(B) If the Secretary finds that there is a reasonable probability that a use of an animal drug authorized under subparagraph (A) may present a risk to the public health, the Secretary may—

(i) establish a safe level for a residue of an animal drug when it is used for such different use authorized by subparagraph (A); and

(ii) require the development of a practical, analytical method for the detection of residues of such drug above the safe level established under clause (i).

The use of an animal drug that results in residues exceeding a safe level established under clause (i) shall be considered an unsafe use of such drug under paragraph (1). Safe levels may be established under clause (i) either by regulation or order.

(C) The Secretary may by general regulation provide access to the records of veterinarians to ascertain any use or intended use authorized under subparagraph (A) that the Secretary has determined may present a risk to the public health.

(D) If the Secretary finds, after affording an opportunity for public comment, that a use of an animal drug authorized under subparagraph (A) presents a risk to the public health or that an analytical method required under subparagraph (B) has not been developed and submitted to the Secretary, the Secretary may, by order, prohibit any such use.

(5) If the approval of an application filed under section 355 of this title is in effect, the drug under such application shall not be deemed unsafe for purposes of paragraph (1) and shall be exempt from the requirements of section 352(f) of this title with respect to a use or intended use of the drug in animals if such use or intended use—

(A) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

(B) is in compliance with regulations promulgated by the Secretary that establish the conditions for the use or intended use of the drug in animals.

(6) For purposes of section 342(a)(2)(D)¹ of this title, a use or intended use of a new animal drug shall not be deemed unsafe under this section if the Secretary establishes a tolerance for such drug and any edible portion of any animal imported into the United States does not contain residues exceeding such tolerance. In establishing such tolerance, the Secretary shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used by the Secretary to establish tolerances for applications for new animal drugs filed under subsection (b)(1) of this section. The Secretary may consider and rely on data submitted by the drug manufacturer, including data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used or data available from a relevant international organization, to the extent such data are not inconsistent with the criteria used by the Secretary to establish a tolerance for ap-

¹ See References in Text note below.

plications for new animal drugs filed under subsection (b)(1) of this section. For purposes of this paragraph, "relevant international organization" means the Codex Alimentarius² Commission or other international organization deemed appropriate by the Secretary. The Secretary may, under procedures specified by regulation, revoke a tolerance established under this paragraph if information demonstrates that the use of the new animal drug under actual use conditions results in food being imported into the United States with residues exceeding the tolerance or if scientific evidence shows the tolerance to be unsafe.

(b) Filing application for uses of new animal drug; contents; patent information; abbreviated application; presubmission conference

(1) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof, of any animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (G) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (H) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe. The applicant shall file with the application the patent number and the expiration date of any patent which claims the new animal drug for which the applicant filed the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

²So in original. Probably should be "Alimentarius".

(2) Any person may file with the Secretary an abbreviated application for the approval of a new animal drug. An abbreviated application shall contain the information required by subsection (n) of this section.

(3) Any person intending to file an application under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j) of this section shall be entitled to one or more conferences prior to such submission to reach an agreement acceptable to the Secretary establishing a submission or an investigational requirement, which may include a requirement for a field investigation. A decision establishing a submission or an investigational requirement shall bind the Secretary and the applicant or requestor unless (A) the Secretary and the applicant or requestor mutually agree to modify the requirement, or (B) the Secretary by written order determines that a substantiated scientific requirement essential to the determination of safety or effectiveness of the animal drug involved has appeared after the conference. No later than 25 calendar days after each such conference, the Secretary shall provide a written order setting forth a scientific justification specific to the animal drug and intended uses under consideration if the agreement referred to in the first sentence requires more than one field investigation as being essential to provide substantial evidence of effectiveness for the intended uses of the drug. Nothing in this paragraph shall be construed as compelling the Secretary to require a field investigation.

(c) Period for submission and approval of application; period for notice and expedition of hearing; period for issuance of order; abbreviated applications; withdrawal periods; effective date of approval; relationship to other applications; withdrawal or suspension of approval; bioequivalence; filing of additional patent information

(1) Within one hundred and eighty days after the filing of an application pursuant to subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either (A) issue an order approving the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for a hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2)(A) Subject to subparagraph (C), the Secretary shall approve an abbreviated application for a drug unless the Secretary finds—

(i) the methods used in, or the facilities and controls used for, the manufacture, process-

ing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(ii) the conditions of use prescribed, recommended, or suggested in the proposed labeling are not reasonably certain to be followed in practice or, except as provided in subparagraph (B), information submitted with the application is insufficient to show that each of the proposed conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i) of this section) have been previously approved for the approved new animal drug referred to in the application;

(iii) information submitted with the application is insufficient to show that the active ingredients are the same as those of the approved new animal drug referred to in the application;

(iv)(I) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug referred to in the application, information submitted in the application is insufficient to show that the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is the same as that of the approved new animal drug, or

(II) if the application is for a drug whose active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed is different from that of the approved new animal drug referred to in the application, no petition to file an application for the drug with the different active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed was approved under subsection (n)(3) of this section;

(v) if the application was filed pursuant to the approval of a petition under subsection (n)(3) of this section, the application did not contain the information required by the Secretary respecting the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which is not the same;

(vi) information submitted in the application is insufficient to show that the drug is bioequivalent to the approved new animal drug referred to in the application, or if the application is filed under a petition approved pursuant to subsection (n)(3) of this section, information submitted in the application is insufficient to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(vii) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the label-

ing approved for the approved new animal drug referred to in the application except for changes required because of differences approved under a petition filed under subsection (n)(3) of this section, because of a different withdrawal period, or because the drug and the approved new animal drug are produced or distributed by different manufacturers;

(viii) information submitted in the application or any other information available to the Secretary shows that (I) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, (II) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included, or (III) in the case of a drug for food producing animals, the inactive ingredients of the drug or its composition may be unsafe with respect to human food safety;

(ix) the approval under subsection (b)(1) of this section of the approved new animal drug referred to in the application filed under subsection (b)(2) of this section has been withdrawn or suspended for grounds described in paragraph (1) of subsection (e) of this section, the Secretary has published a notice of a hearing to withdraw approval of the approved new animal drug for such grounds, the approval under this paragraph of the new animal drug for which the application under subsection (b)(2) of this section was filed has been withdrawn or suspended under subparagraph (G) for such grounds, or the Secretary has determined that the approved new animal drug has been withdrawn from sale for safety or effectiveness reasons;

(x) the application does not meet any other requirement of subsection (n) of this section; or

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

(B) If the Secretary finds that a new animal drug for which an application is submitted under subsection (b)(2) of this section is bioequivalent to the approved new animal drug referred to in such application and that residues of the new animal drug are consistent with the tolerances established for such approved new animal drug but at a withdrawal period which is different than the withdrawal period approved for such approved new animal drug, the Secretary may establish, on the basis of information submitted, such different withdrawal period as the withdrawal period for the new animal drug for purposes of the approval of such application for such drug.

(C) Within 180 days of the initial receipt of an application under subsection (b)(2) of this section or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(D) The approval of an application filed under subsection (b)(2) of this section shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in clause (i) or (ii) of subsection

(n)(1)(G) of this section or in both such clauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in clause (iii) of subsection (n)(1)(G) of this section, the approval may be made effective on the date certified under clause (iii).

(iii) If the applicant made a certification described in clause (iv) of subsection (n)(1)(G) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of 45 days from the date the notice provided under subsection (n)(2)(B)(i) of this section is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the 30 month period beginning on the date of the receipt of the notice provided under subsection (n)(2)(B) of this section or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that if before the expiration of such period—

(I) the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or

(III) the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of 45 days from the date the notice made under subsection (n)(2)(B) of this section is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under section 2201 of title 28 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in clause (iv) of subsection (n)(1)(G) of this section and is for a drug for which a previous application has been filed under this subsection containing such a certification, the application shall be made effective not earlier than 180 days after—

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

(II) the date of a decision of a court in an action described in subclause (III)³ holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within 30 days after such notice, such hearing shall commence not more than 90 days after the expiration of such 30 days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within 90 days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application submitted under subsection (b)(1) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b)(1) of this section, is approved after November 16, 1988, no application may be submitted under subsection (b)(2) of this section which refers to the drug for which the subsection (b)(1) application was submitted before the expiration of 5 years from the date of the approval of the application under subsection (b)(1) of this section, except that such an application may be submitted under subsection (b)(2) of this section after the expiration of 4 years from the date of the approval of the subsection (b)(1) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (n)(1)(G) of this section. The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning 48 months after the date of the approval of the subsection (b) application, the 30 month period referred to in subparagraph (D)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(ii) If an application submitted under subsection (b)(1) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under such subsection, is approved after November 16, 1988, and if such application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b)(2) of this section for the conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of 3 years from the date of the approval of the application under subsection (b)(1) of this section for such drug.

(iii) If a supplement to an application approved under subsection (b)(1) of this section is approved after November 16, 1988, and the supplement contains substantial evidence of the effectiveness of the drug involved, any studies of

³ So in original. Probably should be "clause (iii)(III)".

animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b)(2) of this section for a change approved in the supplement effective before the expiration of 3 years from the date of the approval of the supplement.

(iv) An applicant under subsection (b)(1) of this section who comes within the provisions of clause (i) of this subparagraph as a result of an application which seeks approval for a use solely in non-food producing animals, may elect, within 10 days of receiving such approval, to waive clause (i) of this subparagraph, in which event the limitation on approval of applications submitted under subsection (b)(2) of this section set forth in clause (ii) of this subparagraph shall be applicable to the subsection (b)(1) application.

(v) If an application (including any supplement to a new animal drug application) submitted under subsection (b)(1) of this section for a new animal drug for a food-producing animal use, which includes an active ingredient (including any ester or salt of the active ingredient) which has been the subject of a waiver under clause (iv) is approved after November 16, 1988, and if the application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or human food safety studies (other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species) required for the new approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application (including any supplement to such application) submitted under subsection (b)(2) of this section for the new conditions of approval of such drug in the subsection (b)(1) application effective before the expiration of five years from the date of approval of the application under subsection (b)(1) of this section for such drug. The provisions of this paragraph shall apply only to the first approval for a food-producing animal use for the same applicant after the waiver under clause (iv).

(G) If an approved application submitted under subsection (b)(2) of this section for a new animal drug refers to a drug the approval of which was withdrawn or suspended for grounds described in paragraph (1) or (2) of subsection (e) of this section or was withdrawn or suspended under this subparagraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this paragraph shall be withdrawn or suspended—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or this subparagraph, or

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

(H) For purposes of this paragraph:

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

(ii) A new animal drug shall be considered to be bioequivalent to the approved new animal drug referred to in its application under subsection (n) of this section if—

(I) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses;

(II) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the approved new animal drug referred to in the application when administered at the same dose of the active ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the approved new animal drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective drug concentrations in use, and is considered scientifically insignificant for the drug in attaining the intended purposes of its use and preserving human food safety; or

(III) in any case in which the Secretary determines that the measurement of the rate and extent of absorption or excretion of the new animal drug in biological fluids is inappropriate or impractical, an appropriate acute pharmacological effects test or other test of the new animal drug and, when deemed scientifically necessary, of the approved new animal drug referred to in the application in the species to be tested or in an appropriate animal model does not show a significant difference between the new animal drug and such approved new animal drug when administered at the same dose under similar experimental conditions.

If the approved new animal drug referred to in the application for a new animal drug under subsection (n) of this section is approved for use in more than one animal species, the bioequivalency information described in subclauses (I), (II), and (III) shall be obtained for one species, or if the Secretary deems appropriate based on scientific principles, shall be obtained for more than one species. The Secretary may prescribe the dose to be used in determining bioequivalency under subclause (I), (II), or (III). To assure that the residues of the new animal drug will be consistent with the established tolerances for the approved new animal drug referred to in the application under subsection (b)(2) of this section upon the expiration of the withdrawal period contained in the application for the new animal drug, the Secretary shall require bioequivalency data or residue depletion studies of the new animal drug or such other data or studies as the Secretary considers appropriate based on

scientific principles. If the Secretary requires one or more residue studies under the preceding sentence, the Secretary may not require that the assay methodology used to determine the withdrawal period of the new animal drug be more rigorous than the methodology used to determine the withdrawal period for the approved new animal drug referred to in the application. If such studies are required and if the approved new animal drug, referred to in the application for the new animal drug for which such studies are required, is approved for use in more than one animal species, such studies shall be conducted for one species, or if the Secretary deems appropriate based on scientific principles, shall be conducted for more than one species.

(3) If the patent information described in subsection (b)(1) of this section could not be filed with the submission of an application under subsection (b)(1) of this section because the application was filed before the patent information was required under subsection (b)(1) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the new animal drug for which the application was filed or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b)(1) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than 30 days after November 16, 1988, and if the holder of an approved application could not file patent information under subsection (b)(1) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than 30 days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

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

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

(1) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that—

(A) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such

drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;

(B) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions;

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

(D) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions;

(E) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(F) upon the basis of information submitted to the Secretary as part of the application or any other information before the Secretary with respect to such drug, any use prescribed, recommended, or suggested in labeling proposed for such drug will result in a residue of such drug in excess of a tolerance found by the Secretary to be safe for such drug;

(G) the application failed to contain the patent information prescribed by subsection (b)(1) of this section;

(H) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; or

(I) such drug induces cancer when ingested by man or animal or, after tests which are appropriate for the evaluation of the safety of such drug, induces cancer in man or animal, except that the foregoing provisions of this subparagraph shall not apply with respect to such drug if the Secretary finds that, under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice (i) such drug will not adversely affect the animals for which it is intended, and (ii) no residue of such drug will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (c), (d), and (h) of this section), in any edible portion of such animals after slaughter or in any food yielded by or derived from the living animals;

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearings, the Secretary finds that subparagraphs (A) through (I) do not apply, he shall issue an order approving the application.

(2) In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) the probable consumption of such drug and of any substance formed in or on food because of the use of such

drug, (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substance, (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice. Any order issued under this subsection refusing to approve an application shall state the findings upon which it is based.

(3) As used in this section, the term "substantial evidence" means evidence consisting of one or more adequate and well controlled investigations, such as—

- (A) a study in a target species;
- (B) a study in laboratory animals;
- (C) any field investigation that may be required under this section and that meets the requirements of subsection (b)(3) of this section if a presubmission conference is requested by the applicant;
- (D) a bioequivalence study; or
- (E) an in vitro study;

by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(4) In a case in which an animal drug contains more than one active ingredient, or the labeling of the drug prescribes, recommends, or suggests use of the drug in combination with one or more other animal drugs, and the active ingredients or drugs intended for use in the combination have previously been separately approved pursuant to an application submitted under subsection (b)(1) of this section for particular uses and conditions of use for which they are intended for use in the combination—

(A) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on human food safety grounds unless the Secretary finds that the application fails to establish that—

(i) none of the active ingredients or drugs intended for use in the combination, respectively, at the longest withdrawal time of any of the active ingredients or drugs in the combination, respectively, exceeds its established tolerance; or

(ii) none of the active ingredients or drugs in the combination interferes with the methods of analysis for another of the active ingredients or drugs in the combination, respectively;

(B) the Secretary shall not issue an order under paragraph (1)(A), (1)(B), or (1)(D) refusing to approve the application for such combination on target animal safety grounds unless the Secretary finds that—

(i)(I) there is a substantiated scientific issue, specific to one or more of the active

ingredients or animal drugs in the combination, that cannot adequately be evaluated based on information contained in the application for the combination (including any investigations, studies, or tests for which the applicant has a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted); or

(II) there is a scientific issue raised by target animal observations contained in studies submitted to the Secretary as part of the application; and

(ii) based on the Secretary's evaluation of the information contained in the application with respect to the issues identified in clauses (i)(I) and (II), paragraph (1)(A), (B), or (D) apply;

(C) except in the case of a combination that contains a nontopical antibacterial ingredient or animal drug, the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use other than in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

(i) there is substantial evidence that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to labeled effectiveness;

(ii) each active ingredient or animal drug intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population; or

(iii) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs may be physically incompatible or have disparate dosing regimens, such active ingredients or animal drugs are physically compatible or do not have disparate dosing regimens; and

(D) the Secretary shall not issue an order under paragraph (1)(E) refusing to approve an application for a combination animal drug intended for use in animal feed or drinking water unless the Secretary finds that the application fails to demonstrate that—

(i) there is substantial evidence that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to the labeled effectiveness;

(ii) each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population;

(iii) where a combination contains more than one nontopical antibacterial ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial ingredients or animal drugs makes a contribution to the labeled effectiveness, except that

for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs; or

(iv) where based on scientific information the Secretary has reason to believe the active ingredients or animal drugs intended for use in drinking water may be physically incompatible, such active ingredients or animal drugs intended for use in drinking water are physically compatible.

(5) In reviewing an application that proposes a change to add an intended use for a minor use or a minor species to an approved new animal drug application, the Secretary shall reevaluate only the relevant information in the approved application to determine whether the application for the minor use or minor species can be approved. A decision to approve the application for the minor use or minor species is not, implicitly or explicitly, a reaffirmation of the approval of the original application.

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

(1) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application filed pursuant to subsection (b) of this section with respect to any new animal drug if the Secretary finds—

(A) that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved or the condition of use authorized under subsection (a)(4)(A) of this section;

(B) that new evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved or that subparagraph (I) of paragraph (1) of subsection (d) of this section applies to such drug;

(C) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(D) the patent information prescribed by subsection (c)(3) of this section was not filed within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information;

(E) that the application contains any untrue statement of a material fact; or

(F) that the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the ap-

plication by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application. The supplemental application shall be treated in the same manner as the original application.

If the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the health of man or of the animals for which such drug is intended, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence to suspend the approval of an application shall not be delegated.

(2) The Secretary may also, after due notice and opportunity for hearing to the applicant, issue an order withdrawing the approval of an application with respect to any new animal drug under this section if the Secretary finds—

(A) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under subsection (1) of this section, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection;

(B) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(C) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(3) Any order under this subsection shall state the findings upon which it is based.

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

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d), (e), or (m) of this section, or section 360ccc(c), (d), or (e) of this title refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section, or section 360ccc of this title (other than orders issuing, amending, or repealing regulations) shall be served (1) in person by any officer or employee of the department designated by

the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application filed under subsection (b) or (m) of this section. The provisions of subsection (h) of section 355 of this title shall govern any such appeal.

(i) Publication in Federal Register; effective date and revocation or suspension of regulation

When a new animal drug application filed pursuant to subsection (b) of this section or section 360ccc of this title is approved, the Secretary shall by notice, which upon publication shall be effective as a regulation, publish in the Federal Register the name and address of the applicant and the conditions and indications of use of the new animal drug covered by such application, including any tolerance and withdrawal period or other use restrictions and, if such new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian) applicable to any animal feed for use in which such drug is approved, and such other information, upon the basis of which such application was approved, as the Secretary deems necessary to assure the safe and effective use of such drug. Upon withdrawal of approval of such new animal drug application or upon its suspension or upon failure to renew a conditional approval under section 360ccc of this title, the Secretary shall forthwith revoke or suspend, as the case may be, the regulation published pursuant to this subsection (i) insofar as it is based on the approval of such application.

(j) Exemption of drugs for research; discretionary and mandatory conditions

To the extent consistent with the public health, the Secretary shall promulgate regulations for exempting from the operation of this section new animal drugs, and animal feeds bearing or containing new animal drugs, intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of animal drugs. Such regulations may, in the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such article, of data (including but not limited to analytical reports by investigators) obtained as a result of such investigational use of such article, as the Secretary finds will enable him to evaluate the safety and effectiveness of such article in the event of the filing of an application pursuant to this section. Such regulations, among other things, shall set forth the conditions (if any) upon which animals treated with such articles, and any products of

such animals (before or after slaughter), may be marketed for food use.

(k) Food containing new animal drug considered unadulterated while approval of application for such drug is effective

While approval of an application for a new animal drug is effective, a food shall not, by reason of bearing or containing such drug or any substance formed in or on the food because of its use in accordance with such application (including the conditions and indications of use prescribed pursuant to subsection (i) of this section), be considered adulterated within the meaning of clause (1) of section 342(a) of this title.

(l) Records and reports; required information; regulations and orders; examination of data; access to records

(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) of this section or section 360ccc of this title is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A) of this section, and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

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

(3)(A) In the case of each new animal drug described in paragraph (1) that contains an antimicrobial active ingredient, the sponsor of the drug shall submit an annual report to the Secretary on the amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals, including information on any distributor-labeled product.

(B) Each report under this paragraph shall specify the amount of each antimicrobial active ingredient—

(i) by container size, strength, and dosage form;

(ii) by quantities distributed domestically and quantities exported; and

(iii) by dosage form, including, for each such dosage form, a listing of the target animals, indications, and production classes that are specified on the approved label of the product.

(C) Each report under this paragraph shall—

- (i) be submitted not later than March 31 each year;
- (ii) cover the period of the preceding calendar year; and
- (iii) include separate information for each month of such calendar year.

(D) The Secretary may share information reported under this paragraph with the Antimicrobial Resistance Task Force established under section 247d-5 of title 42.

(E) The Secretary shall make summaries of the information reported under this paragraph publicly available, except that—

- (i) the summary data shall be reported by antimicrobial class, and no class with fewer than 3 distinct sponsors of approved applications shall be independently reported; and
- (ii) the data shall be reported in a manner consistent with protecting both national security and confidential business information.

(m) Feed mill licenses

(1) Any person may file with the Secretary an application for a license to manufacture animal feeds bearing or containing new animal drugs. Such person shall submit to the Secretary as part of the application (A) a full statement of the business name and address of the specific facility at which the manufacturing is to take place and the facility's registration number, (B) the name and signature of the responsible individual or individuals for that facility, (C) a certification that the animal feeds bearing or containing new animal drugs are manufactured and labeled in accordance with the applicable regulations published pursuant to subsection (i) of this section or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc-1(e)(2) of this title and the labeling requirements set forth in section 360ccc-1(h) of this title, and (D) a certification that the methods used in, and the facilities and controls used for, manufacturing, processing, packaging, and holding such animal feeds are in conformity with current good manufacturing practice as described in section 351(a)(2)(B) of this title.

(2) Within 90 days after the filing of an application pursuant to paragraph (1), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall (A) issue an order approving the application if the Secretary then finds that none of the grounds for denying approval specified in paragraph (3) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under paragraph (3) on the question whether such application is approvable. The procedure governing such a hearing shall be the procedure set forth in the last two sentences of subsection (c)(1) of this section.

(3) If the Secretary, after due notice to the applicant in accordance with paragraph (2) and giving the applicant an opportunity for a hearing in accordance with such paragraph, finds, on the basis of information submitted to the Secretary as part of the application, on the basis of a preapproval inspection, or on the basis of any other information before the Secretary—

- (A) that the application is incomplete, false, or misleading in any particular;

- (B) that the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed are inadequate to preserve the identity, strength, quality, and purity of the new animal drug therein; or

- (C) that the facility manufactures animal feeds bearing or containing new animal drugs in a manner that does not accord with the specifications for manufacture or labels animal feeds bearing or containing new animal drugs in a manner that does not accord with the conditions or indications of use that are published pursuant to subsection (i) of this section or an index listing pursuant to section 360ccc-1(e) of this title,

the Secretary shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (C) do not apply, the Secretary shall issue an order approving the application. An order under this subsection approving an application for a license to manufacture animal feeds bearing or containing new animal drugs shall permit a facility to manufacture only those animal feeds bearing or containing new animal drugs for which there are in effect regulations pursuant to subsection (i) of this section or an index listing pursuant to section 360ccc-1(e) of this title relating to the use of such drugs in or on such animal feed.

(4)(A) The Secretary shall, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feeds bearing or containing new animal drugs under this subsection if the Secretary finds—

- (i) that the application for such license contains any untrue statement of a material fact; or
- (ii) that the applicant has made changes that would cause the application to contain any untrue statements of material fact or that would affect the safety or effectiveness of the animal feeds manufactured at the facility unless the applicant has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application.

If the Secretary (or in the Secretary's absence the officer acting as the Secretary) finds that there is an imminent hazard to the health of humans or of the animals for which such animal feed is intended, the Secretary may suspend the license immediately, and give the applicant prompt notice of the action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence shall not be delegated.

(B) The Secretary may also, after due notice and opportunity for hearing to the applicant, revoke a license to manufacture animal feed under this subsection if the Secretary finds—

- (i) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under paragraph (5)(A) of this subsection or section 354(a)(3)(A) of this title, or the applicant has

refused to permit access to, or copying or verification of, such records as required by subparagraph (B) of such paragraph or section 354(a)(3)(B) of this title;

(ii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the methods used in, or the facilities and controls used for, the manufacture, processing, packing, and holding of such animal feed are inadequate to assure and preserve the identity, strength, quality, and purity of the new animal drug therein, and were not made adequate within a reasonable time after receipt of written notice from the Secretary, specifying the matter complained of;

(iii) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the labeling of any animal feeds, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(iv) that on the basis of new information before the Secretary, evaluated together with the evidence before the Secretary when such license was issued, the facility has manufactured, processed, packed, or held animal feed bearing or containing a new animal drug adulterated under section 351(a)(6) of this title and the facility did not discontinue the manufacture, processing, packing, or holding of such animal feed within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(C) The Secretary may also revoke a license to manufacture animal feeds under this subsection if an applicant gives notice to the Secretary of intention to discontinue the manufacture of all animal feed covered under this subsection and waives an opportunity for a hearing on the matter.

(D) Any order under this paragraph shall state the findings upon which it is based.

(5) When a license to manufacture animal feeds bearing or containing new animal drugs has been issued—

(A) the applicant shall establish and maintain such records, and make such reports to the Secretary, or (at the option of the Secretary) to the appropriate person or persons holding an approved application filed under subsection (b) of this section, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section or paragraph (4); and

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

(6) To the extent consistent with the public health, the Secretary may promulgate regulations for exempting from the operation of this subsection facilities that manufacture, process, pack, or hold animal feeds bearing or containing new animal drugs.

(n) Abbreviated applications for new animal drugs; contents, filing, etc.; lists of approved drugs

(1) An abbreviated application for a new animal drug shall contain—

(A)(i) except as provided in clause (ii), information to show that the conditions of use or similar limitations (whether in the labeling or published pursuant to subsection (i) of this section) prescribed, recommended, or suggested in the labeling proposed for the new animal drug have been previously approved for a new animal drug listed under paragraph (4) (hereinafter in this subsection referred to as an “approved new animal drug”), and

(ii) information to show that the withdrawal period at which residues of the new animal drug will be consistent with the tolerances established for the approved new animal drug is the same as the withdrawal period previously established for the approved new animal drug or, if the withdrawal period is proposed to be different, information showing that the residues of the new animal drug at the proposed different withdrawal period will be consistent with the tolerances established for the approved new animal drug;

(B)(i) information to show that the active ingredients of the new animal drug are the same as those of the approved new animal drug, and

(ii) if the approved new animal drug has more than one active ingredient, and if one of the active ingredients of the new animal drug is different from one of the active ingredients of the approved new animal drug and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show that the other active ingredients of the new animal drug are the same as the active ingredients of the approved new animal drug,

(II) information to show either that the different active ingredient is an active ingredient of another approved new animal drug or of an animal drug which does not meet the requirements of section 321(v) of this title, and

(III) such other information respecting the different active ingredients as the Secretary may require;

(C)(i) if the approved new animal drug is permitted to be used with one or more animal drugs in animal feed, information to show that the proposed uses of the new animal drug with other animal drugs in animal feed are the same as the uses of the approved new animal drug, and

(ii) if the approved new animal drug is permitted to be used with one or more other animal drugs in animal feed, and one of the other animal drugs proposed for use with the new animal drug in animal feed is different from one of the other animal drugs permitted to be

used in animal feed with the approved new animal drug, and the application is filed pursuant to the approval of a petition filed under paragraph (3)—

(I) information to show either that the different animal drug proposed for use with the approved new animal drug in animal feed is an approved new animal drug permitted to be used in animal feed or does not meet the requirements of section 321(v) of this title when used with another animal drug in animal feed,

(II) information to show that other animal drugs proposed for use with the new animal drug in animal feed are the same as the other animal drugs permitted to be used with the approved new animal drug, and

(III) such other information respecting the different animal drug or combination with respect to which the petition was filed as the Secretary may require,

(D) information to show that the route of administration, the dosage form, and the strength of the new animal drug are the same as those of the approved new animal drug or, if the route of administration, the dosage form, or the strength of the new animal drug is different and the application is filed pursuant to the approval of a petition filed under paragraph (3), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(E) information to show that the new animal drug is bioequivalent to the approved new animal drug, except that if the application is filed pursuant to the approval of a petition filed under paragraph (3) for the purposes described in subparagraph (B) or (C), information to show that the active ingredients of the new animal drug are of the same pharmacological or therapeutic class as the pharmacological or therapeutic class of the approved new animal drug and that the new animal drug can be expected to have the same therapeutic effect as the approved new animal drug when used in accordance with the labeling;

(F) information to show that the labeling proposed for the new animal drug is the same as the labeling approved for the approved new animal drug except for changes required because of differences approved under a petition filed under paragraph (3), because of a different withdrawal period, or because the new animal drug and the approved new animal drug are produced or distributed by different manufacturers;

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

(H) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the approved new animal drug or which claims a use for such approved new animal drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b)(1) or (c)(3) of this section—

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

(ii) that such patent has expired,

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

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

(I) if with respect to the approved new animal drug information was filed under subsection (b)(1) or (c)(3) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval of an application under subsection (c)(2) of this section, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by subparagraphs (A) through (I).

(2)(A) An applicant who makes a certification described in paragraph (1)(G)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to—

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (c)(1) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application, which contains data from bioequivalence studies, has been filed under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (1)(G)(iv), the notice required by subparagraph (B) shall be given when the amended application is filed.

(3) If a person wants to submit an abbreviated application for a new animal drug—

(A) whose active ingredients, route of administration, dosage form, or strength differ from that of an approved new animal drug, or

(B) whose use with other animal drugs in animal feed differs from that of an approved new animal drug,

such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve a petition for a new animal drug unless the Secretary finds that—

(C) investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which differ from the approved new animal drug, or

(D) investigations must be conducted to show the safety for human consumption of any residues in food resulting from the proposed active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed for the new animal drug which is different from the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug.

The Secretary shall approve or disapprove a petition submitted under this paragraph within 90 days of the date the petition is submitted.

(4)(A)(i) Within 60 days of November 16, 1988, the Secretary shall publish and make available to the public a list in alphabetical order of the official and proprietary name of each new animal drug which has been approved for safety and effectiveness before November 16, 1988.

(ii) Every 30 days after the publication of the first list under clause (i) the Secretary shall revise the list to include each new animal drug which has been approved for safety and effectiveness under subsection (c) of this section during the 30 day period.

(iii) When patent information submitted under subsection (b)(1) or (c)(3) of this section respecting a new animal drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A new animal drug approved for safety and effectiveness before November 16, 1988, or approved for safety and effectiveness under subsection (c) of this section shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or November 16, 1988, whichever is later.

(C) If the approval of a new animal drug was withdrawn or suspended under subsection (c)(2)(G) of this section or for grounds described in subsection (e) of this section or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (c)(2)(G) or (e) of this section, or

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

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

(5) If an application contains the information required by clauses (A), (G), and (H) of subsection (b)(1) of this section and such information—

(A) is relied on by the applicant for the approval of the application, and

(B) is not information derived either from investigations, studies, or tests conducted by or for the applicant or for which the applicant

had obtained a right of reference or use from the person by or for whom the investigations, studies, or tests were conducted,

such application shall be considered to be an application filed under subsection (b)(2) of this section.

(o) "Patent" defined

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

(p) Safety and effectiveness data

(1) Safety and effectiveness data and information which has been submitted in an application filed under subsection (b)(1) of this section or section 360ccc(a) of this title for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

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

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

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

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

(E) upon the effective date of the approval of the first application filed under subsection (b)(2) of this section which refers to such drug or upon the date upon which the approval of an application filed under subsection (b)(2) of this section which refers to such drug could be made effective if such an application had been filed.

(2) Any request for data and information pursuant to paragraph (1) shall include a verified statement by the person making the request that any data or information received under such paragraph shall not be disclosed by such person to any other person—

(A) for the purpose of, or as part of a plan, scheme, or device for, obtaining the right to make, use, or market, or making, using, or marketing, outside the United States, the drug identified in the application filed under subsection (b)(1) of this section or section 360ccc(a) of this title, and

(B) without obtaining from any person to whom the data and information are disclosed an identical verified statement, a copy of which is to be provided by such person to the Secretary, which meets the requirements of this paragraph.

(June 25, 1938, ch. 675, §512, as added Pub. L. 90-399, §101(b), July 13, 1968, 82 Stat. 343; amended Pub. L. 100-670, title I, §§101, 102, 104, 107(a)(2), Nov. 16, 1988, 102 Stat. 3971, 3981, 3982, 3984; Pub. L. 102-108, §2(e), Aug. 17, 1991, 105 Stat. 550; Pub. L. 103-80, §3(r), Aug. 13, 1993, 107 Stat. 777; Pub. L. 103-396, §2(a), (b)(2), (3), Oct. 22, 1994, 108 Stat. 4153, 4154; Pub. L. 104-250, §§2(a)-(d), 3, 4, 5(c), 6(a), (b), Oct. 9, 1996, 110 Stat. 3151-3153, 3155-3157; Pub. L. 105-115, title I, §124(b), Nov. 21, 1997, 111 Stat. 2325; Pub. L. 105-277, div. A, §101(a) [title VII, §737], Oct. 21, 1998, 112 Stat. 2681, 2681-30;

Pub. L. 106-113, div. B, §1000(a)(9) [title IV, §4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A-584; Pub. L. 108-282, title I, §102(b)(2), (3), (5)(I)-(S), Aug. 2, 2004, 118 Stat. 892, 903, 904; Pub. L. 110-316, title I, §105(a), Aug. 14, 2008, 122 Stat. 3513.)

REFERENCES IN TEXT

Section 342(a)(2) of this title, referred to in subsec. (a)(6), was amended by Pub. L. 104-170, title IV, §404, Aug. 3, 1996, 110 Stat. 1514, and, as so amended, no longer contains a subcl. (D). See section 342(a)(2)(C)(ii) of this title.

AMENDMENTS

2008—Subsec. (l)(3). Pub. L. 110-316 added par. (3).

2004—Subsec. (a)(1), (2). Pub. L. 108-282, §102(b)(5)(I), added pars. (1) and (2) and struck out former pars. (1) and (2) which deemed as unsafe new animal drugs and animal feed bearing or containing a new animal drug which did not have in effect certain approvals.

Subsec. (b)(3). Pub. L. 108-282, §102(b)(5)(J), substituted “under paragraph (1), section 360ccc of this title, or a request for an investigational exemption under subsection (j)” for “under paragraph (1) or a request for an investigational exemption under subsection (j)”.

Subsec. (c)(2)(F)(ii), (iii), (v). Pub. L. 108-282, §102(b)(2), substituted “(other than bioequivalence studies or residue depletion studies, except residue depletion studies for minor uses or minor species)” for “(other than bioequivalence or residue studies)”.

Subsec. (d)(4). Pub. L. 108-282, §102(b)(5)(K), substituted “have previously been separately approved pursuant to an application submitted under subsection (b)(1) of this section” for “have previously been separately approved” in introductory provisions.

Subsec. (d)(5). Pub. L. 108-282, §102(b)(3), added par. (5).

Subsec. (f). Pub. L. 108-282, §102(b)(5)(L), substituted “subsection (d), (e), or (m) of this section, or section 360ccc(c), (d), or (e) of this title” for “subsection (d), (e), or (m) of this section”.

Subsec. (g). Pub. L. 108-282, §102(b)(5)(M), substituted “this section, or section 360ccc of this title” for “this section”.

Subsec. (i). Pub. L. 108-282, §102(b)(5)(N), substituted “subsection (b) of this section or section 360ccc of this title” for “subsection (b) of this section” and inserted “or upon failure to renew a conditional approval under section 360ccc of this title” after “or upon its suspension”.

Subsec. (l)(1). Pub. L. 108-282, §102(b)(5)(O), substituted “subsection (b) of this section or section 360ccc of this title” for “subsection (b) of this section”.

Subsec. (m)(1)(C). Pub. L. 108-282, §102(b)(5)(P), substituted “applicable regulations published pursuant to subsection (i) of this section or for indexed new animal drugs in accordance with the index listing published pursuant to section 360ccc-1(e)(2) of this title and the labeling requirements set forth in section 360ccc-1(h) of this title” for “applicable regulations published pursuant to subsection (i) of this section”.

Subsec. (m)(3). Pub. L. 108-282, §102(b)(5)(Q), inserted “or an index listing pursuant to section 360ccc-1(e) of this title” after “subsection (i) of this section” in subpar. (C) and concluding provisions.

Subsec. (p)(1), (2)(A). Pub. L. 108-282, §102(b)(5)(R), (S), substituted “subsection (b)(1) of this section or section 360ccc(a) of this title” for “subsection (b)(1) of this section”.

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

1998—Subsec. (d)(4)(D)(iii). Pub. L. 105-277 inserted before semicolon “, except that for purposes of this clause, antibacterial ingredient or animal drug does not include the ionophore or arsenical classes of animal drugs”.

1997—Subsec. (c)(4). Pub. L. 105-115 added par. (4).

1996—Subsec. (a)(1). Pub. L. 104-250, §6(a), amended par. (1) generally. Prior to amendment, par. (1) read as follows: “A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for the purposes of section 351(a)(5) and section 342(a)(2)(D) of this title unless—

“(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug, and

“(B) such drug, its labeling, and such use conform to such approved application.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee—

“(i) is the holder of an approved application under subsection (m) of this section; or

“(ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved application under subsection (m) of this section.”

Subsec. (a)(2). Pub. L. 104-250, §6(a), amended par. (2) generally. Prior to amendment, par. (2) read as follows: “An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal feed, be deemed unsafe for the purposes of section 351(a)(6) of this title unless—

“(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such drugs, as used in such animal feed,

“(B) there is in effect an approval of an application pursuant to subsection (m)(1) of this section with respect to such animal feed, and

“(C) such animal feed, its labeling, and such use conform to the conditions and indications of use published pursuant to subsection (i) of this section and to the application with respect thereto approved under subsection (m) of this section.”

Subsec. (a)(6). Pub. L. 104-250, §4, added par. (6).

Subsec. (b)(3). Pub. L. 104-250, §2(d), added par. (3).

Subsec. (c)(2)(F)(ii), (iii). Pub. L. 104-250, §2(b)(1), substituted “substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or,” for “reports of new clinical or field investigations (other than bioequivalence or residue studies) and,” and “required for the approval” for “essential to the approval”.

Subsec. (c)(2)(F)(v). Pub. L. 104-250, §2(b)(2), substituted “clause (iv)” for “subparagraph (B)(iv)” in two places, “substantial evidence of the effectiveness of the drug involved, any studies of animal safety,” for “reports of clinical or field investigations” and “required for the new approval” for “essential to the new approval”.

Subsec. (d)(1)(F). Pub. L. 104-250, §3, amended subpar. (F) generally. Prior to amendment, subpar. (F) read as follows: “upon the basis of the information submitted to him as part of the application or any other information before him with respect to such drug, the tolerance limitation proposed, if any, exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended.”

Subsec. (d)(3). Pub. L. 104-250, §2(a), amended par. (3) generally. Prior to amendment, par. (3) read as follows: “As used in this subsection and subsection (e) of this section, the term ‘substantial evidence’ means evidence consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.”

Subsec. (d)(4). Pub. L. 104-250, §2(c), added par. (4).

Subsec. (i). Pub. L. 104-250, §5(c), inserted “and any requirement that an animal feed bearing or containing the new animal drug be limited to use under the professional supervision of a licensed veterinarian” after “(including special labeling requirements”.

Subsec. (m). Pub. L. 104-250, §6(b), amended subsec. (m) generally, substituting provisions relating to application for feed mill licenses, including approval, refusal, revocation, and suspension of such licenses, and provisions for record and reporting requirements for, as well as exemption from, such licenses, for provisions relating to application for uses of animal feed containing new animal drug, including required contents, approval, refusal, and withdrawal of approval or suspension of such usage applications, and provisions for record and reporting requirements of such usage applications.

1994—Subsec. (a)(4), (5). Pub. L. 103-396, §2(a), added pars. (4) and (5).

Subsec. (e)(1)(A). Pub. L. 103-396, §2(b)(2), inserted before semicolon at end “or the condition of use authorized under subsection (a)(4)(A) of this section”.

Subsec. (l)(1). Pub. L. 103-396, §2(b)(3), substituted “relating to experience, including experience with uses authorized under subsection (a)(4)(A) of this section,” for “relating to experience”.

1993—Subsec. (c)(2)(A)(ii). Pub. L. 103-80, §3(r)(1), inserted “in” after “except as provided”.

Subsec. (c)(2)(F)(i). Pub. L. 103-80, §3(r)(2), substituted “subparagraph (D)(iii)” for “subparagraph (C)(iii)”.

Subsec. (c)(2)(H)(ii). Pub. L. 103-80, §3(r)(3), substituted “subclauses” for “subclause” after “bioequivalency information described in” in concluding provisions.

Subsec. (d)(1). Pub. L. 103-80, §3(r)(4), substituted “subparagraphs (A) through (I)” for “subparagraphs (A) through (G)” in concluding provisions.

Subsec. (n)(1). Pub. L. 103-80, §3(r)(5), substituted “section 321(v) of this title” for “section 321(w) of this title” in subpars. (B)(ii)(II) and (C)(ii)(I) and substituted “through (I)” for “through (H)” in concluding provisions.

1991—Subsec. (e)(1)(B). Pub. L. 102-108 substituted “(I)” for “(H)”.

1988—Subsec. (a)(1)(C). Pub. L. 100-670, §107(a)(2), struck out subpar. (C) which read as follows: “in the case of a new animal drug subject to subsection (n) of this section and not exempted therefrom by regulations it is from a batch with respect to which a certificate or release issued pursuant to subsection (n) of this section is in effect with respect to such drug.”

Subsec. (b). Pub. L. 100-670, §§101(a), 102(a), designated existing provisions as par. (1), redesignated cls. (1) to (8) as cls. (A) to (H), respectively, added par. (2), and inserted provisions at end of par. (1) which require applicant to file with application, patent number and expiration date of any patent which claims new animal drug, to amend application to include such information if patent which claims such drug or method of using such drug is issued after filing date but before approval of application, and to publish such information upon approval.

Subsec. (c). Pub. L. 100-670, §§101(c), 102(b)(1), designated existing provisions as par. (1), redesignated cls. (1) and (2) as cls. (A) and (B), respectively, and added pars. (2) and (3).

Subsec. (d)(1). Pub. L. 100-670, §102(b)(3), substituted “(G)” for “(H)” in last sentence.

Subsec. (d)(1)(G) to (I). Pub. L. 100-670, §102(b)(2), added subpar. (G) and redesignated former subpars. (G) and (H) as (H) and (I), respectively.

Subsec. (e)(1)(D) to (F). Pub. L. 100-670, §102(b)(4), added subpar. (D) and redesignated former subpars. (D) and (E) as (E) and (F), respectively.

Subsecs. (n) to (p). Pub. L. 100-670, §101(b), added subsecs. (n) to (p) and struck out former subsec. (n) which related to certification of new drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, and release prior to certification.

EFFECTIVE DATE OF 1999 AMENDMENT

Amendment by Pub. L. 106-113 effective 4 months after Nov. 29, 1999, see section 1000(a)(9) [title IV, §4731] of Pub. L. 106-113, set out as a note under section 1 of Title 35, Patents.

EFFECTIVE DATE OF 1997 AMENDMENT

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

EFFECTIVE DATE OF 1994 AMENDMENT

Pub. L. 103-396, §2(d), Oct. 22, 1994, 108 Stat. 4154, provided that: “The amendments made by this section [amending this section and section 331 of this title] shall take effect upon the adoption of the final regulations under subsection (c) [set out below].” [Final regulations were dated Oct. 22, 1996, filed Nov. 6, 1996, published Nov. 7, 1996, 61 F.R. 57732, and effective Dec. 9, 1996.]

EFFECTIVE DATE OF 1988 AMENDMENT

Pub. L. 100-670, title I, §108, Nov. 16, 1988, 102 Stat. 3984, provided that: “The Secretary of Health and Human Services may not make an approval of an application submitted under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(b)(2)) effective before January 1, 1991.”

EFFECTIVE DATE AND TRANSITIONAL PROVISIONS

Pub. L. 90-399, §108, July 13, 1968, 82 Stat. 353, as amended by Pub. L. 108-282, title I, §102(b)(5)(T), Aug. 2, 2004, 118 Stat. 905, provided that:

“(a) Except as otherwise provided in this section, the amendments made by the foregoing sections [see Short Title of 1968 Amendment note set out under section 301 of this title] shall take effect on the first day of the thirteenth calendar month which begins after the date of enactment of this Act [July 13, 1968].

“(b)(1) As used in this subsection, the term ‘effective date’ means the effective date specified in subsection (a) of this section; the term ‘basic Act’ means the Federal Food, Drug, and Cosmetic Act [this chapter]; and other terms used both in this section and the basic Act shall have the same meaning as they have, or had, at the time referred to in the context, under the basic Act.

“(2) Any approval, prior to the effective date, of a new animal drug or of an animal feed bearing or containing a new animal drug, whether granted by approval of a new-drug application, master file, antibiotic regulation, or food additive regulations, shall continue in effect, and shall be subject to change in accordance with the provisions of the basic Act as amended by this Act [see Short Title of 1968 Amendment note set out under section 301 of this title].

“(3) In the case of any drug (other than a drug subject to section 512(n) of the basic Act as amended by this Act) [subsection (n) of this section] intended for use in animals other than man which, on October 9, 1962, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act [section 321(p) of this title] as then in force, and (C) was not covered by an effective application under section 505 of that Act [section 355 of this title], the words ‘effectiveness’ and ‘effective’ contained in section 201(v) to the basic Act [sic] [section 321(v) of this title] shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

“(4) Regulations providing for fees (and advance deposits to cover fees) which on the day preceding the effective date applicable under subsection (a) of this section were in effect pursuant to section 507 of the basic Act [section 357 of this title] shall, except as the Secretary may otherwise prescribe, be deemed to apply

also under section 512(n) of the basic Act [subsection (n) of this section], and appropriations of fees (and of advance deposits to cover fees) available for the purposes specified in such section 507 [section 357 of this title] as in effect prior to the effective date shall also be available for the purposes specified in section 512(n) [subsection (n) of this section], including preparatory work or proceedings prior to that date.”

REGULATIONS

Pub. L. 104-250, §2(e), Oct. 9, 1996, 110 Stat. 3154, provided that:

“(1) IN GENERAL.—Not later than 6 months after the date of enactment of this Act [Oct. 9, 1996], the Secretary of Health and Human Services shall issue proposed regulations implementing the amendments made by this Act as described in paragraph (2)(A) of this subsection, and not later than 18 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments. Not later than 12 months after the date of enactment of this Act, the Secretary shall issue proposed regulations implementing the other amendments made by this Act as described in paragraphs (2)(B) and (2)(C) of this subsection, and not later than 24 months after the date of enactment of this Act, the Secretary shall issue final regulations implementing such amendments.

“(2) CONTENTS.—In issuing regulations implementing the amendments made by this Act [see Short Title of 1996 Amendments note set out under section 301 of this title], and in taking an action to review an application for approval of a new animal drug under section 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b), or a request for an investigational exemption for a new animal drug under subsection (j) of such section, that is pending or has been submitted prior to the effective date of the regulations, the Secretary shall—

“(A) further define the term ‘adequate and well controlled’, as used in subsection (d)(3) of section 512 of such Act, to require that field investigations be designed and conducted in a scientifically sound manner, taking into account practical conditions in the field and differences between field conditions and laboratory conditions;

“(B) further define the term ‘substantial evidence’, as defined in subsection (d)(3) of such section, in a manner that encourages the submission of applications and supplemental applications; and

“(C) take into account the proposals contained in the citizen petition (FDA Docket No. 91P-0434/CP) jointly submitted by the American Veterinary Medical Association and the Animal Health Institute, dated October 21, 1991.

Until the regulations required by subparagraph (A) are issued, nothing in the regulations published at 21 C.F.R. 514.111(a)(5) (April 1, 1996) shall be construed to compel the Secretary of Health and Human Services to require a field investigation under section 512(d)(1)(E) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(d)(1)(E)) or to apply any of its provisions in a manner inconsistent with the considerations for scientifically sound field investigations set forth in subparagraph (A).”

Pub. L. 103-396, §2(c), Oct. 22, 1994, 108 Stat. 4154, provided that: “Not later than 2 years after the date of the enactment of this Act [Oct. 22, 1994], the Secretary of Health and Human Services shall promulgate regulations to implement paragraphs (4)(A) and (5) of section 512(a) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(a)(4)(A), (5)] (as amended by subsection (a)).”

Pub. L. 100-670, title I, §103, Nov. 16, 1988, 102 Stat. 3982, provided that:

“(a) GENERAL RULE.—The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code, such regulations as may be necessary for the administration of section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b], as amended by sections 101 through 103 of this title,

within one year of the date of enactment of this Act [Nov. 16, 1988].

“(b) TRANSITION.—During the period beginning 60 days after the date of enactment of this Act [Nov. 16, 1988] and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new animal drug applications may be submitted in accordance with the provisions of section 314.55 and part 320 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 512(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(c)] before the date of enactment of this Act. If any such provision of section 314.55 or part 320 is inconsistent with the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (as amended by this title), the Secretary shall consider the application under the applicable requirements of section 512 (as so amended).”

ANTIMICROBIAL ANIMAL DRUG DISTRIBUTION REPORTS

Pub. L. 110-316, title I, §105(b), (c), Aug. 14, 2008, 122 Stat. 3514, provided that:

“(b) FIRST REPORT.—For each new animal drug that is subject to the reporting requirement under section 512(l)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(l)(3)], as added by subsection (a), and for which an approval of an application filed pursuant to section 512(b) or 571 of such Act [21 U.S.C. 360b(b), 360ccc] is in effect on the date of the enactment of this title [Aug. 14, 2008], the Secretary of Health and Human Services shall require the sponsor of the drug to submit the first report under such section 512(l)(3) for the drug not later than March 31, 2010.

“(c) SEPARATE REPORT.—The reports required under section 512(l)(3) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), shall be separate from periodic drug experience reports that are required under section 514.80(b)(4) of title 21, Code of Federal Regulations (as in effect on the date of the enactment of this title).”

DRUGS INTENDED FOR MINOR SPECIES AND MINOR USES

Pub. L. 104-250, §2(f), Oct. 9, 1996, 110 Stat. 3154, provided that: “The Secretary of Health and Human Services shall consider legislative and regulatory options for facilitating the approval under section 512 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b] of animal drugs intended for minor species and for minor uses and, within 18 months after the date of enactment of this Act [Oct. 9, 1996], announce proposals for legislative or regulatory change to the approval process under such section for animal drugs intended for use in minor species or for minor uses.”

TRANSITIONAL PROVISION REGARDING IMPLEMENTATION OF PUB. L. 104-250; APPROVED MEDICATED FEED APPLICATION DEEMED LICENSE

Pub. L. 104-250, §6(c), Oct. 9, 1996, 110 Stat. 3160, provided that: “A person engaged in the manufacture of animal feeds bearing or containing new animal drugs who holds at least one approved medicated feed application for an animal feed bearing or containing new animal drugs, the manufacture of which was not otherwise exempt from the requirement for an approved medicated feed application on the date of the enactment of this Act [Oct. 9, 1996], shall be deemed to hold a license for the manufacturing site identified in the approved medicated feed application. The revocation of license provisions of section 512(m)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(m)(4)], as amended by this Act, shall apply to such licenses. Such license shall expire within 18 months from the date of enactment of this Act unless the person submits to the Secretary a completed license application for the manufacturing site accompanied by a copy of an approved medicated feed application for such site, which license application shall be deemed to be approved upon receipt by the Secretary.”

DRUGS PRIMARILY MANUFACTURED USING
BIOTECHNOLOGY

Pub. L. 100-670, title I, §106, Nov. 16, 1988, 102 Stat. 3984, provided that: "Notwithstanding section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360b(b)(2)], the Secretary of Health and Human Services may not approve an abbreviated application submitted under such section for a new animal drug which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques."

§ 360c. Classification of devices intended for human use

(a) Classes of devices

(1) There are established the following classes of devices intended for human use:

(A) CLASS I, GENERAL CONTROLS.—

(i) A device for which the controls authorized by or under section 351, 352, 360, 360f, 360h, 360i, or 360j of this title or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.

(ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it—

(I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and

(II) does not present a potential unreasonable risk of illness or injury,

is to be regulated by the controls referred to in clause (i).

(B) CLASS II, SPECIAL CONTROLS.—A device which cannot be classified as a class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 360(k) of this title), recommendations, and other appropriate actions as the Secretary deems necessary to provide such assurance. For a device that is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall examine and identify the special controls, if any, that are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide such assurance.

(C) CLASS III, PREMARKET APPROVAL.—A device which because—

(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable

assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and

(ii)(I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or

(II) presents a potential unreasonable risk of illness or injury,

is to be subject, in accordance with section 360e of this title, to premarket approval to provide reasonable assurance of its safety and effectiveness.

If there is not sufficient information to establish a performance standard for a device to provide reasonable assurance of its safety and effectiveness, the Secretary may conduct such activities as may be necessary to develop or obtain such information.

(2) For purposes of this section and sections 360d and 360e of this title, the safety and effectiveness of a device are to be determined—

(A) with respect to the persons for whose use the device is represented or intended,

(B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

(C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

(3)(A) Except as authorized by subparagraph (B), the effectiveness of a device is, for purposes of this section and sections 360d and 360e of this title, to be determined, in accordance with regulations promulgated by the Secretary, on the basis of well-controlled investigations, including 1 or more clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

(B) If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations described in subparagraph (A))—

(i) which is sufficient to determine the effectiveness of a device, and

(ii) from which it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device,

then, for purposes of this section and sections 360d and 360e of this title, the Secretary may authorize the effectiveness of the device to be determined on the basis of such evidence.

(C) In making a determination of a reasonable assurance of the effectiveness of a device for which an application under section 360e of this