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104TH CONGRESS, 2d Session | HOUSE OF REPRESENTATIVES | REPORT 104–823

ANIMAL DRUG AVAILABILITY ACT OF 1996

SEPTEMBER 24, 1996.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. BLILEY, from the Committee on Commerce, submitted the following

R E P O R T

[To accompany H.R. 2508]

[Including cost estimate of the Congressional Budget Office]

The Committee on Commerce, to whom was referred the bill (H.R. 2508) to amend the Federal Food, Drug, and Cosmetic Act to provide for improvements in the process of approving and using animal drugs, and for other purposes, having considered the same, report favorably thereon with an amendment and recommend that the bill as amended do pass.

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AMENDMENT

The amendment is as follows:

Strike out all after the enacting clause and insert in lieu thereof the following:

29–006

SECTION 1. SHORT TITLE; REFERENCE.

(a) SHORT TITLE.—This Act may be cited as the "Animal Drug Availability Act of 1996".

(b) REFERENCE.—Whenever in this Act an amendment or repeal is expressed in terms of an amendment to, or repeal of, a section or other provision, the reference shall be considered to be made to a section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 et seq.).

SEC. 2. EVIDENCE OF EFFECTIVENESS.

(a) ORIGINAL APPLICATIONS.—Paragraph (3) of section 512(d) (21 U.S.C. 360b(d)) is amended to read as follows:

"(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) 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.".

(b) CONFORMING AMENDMENTS.—

(1) Clauses (ii) and (iii) of section 512(c)(2)(F) (21 U.S.C. 360b(c)(2)(F)) are each amended—

(A) by striking "reports of new clinical or field investigations (other than bioequivalence or residue studies) and," and inserting "substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or,"; and

(B) by striking "essential to" and inserting "required for".

(2) Section 512(c)(2)(F)(v) (21 U.S.C. 360b(c)(2)(F)(v)) is amended—

(A) by striking "subparagraph (B)(iv)" each place it appears and inserting "clause (iv)";

(B) by striking "reports of clinical or field investigations" and inserting "substantial evidence of the effectiveness of the drug involved, any studies of animal safety,"; and

(C) by striking "essential to" and inserting "required for".

(c) COMBINATION DRUGS.—Section 512(d) (21 U.S.C. 360b(d)), as amended by subsection (a) is amended by adding at the end the following:

"(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 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; 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.".

(d) PRESUBMISSION CONFERENCE.—Section 512(b) (21 U.S.C. 360b(b)) is amended by adding at the end the following:

"(3) Any person intending to file an application under paragraph (1) or a request for an investigational exemption under subsection (j) 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.".

(e) IMPLEMENTATION.—

(1) IN GENERAL.—Not later than 6 months after the date of enactment of this Act, 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, 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).

(f) MINOR SPECIES AND USES.—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 of animal drugs intended for minor species and for minor uses and, within 18 months after the date of enactment of this Act, 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.

SEC. 3. LIMITATION ON RESIDUES.

Section 512(d)(1)(F) (21 U.S.C. 360b(d)(1)(F)) is amended to read as follows:

"(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;".

SEC. 4. IMPORT TOLERANCES.

Section 512(a) (21 U.S.C. 360b(a)) is amended by adding the following new paragraph at the end:

"(6) For purposes of section 402(a)(2)(D), 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). 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 applications for new animal drugs filed under subsection (b)(1). For purposes of this paragraph, 'relevant international organization' means the Codex Alimentarius 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.".

SEC. 5. VETERINARY FEED DIRECTIVES.

(a) SECTION 503.—Section 503(f)(1)(A) (21 U.S.C. 353(f)(1)(A)) is amended by inserting after "other than man" the following: ", other than a veterinary feed directive drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug,".

(b) SECTION 504.—The Federal Food, Drug, and Cosmetic Act is amended by inserting after section 503 the following:

"VETERINARY FEED DIRECTIVE DRUGS

"SEC. 504. (a)(1) A drug intended for use in or on animal feed which is limited by an approved application filed pursuant to section 512(b) to use under the professional supervision of a licensed veterinarian is a veterinary feed directive drug. Any animal feed bearing or containing a veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice. When labeled, distributed, held, and used in accordance with this section, a veterinary feed directive drug and any animal feed bearing or containing a veterinary feed directive drug shall be exempt from section 502(f).

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

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

"(B) is in compliance with the conditions and indications for use of the drug set forth in the notice published pursuant to section 512(i).

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

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

"(C) Any person who distributes animal feed bearing or containing a veterinary feed directive drug shall upon first engaging in such distribution notify the Secretary of that person's name and place of business. The failure to provide such notification shall be deemed to be an act which results in the drug being misbranded.

"(b) A veterinary feed directive drug and any feed bearing or containing a veterinary feed directive drug shall be deemed to be misbranded if their labeling fails to bear such cautionary statement and such other information as the Secretary may by general regulation or by order prescribe, or their advertising fails to conform to the conditions and indications for use published pursuant to section 512(i) or fails to contain the general cautionary statement prescribed by the Secretary.

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

(c) CONFORMING AMENDMENT.—Section 512 (21 U.S.C. 360b) is amended in subsection (i) by inserting after "(including special labeling requirements" the following: "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".

(d) SECTION 301(e).—Section 301(e) (21 U.S.C. 331(e)) is amended by inserting after "by section 412" the following: ", 504,"; and by inserting after "under section 412," the following: "504,".

SEC. 6. FEED MILL LICENSES.

(a) SECTION 512(a).—Paragraphs (1) and (2) of section 512(a) (21 U.S.C. 360b(a)) are amended to read as follows:

"(a)(1) 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 501(a)(5) and section 402(a)(2)(D) unless —

"(A) there is in effect an approval of an application filed pursuant to subsection (b) 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) holds a license issued under subsection (m) 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) .

"(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 the purposes of section 501(a)(6) unless—

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

"(B) such animal feed is manufactured at a site for which there is in effect a license issued pursuant to subsection (m)(1) to manufacture such animal feed, and

"(C) such animal feed and its labeling, distribution, holding, and use conform to the conditions and indications of use published pursuant to subsection (i).".

(b) SECTION 512(m).—Section 512(m) (21 U.S.C. 360b(m)) is amended to read as follows:

"(m)(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), 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 501(a)(2)(B).

"(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).

"(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),

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) 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 504(a)(3)(A), 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 504(a)(3)(B);

"(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 501(a)(6) 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), 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 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.".

(c) TRANSITIONAL PROVISION.—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, 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, 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.

PURPOSE AND SUMMARY

H.R. 2508, as reported, will facilitate the approval and marketing of new animal drugs and medicated feeds. It builds needed flexibility into the Food and Drug Administration (FDA) animal drug review processes to enable more efficient approval and more expeditious marketing of safe and effective animal drugs. The legislation accomplishes this without decreasing FDA's existing authority to ensure that animal drug products are safe for the animals that use them and for the humans who consume animal food products.

By redefining "substantial evidence," H.R. 2508 provides FDA with greater flexibility to determine what types of studies, including field investigations, are necessary and appropriate for demonstrating the effectiveness of any specific animal drug product. The bill requires FDA to issue regulations defining substantial evidence and the parameters of adequate and well-controlled field investigations. Such regulations must take into account the practical conditions that exist in the field. The bill also requires FDA to hold a presubmission conference at the request of a sponsor submitting a new animal drug application or a request for an investigational exemption.

H.R. 2508 creates a streamlined process for the approval of combination animal drug products when the individual active ingredients or animal drugs used in combination have been approved previously for the particular uses and conditions of use for which they are intended for use in combination. It also authorizes FDA to establish a scientifically-based safe tolerance for new animal drugs.

The bill creates a new class of animal drugs, veterinary feed directive drugs, intended for use in feed under the professional supervision of a licensed veterinarian. The bill eliminates the requirement for feed mills to submit individual medicated feed applications to manufacture certain medicated feeds and allows any medicated feed containing an approved new animal drug to be manufactured at a licensed facility. Finally, the bill authorizes FDA to establish import tolerances for new animal drugs not approved in the United States.

The provisions of the bill are consistent with the initiatives of the Committee on Commerce and the Administration's Reinventing Government proposals to streamline regulatory activities of the FDA.

BACKGROUND AND NEED FOR LEGISLATION

The animal health industry is vital to protecting both humans and animals. Not only does it keep farm animals healthy and protect the food supply, it also safeguards our pets, including some 130 million dogs and cats in the United States. The animal health products industry in the U.S. has sales of $3 billion a year; 90 percent of animal drugs have individual sales of less than $1 million a year. The animal drug industry is one-twentieth the size of the human pharmaceutical industry.

The number of new products approved by the FDA for use in livestock, poultry and pets has dwindled in past years and those who seek to keep animals healthy have an increasingly limited arsenal available for this purpose. Since 1986 FDA has approved only 13 new chemical entities for use in food-producing animals. The swine and turkey industries have had only one new approval in the past decade. This is despite the fact that research and development expenditures by industry now total more than $420 million a year. Manufacturers spend an average of $22 million and 11 years to develop a new animal drug for food animals.

While the law requires a decision on a new animal drug application within 6 months, the process has averaged as high as almost 5 years. Industry reports that these long review times have encouraged a number of pharmaceutical companies to divest themselves of animal drug development capability.

Congress, the Administration, the animal drug industry, veterinarians, and animal producer groups all have recognized the need to streamline the animal drug review process. Thus, representatives of the Administration and affected industries worked successfully with the Committee on Commerce to develop the reforms contained in H.R. 2508, as reported by the Committee. To underscore the success of this negotiation, the Secretary of Health and Human Services wrote a letter to the Committee Chairman on September 19, 1996, in support of H.R. 2508, as reported.

HEARINGS

On February 27, 1996, the Subcommittee on Health and Environment held a hearing on The Need for FDA Reform. Testimony relating to animal drugs was received from the following witnesses: Dr. Kelly F. Lechtenberg, Midwest Veterinary Service, Inc.; Mr. Alexander F. Mathews, President and Chief Executive Officer, Animal Health Institute; and Mr. Brendan P. Fox, President, Elanco Animal Health, on behalf of the Coalition for Animal Health. On May 1 and May 2, 1996, the Subcommittee held hearings on bills relating to FDA reform including H.R. 3200, Title II of which contained legislative language substantially similar to H.R. 2508. Testimony regarding these provisions was presented by FDA Commissioner David A. Kessler and by Mr. Larry Fanella, RoccoTurkeys, Inc., on behalf of the Coalition for Animal Health.

COMMITTEE CONSIDERATION

On September 19, 1996, the Committee on Commerce met in open markup session and ordered H.R. 2508, the Animal Drug

Availability Act of 1996, reported to the House, as amended, by a voice vote, a quorum being present.

ROLLCALL VOTES

Clause 2(l)(2)(B) of Rule XI of the Rules of the House of Representatives requires the Committee to list the recorded votes to report legislation and on amendments thereto. There were no recorded votes taken in connection with ordering H.R. 2508 reported or in adopting the amendment. The voice votes taken in Committee are as follows:

COMMITTEE ON COMMERCE—104TH CONGRESS VOICE VOTES

Bill: H.R. 2508, Animal Drug Availability Act of 1996.

Unanimous Consent Request: Unanimous consent request by Mr. Bliley to discharge the Subcommittee on Health and Environment from further consideration of H.R. 2508 and to proceed to its immediate consideration by the full committee.

Disposition: Agreed to, without objection.

Amendment: Amendment in the nature of a substitute offered by Mr. Klug.

Disposition: Agreed to, by a voice vote.

Motion: Motion by Mr. Bliley to order H.R. 2508 reported to the House, as amended.

Disposition: Agreed to, by a voice vote.

COMMITTEE OVERSIGHT FINDINGS

Pursuant to clause 2(l)(3)(A) of Rule XI of the Rules of the House of Representatives, the Subcommittee on Health and Environment held legislative and oversight hearings and made findings that are reflected in this report.

COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT

Pursuant to clause 2(l)(3)(D) of Rule XI of the Rules of the House of Representatives, no oversight findings have been submitted to the Committee by the Committee on Government Reform and Oversight.

NEW BUDGET AUTHORITY AND TAX EXPENDITURES

In compliance with clause 2(l)(3)(B) of Rule XI of the Rules of the House of Representatives, the Committee states that H.R 2508 would result in no new or increased budget authority or tax expenditures or revenues.

COMMITTEE COST ESTIMATE

In compliance with clause 7(a) of Rule XIII of the Rules of the House of Representatives, the Committee believes that enactment of H.R. 2508 would result in no additional cost to the Federal government. The Committee further adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office (CBO) pursuant to section 403 of the Congressional Budget Act of 1974.

CONGRESSIONAL BUDGET OFFICE ESTIMATE

Pursuant to clause 2(l)(3)(C) of Rule XI of the Rules of the House of Representatives, the following is the cost estimate provided by the Congressional Budget Office pursuant to section 403 of the Congressional Budget Act of 1974:

U.S. CONGRESS,
CONGRESSIONAL BUDGET OFFICE,
Washington, DC, September 20, 1996.

Hon. THOMAS J. BLILEY, Jr.,
Chairman, Committee on Commerce,
House of Representatives, Washington, DC.

DEAR MR. CHAIRMAN: At your request, the Congressional Budget Office (CBO) has reviewed H.R. 2508, the Animal Drug Availability Act of 1996, as ordered reported by the House Committee on Commerce on September 19, 1996. CBO estimates this bill would result in savings to the federal government, although these savings would not be substantial. The bill would not affect direct spending or receipts and thus would not be subject to pay-as-you-go procedures.

The bill would direct the Secretary of Health and Human Services to establish tolerance levels for residues of veterinary drugs in imported animal products intended for human consumption. It would also change the licensing requirements for manufacturers of animal feeds containing veterinary drugs. Both of these provisions would impose new private-sector mandates, as would a provision imposing new recordkeeping requirements on veterinarians and distributors of animal feed directive drugs. Only the new recordkeeping requirements would be likely to impose any significant costs on the private sector, and these costs would be well below the $100 million threshold. The bill contains no intergovernmental mandates as defined in the Unfunded Mandates Reform Act of 1995 (Public Law 104–4) and would impose no costs on state, local, or tribal governments.

Tolerance Standards. Section 4 of the bill would require that the residues from animal drugs in edible animals imported into the United States meet tolerance standards to be set by the Secretary. These animal products could not be deemed unsafe unless their residue levels exceeded the specified tolerance levels. Under current law, the United States Department of Agriculture monitors residues in imported animal food products, sometimes in consultation with the Food and Drug Administration (FDA). However, this section would place a new formal requirement on the importation of edible animals. Based on information from FDA staff, CBO expects that the tolerance standards set by the Secretary would not differ significantly from current practice. Thus, this provision would not have significant costs for the federal government or the private sector.

Recordkeeping Requirements. Section 5(b) of the bill would constitute a private-sector mandate by imposing new recordkeeping requirements on the distributors of veterinary feed directive drugs and on veterinarians that recommend their use. A veterinary feed directive drug is "a drug intended for use in or on animal feed which is limited * * * to use under professional supervision of a

licensed veterinarian." The veterinarian and the distributor of a veterinary feed directive drug would be required to "maintain a copy of the veterinary feed directive applicable to each such feed." Distributors would also be required to provide the Secretary with their names and places of business. Both veterinarians and distributors of veterinary feed directive drugs would be likely to increase their current recordkeeping activities to comply with this mandate, resulting in a small increase in their cost of doing business.

Licensing Requirements. Additionally, the bill would change the licensing requirements for the manufacture of animal feeds containing veterinary drugs. Current law requires manufacturers to file a separate application with the FDA for each type of animal feed they produce that contains a veterinary drug. H.R. 2508 would require each manufacturer to obtain only one license to produce a number of veterinary feed drugs. To apply for this license, manufacturers would need to certify that their products were manufactured and labeled in accordance with the law and good manufacturing practice standards. This change should reduce the overall costs of regulatory compliance for the industry. The reduction in the number of license applications to the FDA would also reduce costs for the federal government.

Drug Approval Process. Two provisions of H.R. 2508 would streamline the approval process for veterinary drugs, resulting in a small savings to the federal government. One provision would require manufacturers of new drugs to submit "one or more adequate and well-controlled investigations" in support of their drugs' efficacy, rather than the multiple investigations required under current law. Another provision would direct the FDA to approve animal drugs containing a combination of drugs, provided each of the individual ingredients had already been approved for use. The agency could refuse to approve these combination drugs only under limited circumstances. These provisions would cut the time needed for the drug approval process by reducing the amount of data that the FDA must review.

Additional provisions would increase the cost of approving new veterinary drugs by escalating the FDA's administrative activities. H.R. 2508 would allow a manufacturer to request one or more conferences with the FDA to establish submission or investigational requirements prior to submission of an application for a new animal drug. The bill would also direct the Secretary to issue new regulations regarding the kind of investigations that must be submitted in support of a new veterinary drug application. CBO estimates that the additional costs associated with these activities would be less than the savings from other provisions of this bill.

If you wish further details on this estimate, we will be pleased to provide them. The staff contacts for this estimate are Anne Hunt (federal cost estimate), John Patterson (state and local estimate), and Anna Cook (private sector mandate estimate).

Sincerely,

JUNE E. O'NEILL, *Director.*

INFLATIONARY IMPACT STATEMENT

Pursuant to clause 2(l)(4) of Rule XI of the Rules of the House of Representatives, the Committee finds that the bill would have no inflationary impact.

ADVISORY COMMITTEE STATEMENT

No advisory committees within the meaning of section 5(b) of the Federal Advisory Committee Act are created by this legislation.

SECTION-BY-SECTION ANALYSIS OF THE LEGISLATION

SECTION 1. SHORT TITLE; REFERENCE

Section 1 provides that the short title of the bill is the "Animal Drug Availability Act of 1996" and specifies that the provisions in the bill refer to the Federal Food, Drug, and Cosmetic Act.

SECTION 2. EVIDENCE OF EFFECTIVENESS

Section 2(a) amends the current definition of "substantial evidence" of effectiveness found in section 512(d)(3). The amended definition of substantial evidence permits the FDA more flexibility in determining the types of studies required to demonstrate that a particular new animal drug is effective for its intended uses and conditions of use. The statutory requirement for a field investigation has been eliminated, but FDA continues to have the authority to require field investigations when necessary. As part of its implementing regulations for this Act, FDA must define by regulation an adequate and well-controlled field investigation, taking into account the practical conditions that exist in the field where such investigations are conducted. Because a field investigation on animal drugs is conducted under actual use conditions, e.g., in feed lots, a determination regarding whether such an investigation is scientifically sound must take into account the differences between field conditions and laboratory conditions.

As in current law, the evidence of effectiveness must consist of one or more adequate and well-controlled studies conducted by qualified experts on the basis of which qualified experts can fairly and reasonably conclude that the drug is effective. The individuals who conduct studies to demonstrate the effectiveness of a new animal drug and the individuals who evaluate those studies must be experts qualified by scientific training and experience to do so.

Section 2(b) makes conforming changes to section 512(c)(2)(F) to reference the revised definition of substantial evidence.

Section 2(c) adds section 512(d)(4) and establishes a streamlined approval process for certain combination animal drugs. Specifically, section 512(d)(4) sets forth the grounds on which FDA may refuse to approve combination animal drugs that contain active ingredients or drugs intended for use in combination that previously have been approved separately for the particular uses and conditions of use for which they are intended for use in the combination.

To establish the human food safety of such a combination animal drug, the application must demonstrate that none of the active ingredients or drugs exceeds its previously established tolerance at the longest withdrawal time of any of the active ingredients or

drugs and that 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.

FDA generally should not require full safety testing of such a combination animal drug to establish target animal safety. However, if there is a substantiated scientific basis for believing that combining the individual ingredients or drugs would endanger target animal safety, or if target animal observations from studies in the application raise a scientific issue regarding animal safety, FDA may require the sponsor of the combination animal drug to conduct additional safety testing. For example, if a drug or active ingredient to be used in combination has a narrow margin of safety to the target animal or is known either to stimulate or inhibit drug metabolism or drug excretion, then FDA may require the sponsor of the combination animal drug to conduct additional safety testing of the combination. Similarly, if during testing of the combination animal drug, clinical signs of morbidity or mortality are observed, FDA may require additional safety testing. FDA should explain to the sponsor the scientific reason for a request for additional safety testing. Unless FDA's substantiation for requiring additional testing is contained in the proprietary files that belong to a different drug applicant, FDA should provide copies of, or citations to, the relevant scientific information.

To establish the effectiveness of a dosage form combination animal drug composed of active ingredients or drugs that previously have been approved separately for particular uses and conditions of use for which they are intended in combination, an application must demonstrate that: (1) there is substantial evidence, as newly defined, that each 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 effectiveness; (2) each active ingredient or animal drug intended for a use different from that of all other active ingredients or animal drugs in the combination provides appropriate concurrent therapy for the intended target population; and (3) the active ingredients or animal drugs are physically compatible and have compatible dosing regimens if such compatibility could affect the effectiveness of the combination. The intent of the third provision (and a similar provision for drugs administered in drinking water) is to authorize FDA to deny approval of a combination animal drug if the physical compatibility or compatibility of the dosing regimens may affect the effectiveness of the combination animal drug and such compatibility is not demonstrated.

In the case of dosage form combination animal drugs that contain any nontopical ingredient or drug intended for use as an antibacterial, the sponsor of such a drug must demonstrate by substantial evidence, as newly defined, that such combination animal drug is effective for its intended uses.

To establish the effectiveness of a combination animal drug (composed of active ingredients or drugs that previously have been approved separately for particular uses and conditions of use for which they are intended in the combination) intended for use in animal feed or drinking water, an application must demonstrate that: (1) there is substantial evidence, as newly defined, 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 effectiveness; (2) each active ingredient or animal drug intended for at least one use different from that of all other active ingredients or animal drugs used in the combination provides appropriate concurrent therapy for the intended target population; (3) when a combination contains more than one antibacterial, each antibacterial ingredient or drug makes a contribution to effectiveness; and (4) if the combination animal drug is intended for use in drinking water, the active ingredients or animal drugs are physically compatible if FDA has a scientific basis to believe they may be incompatible.

Section 2(d) adds section 512(b)(3) to entitle a person intending to file a new animal drug application or a request for investigational new animal drug exemption to request a presubmission conference. The presubmission conference is a forum for the applicant and FDA to discuss what studies the applicant needs to conduct to support FDA's finding that the new animal drug is safe and effective. When FDA and the sponsor reach an agreement on a submission or investigational requirement, such requirement is binding on FDA and the sponsor unless such agreement is changed by mutual agreement or by an FDA order with specific scientific justification. The binding nature of the submission or investigational agreement gives the sponsor assurance that development time and resources will be used efficiently and predictably. As part of a presubmission conference agreement, FDA may, but need not, require a sponsor to conduct an adequate and well-controlled field investigation to demonstrate effectiveness. If FDA concludes that more than one field investigation is essential to demonstrate by substantial evidence, as newly defined, the effectiveness of the specific animal drug and intended uses under consideration, FDA must provide within 25 days after such conference written justification for requiring more than one field investigation.

Assessing the safety and effectiveness of new animal drugs under conditions of use which closely approximate actual field use conditions will remain an important element of many new animal drug approvals. However, there are situations, e.g., approval of many therapeutic animal drugs, in which the effectiveness of the animal drug can be demonstrated without a field investigation. In some instances, laboratory animal studies in the target species on farm settings controlled by the sponsor can fulfill this need. There may be cases in which field investigations would yield no more useful information with regard to an animal drug's effectiveness than can be obtained through laboratory studies. However, there will be cases where at least one field investigation will generally be required. In most instances in which a field investigation is needed, one adequate and well-controlled field investigation which adequately represents the intended target population of animals and conditions of use will be sufficient.

Section 2(e) directs FDA to promulgate regulations to implement the Animal Drug Availability Act of 1996. FDA is directed, within 6 months after enactment, to propose regulations to define "adequate and well-controlled" and to issue final regulations not later than 18 months after enactment. FDA is also required to propose

regulations within 12 months and issue final regulations within 24 months to (1) define "substantial evidence" in a manner that encourages the submission of new animal drug applications and supplemental applications; and (2) to encourage dose range labeling. This section directs FDA, pending the adoption of implementing regulations, to implement the Federal Food, Drug, and Cosmetic Act, as amended by this Act, in a manner consistent with the policies set forth in this bill for all pending and future applications and supplemental applications from the date of enactment.

Section 2(f) requires FDA to consider regulatory and legislative options for facilitating the approval of animal drugs intended for use in minor species and for minor uses, and to announce proposals for regulatory or legislative change within 18 months of enactment of this Act. Because the population for which such drugs are intended is small, it is often difficult or impossible to design and conduct studies to establish safety and efficacy under the traditional approval processes. Furthermore, there may not be economic incentives for a sponsor to conduct such studies in light of the potential market for the product. FDA is directed to consider regulatory and legislative options for implementing an approval process that takes into account these special circumstances and ensures that more drugs are available for minor species and for minor uses and that such drugs do not endanger the public health.

SECTION 3. LIMITATION ON RESIDUES

Section 3 amends section 512(d)(1)(F) which, under existing law, requires FDA not to approve a new animal drug application if the tolerance limitation proposed exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended. This provision of the current statute derives from similar language relating to the regulation of food additives, and directs the agency to (1) determine, and to establish as a condition of use for new animal drugs intended for use in food animals, the minimum dose necessary to accomplish the intended effect; and (2) limit tolerances based on such use conditions. The current requirement to establish the minimum dose creates a burden on the applicant and FDA to determine dose to a level of specificity which is not scientifically necessary for the safe use of all new animal drugs intended for use in food animals. Furthermore, for a number of therapeutic drugs, use of the drug at the minimum effective dose is not consistent with the best medical practice. The change implemented by section 3 would permit FDA to use the concept of dose-ranging in new animal drug development and labeling to a greater extent and to establish tolerances solely on the basis of scientifically valid risk assessment procedures. The safeguards to animal and human health built into the current statute will continue.

SECTION 4. IMPORT TOLERANCES

Section 4 amends section 512(a) to permit FDA to establish a tolerance for residues of an animal drug in human foods, when the drug is not approved for use in the United States but imported food products of animal origin may contain residues of that drug.

There are appropriate instances in which food producing animals raised in other countries are treated with animal drugs that are

not approved in the United States. For example, the disease or condition treated by the drug does not occur in the United States. There have been concerns about residues of such drugs in food products derived from these animals, imported into the United States. This provision authorizes FDA to establish a safe tolerance using criteria similar to those that it would apply in reviewing the human food safety aspects of an animal drug for which approval is sought in the United States. FDA may rely on data generated by the drug manufacturer or on data from a relevant international organization such as the Codex Alimentarius Commission. This is a step in the direction of international harmonization of regulatory requirements.

If an international standard on which FDA relied changes or new information (from either experience or scientific data) shows the tolerance is no longer safe, FDA may change or revoke the tolerance. In addition, section 4 provides that the tolerance may be revoked if information shows use of the animal drug under actual use conditions results in food being imported into the United States with residues exceeding the tolerance.

SECTION 5. VETERINARY FEED DIRECTIVES

Section 5 adds a new section 504, Veterinary Feed Directive Drugs. Veterinary feed directive drugs are animal drugs intended for use in or on animal feed which are limited, by an approved application filed pursuant to section 512(b), to use under the professional supervision of a licensed veterinarian in the course of the veterinarian's professional practice.

A significant number of animal drugs are administered through animal feed. All commercially available animal drugs intended for use in feed are now available to animal owners and producers without the involvement of the veterinarian. However, FDA has determined that in the future certain animal drugs can be approved for feed use only if they are used under a veterinarian's supervision. Under the existing law, an animal drug limited by an approved application to use under the professional supervision of a licensed veterinarian is a prescription animal drug. Because the distribution system for medicated feeds is more complex than the distribution system for dosage form animal drugs, regulation of animal feeds under traditional prescription systems is not practical. This bill provides that veterinary feed directive drugs and medicated feeds containing them are not "prescription" articles under any Federal or State law.

Under this bill, the labeling, distribution, holding, or use of a veterinary feed directive drug or feed in a manner inconsistent with its approval results in the drug or feed being deemed adulterated. This bill requires each person involved in the distribution or use of a veterinary feed directive medicated feed and the veterinarian issuing the veterinary feed directive to maintain a copy of the applicable feed directive, except that a person distributing the feed to another person for further distribution is required to maintain a copy of a written acknowledgment from the consignee stating that veterinary feed directive distribution limitations will be followed. FDA is given correlative authority to inspect and copy the veterinary feed directives and written acknowledgments. Persons distrib-

uting veterinary feed directive medicated feeds must provide a one-time notice to FDA.

While this section authorizes FDA to promulgate implementing regulations for veterinary feed directive drugs and feeds, FDA should not delay any drug approvals pending the promulgation of such regulations. In the absence of such regulations, FDA should set forth all necessary conditions related to the labeling, advertising, distribution, holding, or use of a veterinary feed directive drug or feed in the new animal drug approval notice required by section 512(i).

SECTION 6. FEED MILL LICENSES

Section 6 amends sections 512(a) and 512(m) to establish a new regulatory system for licensing feed mills to manufacture any or all medicated feeds that, under existing law, are the subject of drug specific medicated feed applications (MFAs). The underlying standards for the issuance of a license and for revoking a license do not differ substantively from the existing standards applicable to MFAs. As under existing law dealing with MFAs, the principal criterion for the issuance of a feed mill license is whether the establishment is operating within current good manufacturing practices, as represented in the application filed by the applicant and confirmed by FDA or State inspections. But, by requiring a feed mill to submit for approval an application for a single license for the facility, this section eliminates a paperwork and administrative burden on industry to file multiple product specific MFAs.

Persons holding an approved MFA under existing law are deemed to hold a feed mill license for the site identified in the MFA. Such license will expire within 18 months from enactment of this bill unless the person submits a completed license application for the manufacturing site along with a copy of an approved MFA for such site.

CHANGES IN EXISTING LAW MADE BY THE BILL, AS REPORTED

In compliance with clause 3 of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italics, existing law in which no change is proposed is shown in roman):

FEDERAL FOOD, DRUG, AND COSMETIC ACT

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CHAPTER III—PROHIBITED ACTS AND PENALTIES

PROHIBITED ACTS

SEC. 301. The following acts and the causing thereof are hereby prohibited:

(a) * * *

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(e) The refusal to permit access to or copying of any record as required by section 412*, 504,* or 703; or the failure to establish or maintain any record, or make any report, required under section 412, *504,* 505 (i) or (k), 507(d) or (g), 512(a)(4)(C), 512 (j), (l) or (m), 515(f), or 519 or the refusal to permit access to or verification or copying of any such required record.

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CHAPTER V—DRUGS AND DEVICES

SUBCHAPTER A—DRUGS AND DEVICES

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EXEMPTIONS AND CONSIDERATION FOR CERTAIN DRUGS, DEVICES, AND BIOLOGICAL PRODUCTS

SEC. 503. (a) * * *

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(f)(1)(A) A drug intended for use by animals other than man*, other than a veterinary feed directive drug intended for use in animal feed or an animal feed bearing or containing a veterinary feed directive drug,* which—

(i) because of its toxicity or other potentiality or harmful effect, or the method of its use, or the collateral measures necessary for its use, is not safe for animal use except under the professional supervision of a licensed veterinarian, or

(ii) is limited by an approved application under subsection (b) of section 512 to use under the professional supervision of a licensed veterinarian,

shall be dispensed only by or upon the lawful written or oral order of a licensed veterinarian in the course of the veterinarian's professional practice.

* * * * * * *

VETERINARY FEED DIRECTIVE DRUGS

SEC. 504. (a)(1) A drug intended for use in or on animal feed which is limited by an approved application filed pursuant to section 512(b) to use under the professional supervision of a licensed veterinarian is a veterinary feed directive drug. Any animal feed bearing or containing a veterinary feed directive drug shall be fed to animals only by or upon a lawful veterinary feed directive issued by a licensed veterinarian in the course of the veterinarian's professional practice. When labeled, distributed, held, and used in accordance with this section, a veterinary feed directive drug and any animal feed bearing or containing a veterinary feed directive drug shall be exempt from section 502(f).

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

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

(B) is in compliance with the conditions and indications for use of the drug set forth in the notice published pursuant to section 512(i).

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

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

(C) Any person who distributes animal feed bearing or containing a veterinary feed directive drug shall upon first engaging in such distribution notify the Secretary of that person's name and place of business. The failure to provide such notification shall be deemed to be an act which results in the drug being misbranded.

(b) A veterinary feed directive drug and any feed bearing or containing a veterinary feed directive drug shall be deemed to be misbranded if their labeling fails to bear such cautionary statement and such other information as the Secretary may by general regulation or by order prescribe, or their advertising fails to conform to the conditions and indications for use published pursuant to section 512(i) or fails to contain the general cautionary statement prescribed by the Secretary.

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

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NEW ANIMAL DRUGS

SEC. 512. [(a)(1) 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 501(a)(5) and section 402(a)(2)(D) 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.

[(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 the purposes of section 501(a)(6) unless—

[(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such drug, 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.]

(a)(1) 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 501(a)(5) and section 402(a)(2)(D) unless—

(A) there is in effect an approval of an application filed pursuant to subsection (b) 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) holds a license issued under subsection (m) 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) .

(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 the purposes of section 501(a)(6) unless—

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

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

(C) such animal feed bears approved labeling and such use conforms to the conditions and indications of use published pursuant to subsection (i).

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(6) For purposes of section 402(a)(2)(D), 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). 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 applications for new animal drugs filed under subsection (b)(1). For purposes of this paragraph, "relevant international organization" means the Codex Alimenterius 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)(1) * * *

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(3) Any person intending to file an application under paragraph (1) or a request for an investigational exemption under subsection (j) 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)(1) * * *

(2)(A) * * *

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(F)(i) * * *

(ii) If an application submitted under subsection (b)(1) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another applica-

tion approved under such subsection, is approved after the date of enactment of this paragraph and if such application contains [reports of new clinical or field investigations (other than bioequivalence or residue studies) and,] *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 or residue studies) [essential to] *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) 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) for such drug.

(iii) If a supplement to an application approved under subsection (b)(1) is approved after the date of enactment of this paragraph and the supplement contains [reports of new clinical or field investigations (other than bioequivalence or residue studies) and,] *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 or residue studies) [essential to] *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) for a change approved in the supplement effective before the expiration of 3 years from the date of the approval of the supplement.

* * * * * * *

(v) If an application (including any supplement to a new animal drug application) submitted under subsection (b)(1) 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 [subparagraph (B)(iv)] *clause (iv)* is approved after the date of enactment of this paragraph, and if the application contains [reports of clinical or field investigations] *substantial evidence of the effectiveness of the drug involved, any studies of animal safety,* or human food safety studies (other than bioequivalence or residue studies) [essential to] *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) 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) 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 [subparagraph (B)(iv)] *clause (iv).*

* * * * * * *

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

(A) * * *

* * * * * * *

[(F) 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;]

(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;

* * * * * * *

[(3) As used in this subsection and subsection (e), 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.]

(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) 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 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; 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.

* * * * * * *

(i) When a new animal drug application filed pursuant to subsection (b) 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, 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.

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[(m)(1) Any person may file with the Secretary an application with respect to any intended use or uses of an animal feed bearing or containing a new animal drug. Such person shall submit to the Secretary as part of the application (A) a full statement of the composition of such animal feed, (B) an identification of the regulation or regulations (relating to the new animal drug or drugs to be used in such feed), published pursuant to subsection (i), on which he relies as a basis for approval of his application with respect to the use of such drug in such feed, (C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed, (D) specimens of the labeling proposed to be used for such animal feed, and (E) if so requested by the Secretary, samples of such animal feed or components thereof.

[(2) Within ninety days after the filing of an application pursuant to subsection (m)(1), 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 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).

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

[(A) that there is not in effect a regulation under subsection (i) (identified in such application) on the basis of which such application may be approved;

[(B) that such animal feed (including the proposed use of any new animal drug therein or thereon) does not conform to an applicable regulation published pursuant to subsection (i) referred to in the application, or that the purposes and conditions or indications of use prescribed, recommended, or suggested in the labeling of such feed do not conform to the applicable purposes and conditions or indications of use (including warnings) published pursuant to subsection (i) or such labeling omits or fails to conform to other applicable information published pursuant to subsection (i);

[(C) 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

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

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (D) do not apply, he shall issue an order approving the application. An order under this subsection approving an application with respect to an animal feed bearing or containing a new animal drug shall be effective only while there is in effect a regulation pursuant to subsection (i), on the basis of which such application (or a supplement thereto) was approved, relating to the use of such drug in or on such feed.

[(4)(A) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application with respect to any animal feed under this subsection if the Secretary finds—

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

[(ii) 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 application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an ap-

proval 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 animal feed 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 shall not be delegated.

[(B) 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 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 the applicant has refused to permit access to, or copying or verification of, such records as required by subparagraph (B) of such paragraph;

[(ii) that on the basis of new information before him, evaluated together with the evidence before him when such application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing 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; or

[(iii) 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 animal feed, 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.

[(C) Any order under paragraph (4) of this subsection shall state the findings upon which it is based.

[(5) In the case of any animal feed for which an approval of an application filed pursuant to this subsection is in effect—

[(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), 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 paragraph (4) of this subsection.

[(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 Sec-

retary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.]

(m)(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), 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 501(a)(2)(B).

(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).

(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),

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) 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 504(a)(3)(A), 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 504(a)(3)(B);

(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 501(a)(6) and the facility did not discontinue the manufacture, processing, packing, or holding of such animal feed within a reasonable time after re-

ceipt 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), 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 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.

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