104TH CONGRESS
2D SESSION

S. 773

AN ACT

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.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

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 in-

gredients 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 US.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 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.''.

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 direc-

tive 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 sub-

section 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 li-

cense application shall be deemed to be approved upon receipt by the Secretary.

Passed the Senate September 24, 1996.

Attest:

Secretary.

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S 773 ES——2

S 773 ES——3

S 773 ES——4

S 773 ES——5