

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-N-0528]

Unapproved Animal Drugs

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency) is soliciting comments from stakeholders on strategies to address the prevalence of animal drug products marketed in the United States without approval or other legal marketing status. FDA is concerned that the safety and effectiveness of these actively-marketed products has not been demonstrated. Therefore, the Agency is requesting comments on approaches for increasing the number of legally-marketed animal drug products, as well as on the use of enforcement discretion for some unapproved animal drug products in certain limited circumstances.

DATES: Submit either electronic or written comments by February 18, 2011.

ADDRESSES: Submit electronic comments to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Tracey H. Forfa, Center for Veterinary Medicine (HFV-1), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240-276-9000. e-mail: tracey.forfa@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Purpose

FDA is soliciting comments from all stakeholders, including the regulated industry, veterinary professionals, and the public on strategies to address the prevalence of animal drug products marketed in the United States without approval or other legal marketing status. The Agency is concerned that the safety and effectiveness of these marketed products has not been demonstrated. FDA recognizes that the continued availability of a number of these products is important to meet the health needs of animals. FDA is requesting comments on approaches for increasing the number of currently marketed animal drug products that have legal marketing status. Our focus at this time is not on revising the current new animal drug approval process. Instead, we wish to explore additional

mechanisms that utilize FDA's existing regulatory framework as well as novel strategies not currently employed by the agency to increase the number of approved or otherwise legally marketed animal drugs. Furthermore, we are requesting comment on the use of limited enforcement discretion as an element of the overall strategy.

II. Background

New animal drugs cannot be legally marketed unless they have been reviewed and approved, conditionally approved, or index-listed by FDA. The Federal Food, Drug, and Cosmetic Act (the FD&C Act) defines the term "drug" to include articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, and articles (other than food) intended to affect the structure or any function of the body of man or other animals (section 201(g)(1) of the FD&C Act (21 U.S.C. 321(g)(1)). The FD&C Act also defines the term "new animal drug." A "new animal drug" includes any drug intended for use for animals that is not generally recognized as safe and effective for use under the conditions listed in the drug's labeling (section 201(v) of the FD&C Act).

Under the FD&C Act, a new animal drug may not be legally introduced into interstate commerce unless it is the subject of an approved new animal drug application (NADA) or abbreviated new animal drug application (ANADA) under section 512 of the FD&C Act (21 U.S.C. 360b), a conditional approval (CNADA) under section 571 of the FD&C Act (21 U.S.C. 360ccc), an index listing under section 572 of the FD&C Act (21 U.S.C. 360ccc-1), or an investigational new animal drug exemption (INAD) under section 512(j) of the FD&C Act (21 U.S.C. 360b(j)). When this notice refers to an "unapproved animal drug," we mean an animal drug that does not have a necessary approval, conditional approval, index listing, or INAD exemption.

The FD&C Act's new animal drug approval requirements provide important protection for humans and animals. Animal drugs that are marketed without required FDA review and approval may not meet requirements and standards for, among other things, safety and effectiveness. The FDA drug approval process ensures, through an evaluation of scientific evidence, that animal drugs are safe and effective. The approval process also provides a review of product-specific information that is critical to ensuring the safety and effectiveness of the

finished animal drug product. For instance, the sponsor of an NADA must demonstrate that the manufacturing processes can reliably produce drug products of expected identity, strength, quality, and purity. Furthermore, FDA's review of the applicant's labeling assures that veterinarians, animal owners and other consumers have the information necessary to understand a drug product's risks. In addition, firms marketing approved animal drug products must report adverse events associated with their product's use, which helps FDA continuously assess the risks associated with a particular product. Although the conditional approval and indexing requirements differ in some ways from the animal drug approval process, they all provide for a science-based review to assure the drug will be safe for its intended use. FDA employs these standards in the new animal drug approval process to protect both human and animal health.

For many years, FDA has been aware that a wide variety of animal drug products are being marketed that meet the definition of "drug" and "new animal drug" as defined in the FD&C Act, but are not approved, conditionally approved, or indexed. Many of these unapproved animal drugs were, and some continue to be, the standard of care in treating animals, and some are essential to protecting animal health and ensuring an adequate food supply.

In general, the types of unapproved animal drugs being marketed include, but are not limited to, injectable vitamins, various topical solutions, shampoos, and liniments, electrolyte and glucose solutions, and antidotes. In addition, there are a variety of anti-infective and other animal drug products marketed for use in a variety of animal species. The Agency determined, based on available information, that some of these animal drug products or categories of products did not raise safety concerns. With respect to those products, the Agency historically exercised its enforcement discretion, even though such products lacked the required FDA marketing approval. This approach has been important for setting enforcement priorities and for making decisions as to whether to take action against an illegally marketed unapproved drug or class of drugs under particular circumstances.

Some of these unapproved drugs which did not raise safety concerns have been marketed under an FDA letter of "no objection," issued in response to a firm's request, stating that FDA did not at the time object to the marketing of a particular unapproved new animal

drug. In addition, some unapproved drugs have been marketed under the auspices of Compliance Policy Guides issued by FDA to let its staff, the public, and industry know the conditions under which FDA would consider enforcement action with respect to these unapproved drugs. This practice of proactively announcing the Agency's intent to exercise enforcement discretion with respect to particular types of unapproved drugs under specified conditions has been used in certain circumstances because of the relatively limited number of approved animal drugs available to meet the animal health needs of a diverse number of animal species.

FDA recognizes that it will be necessary to continue to exercise enforcement discretion in limited circumstances for certain essential unapproved animal drug products or categories of products as the Agency works to develop new ways to increase the availability of products that are approved or otherwise legally marketed. However, it is the Agency's general expectation that new animal drugs must be approved or otherwise legally marketed as required by the FD&C Act. Therefore, any exercise of the Agency's enforcement discretion with respect to unapproved animal drugs should be limited to the greatest extent possible. To that end, the Agency is seeking comment on strategies for increasing the number of animal drug products that are legally marketed, and thus decreasing the number of currently marketed products that lack approval or other legal marketing status. Such strategies may include alternative pathways to achieve legal marketing status that assure animal drug products meet safety and effectiveness standards, including human food safety standards. However, even after alternative pathways to legal marketing are established, some drugs may not be well-suited to such alternatives and may be required to go through the new animal drug approval process, especially in cases where there are safety or effectiveness concerns. For example, certain drug products intended for use in food-producing animals may only be able to achieve legal marketing status through the traditional new animal drug approval process because of concerns about drug residues appearing in edible tissues.

III. Agency Request for Comments

FDA is soliciting public comment on potential actions the Agency can take to help achieve the goal of obtaining legal marketing status, as appropriate, for unapproved animal drugs that are currently being marketed in the United

States. We are interested in comments on strategies that utilize FDA's existing regulatory framework for addressing this issue as well as comments on novel strategies not currently employed by the Agency. In conjunction with pursuing this goal, the Agency recognizes the need for maintaining the availability of essential animal drugs for pet owners, veterinarians, and animal producers.

FDA is also specifically requesting comments and information on the questions and subjects below. This list is not all-inclusive, however, and is not intended to limit the range of options available for public comment. The Agency asks that comments be as detailed as possible, with explanations and information to assist FDA in evaluating whether the approaches will help accomplish the goal of increasing the number of currently marketed animal drug products that have approval or other legal marketing status. FDA's intent is that of inquiry and not for anyone to read this list as any indication of the Agency's position on a particular approach or a determination that the Agency has the resources to implement such an approach.

A. Increasing the Availability of Legally Marketed Animal Drug Products

In general, the types of unapproved animal drugs being marketed include, but are not limited to: Injectable vitamins; various topical solutions, shampoos, and liniments; electrolyte and glucose solutions; and antidotes. In addition, there are a variety of anti-infective and other animal drug products marketed for use in a variety of animal species. Given the broad array of animal drug products that are important for meeting the health needs of a diverse number of animal species, FDA is interested in exploring alternative approaches (*i.e.*, alternatives to the existing new animal drug approval process) by which those products could be legally marketed. Some examples of alternative approaches are discussed in sections III.A.1 and III.A.2 of this document.

1. Monographs

Certain over-the-counter (OTC) drugs for humans are marketed under monographs that establish the conditions under which these drugs are generally recognized as safe and effective and not misbranded. The monographs specify active ingredients, dosage forms, product strengths, indications for use, labeling, and other conditions. Human OTC drug products that comply with all of a monograph's conditions and the provisions in 21 CFR part 330 may be manufactured and

distributed without applications or any other premarket review. Monographs are developed after review of available information about safety and effectiveness, including published and unpublished data and information submitted to the Agency, and must be supported by adequate and well-controlled studies.

Does published literature of sufficient quality exist for some currently marketed unapproved animal drugs such that monographs might be a feasible approach? For which drugs might this be feasible? What are the attributes that make the published literature suitable for this purpose? What criteria should be used to determine whether an animal drug is potentially suitable for a monograph to ensure that quality, safety and effectiveness would not be compromised in the absence of premarket review?

2. Use of Publicly Available Information

In some cases, human prescription drugs have been approved and marketed after FDA reviewed the existing literature and data regarding a particular drug or class of drugs. Examples of drugs for which FDA has used this approach include the following:

- Prussian Blue (*see* "Guidance for Industry on Prussian Blue for Treatment of Internal Contamination With Thallium or Radioactive Cesium; Availability" (68 FR 5645, February 4, 2003)) and
- Pancreatic Enzymes (*see* "Exocrine Pancreatic Insufficiency Drug Products" (69 FR 23410, April 28, 2004), "Exocrine Pancreatic Insufficiency Drug Products for Over-the-Counter Human Use" (56 FR 32282, July 15, 1991), and "Guidance for Industry: Exocrine Pancreatic Insufficiency Drug Products— Submitting NDAs," issued in April 2006 and available online at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071651.pdf>).

For each of these drugs, FDA reviewed the publicly available information and published in the **Federal Register** a discussion regarding the drug's safety and effectiveness, and any conclusions reached by the Agency based on that review. Firms then submitted drug applications referencing the public information and/or the **Federal Register** notice to address certain information requirements needed for an application.

Does published literature of sufficient quality exist for some animal drugs that could be used to support safety and effectiveness evaluations for these

currently unapproved marketed drugs? For which drugs might this be feasible? What attributes make published literature of sufficient quality to contribute to such an evaluation?

B. Limiting the Use of Enforcement Discretion

As stated previously, the Agency acknowledges that the practice of exercising enforcement discretion in certain circumstances is necessary to ensure the availability of some essential animal drug products. This practice of exercising enforcement discretion (*i.e.*, a decision on the part of the Agency to not take enforcement action in certain circumstances) is not only important for managing limited Agency resources related to compliance activities but is also important for assuring that certain animal drug products remain available for addressing the health needs of animals. However, FDA's goal is to limit, to the extent possible, its use of enforcement discretion for unapproved animal drugs.

What factors should the Agency consider when determining which unapproved animal drug products or categories of products should be the subject of enforcement discretion?

IV. Comments

Interested persons may submit to the Division of Dockets Management (*see ADDRESSES*) either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket

number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: December 15, 2010.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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BILLING CODE 4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Submission for OMB; Comment Request; National Epidemiologic Survey on Alcohol and Related Conditions—III

SUMMARY: In compliance with the requirement of Section 3507(a)(1)(D) of the Paperwork Reduction Act of 1995, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institutes of Health (NIH) has submitted to the Office of Management and Budget (OMB) a request for review and approval of the information collection listed below. This proposed information collection was previously published in the *Federal Register* on October 15, 2010, and allowed 60-days for public comment. No public comments were received. The purpose of this notice is to allow an additional 30 days for public comment. The National Institutes of Health may not conduct or sponsor, and the respondent is not required to respond to, an information collection

that has been extended, revised, or implemented on or after October 1, 1995, unless it displays a currently valid OMB control number.

Proposed Collection: Title: National Epidemiologic Survey on Alcohol and Related Conditions—III. *Type of Information Collection Request:* NEW. *Need and Use of Information Collection:* This study will determine the prevalence of alcohol use patterns and alcohol use disorders and their associated disabilities in a representative sample of adults in the United States population. The primary objectives of this study are to: (1) Understand the relationships between alcohol use patterns and alcohol use disorders and their related psychological and medical disabilities with a view toward designing more effective treatment, prevention and intervention programs; (2) identify subgroups at high risk for alcohol use disorders that are complicated by associated disabilities; (3) understand treatment utilization, unmet treatment need, barriers to treatment, health disparities, and economic costs of alcohol use disorders and their associated disabilities; and (4) identify environmental and genetic risk factors and their interactions that are associated with harmful consumption patterns and alcohol use disorders and their associated disabilities. *Frequency of Response:* On occasion. *Affected Public:* Individuals. *Type of Respondents:* Adults.

ESTIMATED TOTAL ANNUAL BURDEN

Type of respondents	Estimated number of respondents	Estimated number of responses per respondent	Average burden hours per response	Estimated total annual burden hours requested
Adults	44,900	1	1.0	44,900
Adults	1,700	2	1.7	2,890
Total	47,790

The annualized cost to respondents is estimated to be \$936,684.00. There are no Capital Costs to report. There are no Operating or Maintenance Costs to report.

Request for Comments: Written comments and/or suggestions from the public and affected agencies are invited on one or more of the following points: (1) Whether the proposed collection of information is necessary for the proper performance of the function of the agency, including whether the information will have practical utility;

(2) The accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) Ways to enhance the quality, utility, and clarity of the information to be collected; and (4) Ways to minimize the burden of the collection of information on those who are to respond, including the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

Direct Comments to OMB: Written comments and/or suggestions regarding the item(s) contained in this notice, especially regarding the estimated public burden and associated response time, should be directed to the: Office of Management and Budget, Office of Regulatory Affairs, *OIRA_submission@omb.eop.gov* or by fax to 202-395-6974, Attention: Desk Officer for NIH. To request more information on the proposed project or to obtain a copy of the data collection plans and instruments, contact: Dr.