#79

Guidance for Industry

DISPUTE RESOLUTION PROCEDURES FOR SCIENCE-BASED DECISIONS ON PRODUCTS REGULATED BY THE CENTER FOR VETERINARY MEDICINE (CVM)

This guidance document describes the procedures for handling a request for an internal review of scientific controversies relating to a decision affecting animal drugs or other products that are regulated by CVM. PPM 1240.3130 (Center Appeals Procedure Guide) of the CVM Program Policy and Procedures (P&P) Manual describes CVM's appeals procedure. Because this Guide predates the Food and Drug Administration Modernization Act (FDAMA), CVM is revising its procedures. This guidance supersedes PPM 1240.3130, which has been deleted from the P&P Manual.

Submit comments on this guidance at any time. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments on the guidance at http://www.regulations.gov. All written comments should be identified with the Docket No. .03D-0167.

For further information regarding this guidance document, contact Marcia Larkins, Center for Veterinary Medicine (HFV-3), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9015. E-mail: marcia.larkins@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at either http://www.fda.gov/AnimalVeterinary/default.htm or http://www.regulations.gov .

Paperwork Reduction Act (PRA) Public Burden Statement

According to the Paperwork Reduction Act of 1995, a collection of information should display a valid OMB control number. The valid OMB control number for this information collection is 0910-0566.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
July 19, 2005

DISPUTE RESOLUTION PROCEDURES FOR SCIENCE-BASED DECISIONS ON PRODUCTS REGULATED BY CVM

This guidance represents the Food and Drug Administration's current thinking on resolving scientific disputes concerning the products regulated by CVM. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidances means that something is suggested or recommended, but not required.

This guidance document describes a recommended approach for resolution of disputes relating to scientific controversies. A scientific controversy involves issues that arise within the context of the Center's regulation of a specific product and are related to matters of technical expertise that require some specialized education, training, or experience in order to be understood and resolved. The guidance document describes the dispute resolution procedures that we recommend be followed by sponsors, applicants, and manufacturers when requesting review of FDA decisions related to regulated products for animals. (Hereafter in this document, the term applicant includes a sponsor, applicant, or manufacturer.)

II. BACKGROUND

On November 21, 1997, the President signed the Food and Drug Modernization Act of 1997 (FDAMA) into law (Public Law 105-115). Section 404 of FDAMA amends the Federal Food, Drug, and Cosmetic Act (the act) by adding a provision (Section 562, 21 U.S.C. § 360bbb-1) for dispute resolution. If a procedure under which an applicant could request a review of a scientific controversy related to human drugs, animal drugs, human biologics, or devices did not already exist, either as a provision in the act or a regulation promulgated under the act, FDAMA required FDA to establish a procedure by regulation through which an applicant may request review of such scientific controversy, including a review by an appropriate scientific advisory panel or advisory committee. Prior to FDAMA, a procedure for review of such controversies was provided under §10.75 (21

CFR 10.75), Internal agency review of decisions. § 10.75 provides for internal agency review of a decision through "the established agency channels of supervision or review." To implement Section 562, FDA amended 21 CFR Part 10 (Administrative Practices and Procedures) to add the following:

> A sponsor, applicant, or manufacturer of a drug or device regulated under the act or the Public Health Service Act (42 U.S.C. 262), may request review of a scientific controversy by an appropriate scientific advisory panel as described in section 505(n) of the act, or an advisory committee as described in section 515(g)(2)(B) of the act. The reason(s) for any denial of a request for such review shall be briefly set forth in writing to the requester. Persons who receive a Center denial of their request under this section may submit a request for review of the denial. The request should be sent to the Chief Mediator and Ombudsman. (21 CFR 10.75(b)(2), 63 FR 63982, November 18, 1998)

There are significant differences in the statutory provisions that govern the regulation of the various products regulated by FDA's Centers, and similarly in the existing appeal and dispute resolution mechanisms and approaches to advisory committee management. Therefore, FDA did not include in § 10.75 specific procedures for requesting reviews of scientific controversies, but has instead adopted a Center-based approach to resolving such disputes for drugs or devices. Each affected Center is responsible for developing and administering its own processes for handling requests for reviews of scientific controversies. This guidance sets forth CVM's recommended processes. Although section 404 of FDAMA only required the agency to establish dispute resolution procedures for scientific controversies involving drugs and devices and § 10.75(b)(2) only applies to drugs and devices, the procedure in this guidance may also be used by applicants for other products regulated by CVM.

III. SCIENTIFIC CONTROVERSIES ELIGIBLE FOR DISPUTE RESOLUTION

It is not CVM's intent for applicants to use the dispute resolution procedure as their initial response to "incomplete letters" that the Center sends to applicants when the Center needs more information than contained in a submission in order to make a decision issued as a result of INAD (Investigational New Animal Drug), NADA (New Animal Drug Application), ANADA (Abbreviated New Animal Drug Application), IFA (Investigational Feed Additive), or FAP (Feed Additive Petition) review. A scientific controversy may be considered eligible for dispute resolution when there is an unresolved disagreement between applicants and Division Directors on scientific decisions made by CVM including, but not limited to, the following examples:

A. CVM requests specific studies from an applicant in order to meet minimum pre-approval data requirements (e.g., a request for more than one field trial, or a request for antimicrobial resistance studies, or a request based on a recently implemented regulation/guidance).

B. In compliance with the provisions of section 512(b)(3) (21 U.S.C. 360b(b)(3)) of the act, CVM changes the data/ protocol requirements that it had previously agreed to with the applicant (e.g., based on new information discovered after a pre-submission conference).

C. CVM determines that the information submitted by an applicant is inadequate (e.g., because the description of a particular aspect of a study in the protocol is inadequate, or because a study is not acceptable for or applicable to a particular indication or assessment of safety, or because the inferential value of an efficacy study is insufficient to support a claim).

D. CVM and an applicant have different interpretations of the results/data from a study.

IV. DISPUTE RESOLUTION PROCEDURE

We recommend the applicant follow the dispute resolution procedure as explained below when requesting review of a written scientific decision. The key features of the dispute resolution procedure are also summarized in APPENDIX I, CVM Decision Review Process.

A. Review by the Supervisory Chain of Command

The Code of Federal Regulations at § 10.75 states that any interested person may obtain review of any agency decision by raising the matter through established agency channels of supervision or review. CVM encourages applicants to begin the resolution of science-based disputes with discussions with the review team/group, including the Team Leader or Division Director. The Center prefers that differences of opinion regarding science or science-based policy be resolved between the review team/group and the applicant**.** If the matter is not resolved by that method, we recommend that the applicant follow the procedure below.

1. Office Level Appeals Procedure

a) When an applicant has a scientific disagreement with a written decision by FDA, the applicant may submit to the Division Director, who is responsible for the team/group/individual that communicated the decision, a request for review of that decision. The initial appeal should identify the information in the administrative file (the file) upon which the request is based. If the appeal contains new information, not previously contained in the administrative file, the matter will, in accordance with § 10.75(d), be returned to the appropriate lower level in the agency for reevaluation based on the new information. A reevaluation, based on the new information, is subject to the corresponding review times provided by statute or regulation (e.g., 180 days for a NADA).

b) The Division Director should prepare a written response to the applicant's request within 30 calendar days of receiving the request for review. The response should include the reasoning/rationale for the decision.

c) If the applicant disagrees with the Division Director’s response, the applicant may appeal in writing to the Office Director. The Office Director should prepare a written response to the applicant’s appeal within 40 calendar days of receiving the formal appeal. The response should include the

reasoning/rationale for the decision. The following options outlined below are some but not all of the options available to the Office Director:

i. If the Office Director agrees with the applicant's position, the Office Director should document his or her decision in writing and return the file to the Division Director. The Division Director should expeditiously take appropriate action to implement the Office Director's decision and after obtaining the Office Director's concurrence on the response, communicate the action (including the reasoning/rationale) to the applicant.

ii. If the Office Director disagrees in whole or in part with the applicant's position, he or she should document the decision in writing and return the file to the Division Director. The Division Director should obtain the Office Director's concurrence on the response and notify the applicant of the decision (including the reasoning/rationale for the decision) and of the applicant's right to have the issue forwarded to the CVM Ombudsman with a request for either 1) consideration by a Deputy Center Director Ad Hoc Appeals Committee (Ad Hoc Appeals Committee) or 2) review by the Veterinary Medicine Advisory Committee (VMAC) if the product is a drug or device as required by § 10.75(b)(2). Applicants of other products regulated by CVM may also request review by VMAC. These two options for appeal are described below. Either request should be sent in writing to the CVM Ombudsman with courtesy copies to the appropriate Division and Office Directors. It is the applicant's responsibility to decide whether to continue to pursue the review of a scientific decision. If the applicant requests consideration by the Ad Hoc Appeals Committee, the CVM Ombudsman should provide written acknowledgement to the applicant, within 14 days, and forward the request to the CVM Deputy Director. If the applicant requests consideration by VMAC, the CVM Ombudsman should provide similar acknowledgement and forward the request to the CVM Director.

2. Deputy Center Director Ad Hoc Appeals Committee Procedure:

a) The Committee should generally consist of the CVM Deputy Director (or on rare occasions, an alternate senior level Center manager), who acts as the Chair, and a minimum of three members from the Center's management and other experts from the federal government appointed by the Chair. Selection of these individuals should be on an ad hoc basis, depending on the issue involved. It is expected that the Committee may also seek expert advice by consulting on an individual, as-needed basis with others inside the Agency as well as outside the Agency or the government, who possess expertise on the matter under consideration.

b) The Chair should provide, in writing, an opportunity for the applicant to submit written arguments and to meet with the Committee. If the applicant decides to meet with the Committee, the applicant may bring as many consultants as the applicant wishes. The meeting is to provide an opportunity for the full exchange of information and views between the Committee and the applicant. The meeting should be structured to allow for presentation by the applicant, input by the appropriate CVM reviewing Division, and appropriate discussion. Finally, after the meeting, the Chair and the Committee members should deliberate without the applicant, the applicant's consultants, or personnel from the CVM reviewing Division.

c) Following the deliberations, the Chair, with the advice of the Committee, should make a decision on the issue and take appropriate action to implement the decision. The Chair should provide the decision or a status report on the appeal to the applicant in writing within 60 calendar days following the Committee meeting. The response should include the reasoning/rationale for the decision.

d) If the Chair disagrees with the applicant's position, and the applicant is not satisfied with the decision, the applicant may appeal the Committee decision to the Center Director by letter. The Center Director should respond in writing to the applicant's appeal within 40 calendar days of receipt. The response should include the reasoning/rationale for the decision. If the Center Director also disagrees with the applicant's position, the applicant may submit an appeal by letter to the Office of the Commissioner either directly or through the Office of the FDA Ombudsman.

B. Veterinary Medicine Advisory Committee (VMAC) Procedure

CVM has one standing advisory committee, the VMAC. The committee consists of 13 members representing a wide spectrum of disciplines and interests associated with veterinary medicine. The committee meets once or twice a year to give advice on broad scientific issues identified by CVM and the agency. In cases involving broad scientific matters having a general impact on the veterinary drug industry, and if time and budgetary constraints permit, the Center may refer a request for the review of a scientific controversy to VMAC. A request for review by VMAC from an applicant should relate to agency action on the applicant's own product.

1. Upon the applicant's request, the Center may refer a scientific controversy to VMAC for review after the applicant has requested review by the supervisory chain of command through the level of the Office Director, as described in IV(A). The applicant may submit a written request for review by VMAC to the CVM Ombudsman for consideration by the Center Director. CVM recommends that applicants filing a request for review by VMAC provide the CVM Ombudsman with a concise summary of the scientific issue in dispute, including a summary of the particular FDA action or decision to which the applicant objects, the results of all efforts that have been made to resolve the dispute to date, and a clear articulated

summary of the arguments and relevant data and information. The information collected will form the basis for resolving the dispute between the applicant and FDA. The Center Director should determine whether review by VMAC is appropriate or, depending on the scientific issue involved, whether the Ad Hoc Appeals Committee review procedure might provide a more efficient means of resolving the scientific controversy.

2. The Center should send a written response to the applicant's request for VMAC review within 30 calendar days of receiving the request. If the CVM Director denies a request for VMAC review, the reasons for the denial must be briefly set forth in writing to the applicant, if the product is a drug or device, as required by §10.75 (b)(2). The reasons for the denial should also be briefly set forth in writing to applicants of other products regulated by CVM. The applicant may submit to the FDA Ombudsman a request for review of the denial. The FDA Ombudsman should not make an independent determination of whether a VMAC review should be granted, but should work informally with the Center and the person denied VMAC review to develop a mutually acceptable approach, taking into account all relevant factors (63 FR 63978 at 63979).

3. If the Center Director grants a request for VMAC review of the scientific controversy, VMAC should make a recommendation to the Center Director who should consider it in making a decision. While the purpose of an advisory committee is to provide expert scientific advice and recommendations, the conclusions of the VMAC are not binding on the agency. The Center Director should issue a written decision, including the reasoning/rationale for that decision within 60 calendar days following the VMAC meeting. If the Center Director disagrees with the applicant's position, and the applicant is not satisfied with the decision, the applicant may choose to request further review by the Office of the Commissioner.

Unless otherwise provided by law, the resolution of a scientific dispute by CVM is not final agency action for purposes of judicial review.

V. THE ROLE OF THE OMBUDSMAN

CVM's Ombudsman plays an important role in the dispute resolution process. This person is committed to handling disputes in a neutral and confidential manner and to helping achieve equitable solutions. The Ombudsman can help ensure that the process proceeds as smoothly and fairly as possible.

A May 1, 1998, Presidential memorandum directs each federal agency to "promote greater use of mediation, arbitration, early neutral evaluation, agency ombudsman and other ADR [alternative dispute resolution] techniques." Ref. 1. In addition to FDA's formal processes, several ombudsman offices, including one in CVM, have been established to facilitate the resolution of disputes informally. FDA has established the Office of the Ombudsman within the Commissioner's Office to resolve inter-center disputes, hear appeals of decisions of the Center Directors, and to resolve other disputes

where the complainant has concerns about raising the issue with a Center. (See 63 FR 63978).

In a memo dated June 29, 1995, the Commissioner of Food and Drugs (the Commissioner) reminded all FDA employees that companies are free to vigorously challenge agency positions and requirements, and to freely voice their views. Ref. 2. By letter of the same date, the Commissioner assured members of Congress that any act or threat of retaliation by any FDA employee is totally unacceptable and will not be tolerated. Anyone who believes retaliation has occurred, or is likely to occur, is urged to contact the CVM Ombudsman, Center management, or the Office of the FDA Ombudsman.

The function of the CVM Ombudsman is to help resolve disputes at the Center level, typically in accordance with the procedures described in this guidance. The CVM Ombudsman facilitates the resolution of disputes by operating in a neutral role, to help achieve equitable solutions. The Ombudsman is also the Center's point of contact for information on the dispute resolution process (see 63 FR 63978) and is also responsible for assuring the effective implementation of the process. An applicant may contact the Ombudsman when the applicant does not know where or how to begin an appeal, little progress is being made going up the chain of command, or a matter is not resolved in the supervisory chain of command procedure (see IV. A. above). The Ombudsman helps to facilitate administratively the formal appeals process above the Office level. The Ombudsman serves as a neutral and may suggest alternatives to the procedures described in this guidance for resolving disputes during the appeals process, subject to mutual agreement by the applicant and CVM as described in the Administrative Dispute Resolution Act (ADRA) of 1996. 5 U.S.C. 571 (3) and (9), 573 (b).

Additionally, anyone who believes that an employee has not followed proper good guidance practices or has treated this or any guidance document as a binding document may also ask the CVM Ombudsman for assistance. If the issue is not resolved at the Center level the complainant may ask FDA's Office of the Ombudsman to become involved. 21 CFR 10.115(o).

VI. REFERENCES

1. President William J. Clinton. Memorandum for Heads of Executive Departments and Agencies. Designation of Interagency Committees to Facilitate and Encourage Agency Use of Alternate Means of Dispute Resolution and Negotiated Rulemaking. May 1, 1998.

2. Commissioner David A. Kessler. Memorandum to All FDA Employees. Allegations of Retaliation. June 29, 1995.

CVM DECISION REVIEW PROCESS