Guidance for Industry

Formal Dispute Resolution: Appeals Above the Division Level

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Procedural
February 2000

OMB Control Number 0910-0430
Expiration Date: 08/31/2012
See additional PRA statement in Section V of this guidance
(Note: PRA information added 05/04/2011)

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Additional copies of this Guidance are available from:

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Division of Communications Management
Drug Information Branch, HFD-210
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, Rockville, MD 20857
(Phone 301-827-4573)
Internet: http://www.fda.gov/cder/guidance/index.htm.

or

Office of Communication, Training and
Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
Internet: http://www.fda.gov/cber/guidelines.htm.
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I. INTRODUCTION

This document is intended to provide guidance for industry on procedures adopted by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) for resolving scientific and procedural disputes that cannot be resolved at the Division level. This guidance describes procedures for formally appealing[2] such disputes to the Office or Center level and for submitting information to assist Agency officials in resolving the issue(s) presented.

Scientific (including medical) disputes and procedural (including administrative) disputes will inevitably arise during the drug development, new drug review, generic drug review, and postmarketing oversight processes. As these disputes can involve complex judgments and issues that are scientifically and commercially important, it is critical that there be procedures in place that will encourage open, prompt discussion of such disputes, which will usually lead to their resolution. The procedures and policies described in this guidance document are intended to promote rapid resolution of scientific and procedural disputes between sponsors and the Agency. For the purposes of this document, the term *sponsor* includes any sponsor, applicant, or manufacturer of a new drug, generic drug, or biologic product regulated by the Agency under the Federal Food, Drug, and Cosmetic Act (the Act) or section 351 of the Public Health Service Act (the PHS Act).

FDA regulations (21 CFR 10.75) provide a mechanism for any interested person[3] to obtain formal review of any Agency decision by raising the matter with the supervisor of the employee who made the decision. If the issue is not resolved at the primary supervisory level, the interested person may request that the matter be reviewed at the next higher supervisory level. This process may continue through the Agency's chain of command, through the Centers to the Commissioner of Food and Drugs. Regulations for dispute resolution during the IND process

[1]This guidance has been prepared by the Review Management Working Group in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration. This guidance document represents CDER's and CBER=s current thinking on dispute resolution. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

[2]As used in this guidance document, an appeal is a request for formal dispute resolution.

[3]An *interested person* is a person who submits a petition, comment, or objection or otherwise asks to participate in an informal or formal administrative proceeding or court action (21 CFR 10.3). This definition of interested person includes a sponsor, applicant, or manufacturer of a drug or biological product.

(21 CFR 312.48) and the NDA/ANDA process (21 CFR 314.103) specifically establish similar procedures for the resolution of scientific and procedural matters at the Division level and subsequent formal review of decisions through Center management. CDER and CBER regulations also provide that a sponsor may request that the Agency seek the advice of outside experts, including an appropriate advisory committee, in resolving the matter (312.48(c)(3) and 314.103(c)(3)).

Section 404 of the Food and Drug Administration Modernization Act of 1997 creates new section 562 of the Act (21 U.S.C. 360bbb-1). Section 562 of the Act provides that if, regarding an obligation concerning drugs or devices under the Act or section 351 of the PHS Act, there is a scientific dispute between the Agency and a sponsor, applicant, or manufacturer and no specific provision of the Act or regulation provides a right of review of the matter in controversy, FDA shall, by regulation, establish a procedure under which such sponsor, applicant, or manufacturer may request a review of the controversy, including review by an advisory committee. Section 562 of the Act further provides that such review of the controversy, if granted, shall take place in a timely manner.

In the *Federal Register* of November 18, 1998 (63 FR 63978), FDA amended 21 CFR 10.75 to explicitly state that a sponsor, applicant, or manufacturer of a drug or device may request review of a scientific controversy by an appropriate advisory committee. In recognition of the Agency's authority to determine whether to seek the advice of an advisory committee in resolving a scientific dispute, the amendment to the regulation states that the reason(s) for any denial of a request for advisory committee review will be set forth in writing to the requester. A person whose request has been denied at the Center level may submit a request for review of the denial at the Commissioner's Office level. Such request should be sent to the Agency's Chief Mediator and Ombudsman. In the preamble to the final rule, FDA stated that implementation of this provision would be undertaken by the individual FDA Centers and would be described in guidance documents. This document is intended to meet that commitment.

A. PDUFA Products

The Prescription Drug User Fee Act of 1992 (PDUFA) was reauthorized in November 1997 (PDUFA 2). In conjunction with PDUFA 2, FDA agreed to specific performance goals (PDUFA goals) for activities associated with the development and review of products in human drug applications as defined in section 735(1) of the Act (21 U.S.C. 379g(1)) (PDUFA products). The PDUFA goals are summarized in "PDUFA Reauthorization Performance Goals and Procedures," an enclosure to a letter dated November 12, 1997, from the Secretary of Health and Human Services, Donna E. Shalala, to Senator James M. Jeffords. The PDUFA goals for major dispute resolution provide the following time frames for Agency response to formal appeals regarding scientific or procedural matters:

Fiscal Year (FY) 1999	70% acted upon within 30 calendar days
FY 2000	80% acted upon within 30 calendar days
FY 2001 and subsequent years	90% acted upon within 30 calendar days

Acted upon, in this context, includes, but is not limited to, requesting additional information, scheduling a meeting with the sponsor (ordinarily such meetings will be considered type A meetings[4]), deciding to submit the issue(s) for presentation to an advisory committee, requesting an opinion from the Office of Chief Counsel, granting the appeal, or denying the appeal.

B. Scope of the Guidance

The policies and procedures described in this guidance document implement section 562 of the Act, Agency regulations, and the PDUFA goals for dispute resolution. Unless otherwise stated, this guidance applies to PDUFA products and non-PDUFA products (e.g., generic drugs).

At any time, a sponsor may choose not to follow the formal dispute resolution process and may informally raise a procedural or administrative matter with the CDER or CBER Ombudsman (ээ 312.48 and 314.103). A sponsor who remains dissatisfied with the procedure used by the Center in formal resolution of a dispute after the Center Director has made a determination on the issue(s) involved may also seek the assistance of the CDER or CBER Ombudsman in facilitating resolution of the matter. The procedures described in this guidance do not apply to such informal dispute resolution through the CDER or CBER Ombudsman. Furthermore, such informal contacts with the Ombudsman concerning PDUFA products are not subject to the PDUFA goals and therefore progress on the resolution of the issue(s) will not be formally tracked in CDER or CBER databases.

II. FORMAL DISPUTE RESOLUTION

As described in Agency regulations (21 CFR 10.75, 312.48, 314.103), a sponsor should initially seek resolution of any scientific or procedural dispute at the Division level using formal or informal mechanisms, as appropriate. If these mechanisms do not lead to resolution, the sponsor may formally request reconsideration of the matter by the Division after providing the Division an opportunity to review any materials the sponsor intends to rely on in an appeal to the next level. *Because all Agency decisions on the matter must be based on information in the matter's administrative file (э 10.75(d)), no new information should be submitted as part of a request for reconsideration or appeal*. If the sponsor has new information that may affect the original decision, any appeal should be deferred and the new information should be submitted and reviewed by the Division. For example, a response to an action letter should initially be submitted to the Division for review. If an issue is still not resolved to the satisfaction of the sponsor at the Division level, the sponsor may appeal the matter to the appropriate Office Director. If the sponsor is not satisfied with the decision made by the Office Director with respect to the issue(s), the sponsor may appeal the matter to the appropriate Deputy Center

[4] In February 1999 (64 FR 13591), FDA made available for comment a draft guidance for industry, *Formal Meetings with Sponsors and Applicants for PDUFA Products*, describing policies and procedures that will be adopted by CDER and CBER to enhance the productivity of meetings between the Agency and sponsors of PDUFA products.

Director. If the sponsor is not satisfied with the decision made by the Deputy Center Director with respect to the issue(s), the sponsor may appeal the matter to the Center Director.

At any point in the formal dispute resolution process, a sponsor may request that a scientific dispute be reviewed by an appropriate advisory committee. Such a request for advisory committee review may be part of the original formal appeal or may be an amendment to the formal appeal. If a sponsor believes that review by an advisory committee is the most appropriate venue for resolution of a scientific controversy, such a request should be made as early in the dispute resolution process as feasible. Such early notice will enable the Center to evaluate at every step in the process whether to send the matter to an advisory committee.

III. PROCEDURES FOR SUBMITTING A REQUEST FOR FORMAL DISPUTE RESOLUTION

A. How to Request Formal Dispute Resolution

A sponsor interested in requesting formal dispute resolution by the Office or Center should do so only if an attempt for resolution at the previous supervisory level was unsuccessful. The sponsor should submit a written request and supporting documentation to the appropriate CDER or CBER component as follows, with a copy submitted as an amendment to the application to the appropriate Division document room.

Requests for formal dispute resolution with CDER should be submitted to the Center Formal Dispute Resolution Project Manager (DRPM) *except* requests for formal dispute resolution concerning generic drugs should be submitted directly to the Office of Generic Drugs.

For CDER issues other than generic drug issues the following address should be used:

Formal Dispute Resolution Project Manager (DRPM)
Food and Drug Administration
Center for Drug Evaluation and Research
Mail Code HFD-002
5600 Fishers Lane
Rockville, MD 20857

For CDER generic drug issues the following address should be used:

Director
Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Mail Code HFD-600
7500 Standish Place
Rockville, MD 20855

All requests for formal dispute resolution with CBER should be submitted to:

Formal Dispute Resolution Project Manager (DRPM)
Food and Drug Administration
Center for Biologics Evaluation and Research
Mail Code HFM-007
1401 Rockville Pike
Rockville, MD 20852

B. Supporting Information

To make the most efficient use of Agency and industry resources, any request for formal dispute resolution should include adequate information to explain the nature of the dispute and to allow the Agency to determine the necessary steps to resolve the matter quickly and efficiently. Each request should include the following:

1. Cover sheet that clearly identifies the submission as FORMAL DISPUTE RESOLUTION REQUEST in bold, uppercase letters.
2. Application number (IND, NDA, BLA, ANDA), if applicable.
3. Proprietary name and established name for a product in CDER; proper name and trade name for a product in CBER.
4. Division or Office where the application is filed.
5. Proposed indication(s), if applicable.
6. Brief, but comprehensive statement of each issue to be resolved:
   - ! Clearly describe the issue to be resolved.
   - ! Identify the issue as scientific, procedural, or both.
   - ! State the steps that have been taken to resolve the issue, including informal dispute resolution.
   - ! Identify possible solutions, including, for scientific issues, whether an advisory committee review is requested.
   - ! State expected outcome.
7. Statement identifying the division that issued the original decision on the matter and, if applicable, the last Agency official who attempted to formally resolve the matter.
8. List of documents previously submitted to the Agency that are deemed necessary for resolution of the issue(s). If a sponsor prefers, copies of such documents may be resubmitted to the Agency.
9. Statement that the previous supervisory level has received and had the opportunity to review all of the material relied on for dispute resolution.
10. Name, title, and telephone and fax numbers of company contact for the appeal.

All Agency decisions on a matter are based on the information in the matter's administrative file (ə 10.75(d)). In general, new information, not seen at the review division or previous supervisory levels of review, should not be provided. If a sponsor presents new information about an issue in requesting formal dispute resolution, the matter will be returned to the Division for reevaluation based on the new information.

IV. AGENCY ACTION

The DRPM will forward the formal request to the appropriate CDER or CBER official (the Official) to respond to the formal appeal as established under the Center chain of command, enter the necessary information into the appropriate tracking system, and send an acknowledgment letter to the sponsor. The Official will review the matter's administrative record and provide a response. The response could be a decision on the matter, but could also be a decision to seek advice from an advisory committee or other internal or external experts or to ask the sponsor for more information.

A. Written Response

FDA will generally send a written response to a sponsor who requests formal dispute resolution. The written response should specifically agree or disagree with the outcome desired by the sponsor, agree or disagree with parts of the proposed outcome, or indicate a resolution that is different than that proposed by the sponsor. If the Agency does not agree with the sponsor's position, the response should include reasons for the disagreement and any actions that the sponsor can take to address issues the Agency has raised.

1. PDUFA Products

If the product underlying a procedural or scientific dispute is a PDUFA product, the Official should complete the review within 30 calendar days from the DRPM's receipt of the formal request. The Official should contact the sponsor within the 30 day window via written response or telephone response (*30 day response*). If the response is by telephone, the reviewing Official should provide a written confirmation of the formal dispute resolution outcome to the sponsor or applicant within 14 calendar days from the date of the telephone call. If FDA is unable to complete the review and respond within 30 days, the Official should notify the sponsor, explain the reasons for the delay, and discuss the time frame for completing the review.

Where additional data or input from others are needed to reach a decision on the appeal, the 30 day response should be a description of the plan for obtaining the information (e.g., requesting further information from the sponsor, deciding to schedule a meeting with the sponsor, bringing the issue for discussion at an advisory committee). In such cases, once the required information is received by the Agency, the Official will again have 30 calendar days from the receipt of the required information in which to respond to the appeal and state whether the Agency agrees or disagrees with the sponsor=s stated position.

2. Non-PDUFA Products

If the matter under appeal does not pertain to a PDUFA product, the Official should make all reasonable efforts to resolve the dispute as expeditiously as possible, taking into consideration available resources, and should provide a written or telephone response to the sponsor in a timely fashion. If the response is by telephone, the reviewing Official should subsequently provide a written confirmation of the formal dispute resolution outcome to the sponsor.

B. Response to a Request for Advisory Committee Review

If a sponsor seeking resolution of a scientific dispute requests advisory committee review of the matter, the Official will determine whether such review is appropriate and would be helpful to the Agency at that time in the formal appeal process. The Official will communicate this determination to the sponsor following the procedures described in **Written Response** above.

An issue may be appropriate for advisory committee review if it is related to matters of technical expertise that require some specialized education, training, or experience to understand and resolve. Issues that generally are not appropriate for advisory committee review include those that involve: (1) potential criminal activity (e.g., data fraud, submission of false information, unauthorized disclosure of proprietary information); (2) allegations of intellectual or regulatory bias, including differential treatment, on the part of FDA employees, members of FDA advisory committees, or other special Government employees; (3) regulatory jurisdiction (e.g., which FDA component will have lead regulatory responsibility for a particular matter) or other matters in which regulatory policy or procedures are the dominant concerns; and (4) matters for which the Center Director has not been delegated authority.

The Official may decide not to send the matter to an advisory committee and may consult with one or more of the members of the advisory committee or other internal or external experts in resolving the matter.

1. Advisory committee review

If the request for review by an advisory committee is granted, the matter will be brought to the next scheduled advisory committee meeting for which there is time available on the agenda for adequate discussion of the issue. Due to administrative concerns related to organizing each advisory committee meeting (e.g., establishing an agenda, sending background information to the advisory committee members prior to the meeting), it may not be feasible to raise the matter at the next scheduled meeting.

As discussed in Agency regulations (ə 14.5(b)) and the preamble to the final rule amending ə 10.75, the advice and recommendations of an advisory committee after review of a scientific dispute would not bind the Agency to a particular action or policy. After receiving the advice of the appropriate advisory committee, the Agency should notify the sponsor of its determination on the matter within 30 days. Unless otherwise provided by law, an FDA decision based on an advisory committee recommendation is not final Agency action subject to judicial review.

2. Denial of a request for advisory committee review

If the Official does not grant advisory committee review, the Official will notify the sponsor in writing of such decision, including the reason(s) for the denial. This notification may be included in the written response to the formal dispute resolution.

A sponsor denied advisory committee review of a scientific dispute may appeal the denial up the chain of command in the Center as part of any subsequent request for dispute resolution of the underlying matter. After exhausting the Center's mechanisms for appealing the decision denying advisory committee review, a sponsor may request review of the Center's decision through the Agency's supervisory chain of command to the Commissioner of Food and Drugs. As stated in ə 10.75, requests for such review should be submitted to the Agency's Chief Mediator and Ombudsman. Although not formally in the chain of command, the Chief Mediator and Ombudsman will work with the Center and the sponsor attempting to develop a mutually acceptable approach, taking into account all relevant factors. Unless otherwise provided by law, an FDA decision to deny a request for advisory committee review is not final Agency action subject to judicial review.

V. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 8 hours to prepare and submit a request for formal dispute, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to: Office of Regulatory Policy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002.

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information for FDA Form 1571 have been approved under OMB Control No. 0910-0014 and for FDA Form 356h have been approved under OMB Control No. 0910-0338.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0430 (expires 08/31/2012).