
Formal Dispute Resolution: Sponsor Appeals Above the Division Level

Guidance for Industry and Review Staff

Good Review Practice

**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)**

**November 2017
Procedural**

Revision 1

**OMB Control Number 0910-0430
Expiration Date: 02/28/2019
See additional PRA statement in section VII of this guidance**

Formal Dispute Resolution: Sponsor Appeals Above the Division Level Guidance for Industry and Review Staff

Good Review Practice

Additional copies are available from:

*Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002*

*Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353; Email: druginfo@fda.hhs.gov
<https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>*

and/or

*Office of Communication, Outreach, and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, rm. 3128
Silver Spring, MD 20993-0002*

*Phone: 800-835-4709 or 240-402-8010; Email: ocod@fda.hhs.gov
<https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>*

**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)**

**November 2017
Procedural**

Revision 1

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	BACKGROUND	2
A.	Regulatory Framework	2
B.	Formal Dispute Resolution User Fee Performance Goals	3
III.	CONSIDERATIONS FOR SPONSORS: BEFORE SUBMITTING A REQUEST FOR FORMAL DISPUTE RESOLUTION	4
A.	What Is an Appropriate Matter for a Formal Dispute Resolution Request?	4
B.	When Is a Matter Not Appropriate for a Formal Dispute Resolution Request?	5
C.	Is There New Information and/or Are There New Analyses of Previously Reviewed Data That the Sponsor Believes Is/Are Relevant?	6
D.	Can a Sponsor Request a Meeting as Part of an FDRR?	6
E.	Can a Sponsor Request an Advisory Committee Meeting as Part of FDR?	7
IV.	PROCEDURES FOR SUBMITTING A REQUEST FOR FORMAL DISPUTE RESOLUTION	7
A.	How to Request Formal Dispute Resolution	7
1.	<i>Requests for CDER</i>	7
2.	<i>Requests for CBER</i>	7
B.	Content and Format of an FDRR	8
V.	FDA ACTION	9
A.	Responses to an Appeal	9
1.	<i>Timelines for Reviewing Formal Dispute Resolution Requests for Human Drug Applications Covered by PDUFA, BsUFA, or GDUFA</i>	10
2.	<i>Timelines for Reviewing Formal Dispute Resolution Requests for Applications and Submissions Not Covered by PDUFA, BsUFA, or GDUFA</i>	11
B.	Additional Considerations Regarding Responses to Appeals That Request Advisory Committee Review	11
1.	<i>Granting a Request for Advisory Committee Review</i>	11
2.	<i>Denial of a Request for Advisory Committee Review</i>	12
VI.	REPEAT APPEALS	12
VII.	PAPERWORK REDUCTION ACT OF 1995	12

Formal Dispute Resolution: Sponsor Appeals Above the Division Level Guidance for Industry and Review Staff¹

Good Review Practice

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides recommendations for industry and review staff on the procedures in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) for resolving scientific and/or medical disputes² between CDER or CBER and sponsors³ that cannot be resolved at the division level. This guidance describes the formal dispute resolution (FDR) procedures for sponsors that wish to appeal⁴ a scientific and/or medical issue to the office or center level and provides a structured process for resolving disputes.

During the course of review of an investigational new drug application (IND), new drug application (NDA), biologics license application (BLA), or abbreviated new drug application (ANDA), a wide variety of important scientific and/or medical issues are considered that are central to product development. Sometimes, a sponsor may disagree with the Agency on a matter, and a dispute arises. Because these disputes often involve complex scientific and/or

¹ This guidance has been prepared by the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

² The FDA considers scientific and/or medical disputes to encompass procedural matters that may arise in the context of a larger scientific and/or medical dispute. For example, if a sponsor is disputing a clinical hold action for an investigational new drug application (IND), the formal dispute resolution request could include consideration of related procedural matters, such as inadequate communication between the sponsor and the review division at the time of the clinical hold decision.

³ For purposes of this guidance, the term *sponsor* includes any sponsor of an IND or applicant for a new drug application, abbreviated new drug application, or biologics license application under section 505 of the Federal Food, Drug, and Cosmetic Act or section 351 of the Public Health Service Act.

⁴ For purposes of this guidance, an *appeal* is a sponsor request for FDR.

Contains Nonbinding Recommendations

medical matters, it is critical to have procedures in place to help ensure open and prompt discussion. The procedures and policies described in this guidance are intended to promote rapid and fair resolution of scientific and/or medical disputes between a sponsor and CDER or CBER.⁵

In general, FDA's guidance documents 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. Although guidance documents do not legally bind the FDA, review staff may depart from guidance documents only with appropriate justification and supervisory concurrence.

II. BACKGROUND

A. Regulatory Framework

In 1997, Congress enacted section 562 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-1), which directed the FDA to ensure that it had adequate dispute resolution procedures to provide for appropriate review of scientific controversies between the FDA and members of regulated industry, including possible review by a scientific advisory committee.⁶ The Agency's implementation of section 562 was two-fold. First, the FDA amended 21 CFR 10.75, the general appeal regulation applicable across all FDA components, to provide for advisory committee review (21 CFR 10.75(b)(2); 63 FR 63978, November 18, 1998). Second, the Agency adopted an individual, center-based approach to the specific implementation of section 562's mandates, which would be detailed in center-issued guidances (63 FR at 63979).

At the time of section 562's enactment, in addition to the general, Agency-wide regulation set forth at 21 CFR 10.75, CDER and CBER had dispute resolution regulations that pertained to the IND and NDA processes (21 CFR 312.48, 314.103). Nonetheless, in response to the enactment of section 562, CDER and CBER created FDR. The guidance for industry *Formal Dispute Resolution: Appeals Above the Division Level* issued in February 2000 (2000 guidance) outlined the basic elements of FDR. The 2000 guidance brought together under the FDR umbrella

⁵ This guidance does not apply to purely internal disputes involving FDA staff. Additionally, this guidance is not intended to address the alternate dispute resolution pathway of appealing a dispute to the Drug Safety Oversight Board that exists for risk evaluation and mitigation strategies modified or required after initial drug approval (21 U.S.C. 355-1(h)(5)). For guidance on how to resolve disputes of scientific and technical issues relating to current good manufacturing practice requirements, see the guidance for industry *Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP*. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

⁶ Although section 562 refers to obligations concerning both drugs and devices, this guidance addresses FDR only as it pertains to CDER- and CBER-regulated products. Medical devices regulated by CBER are addressed in section II.B., Formal Dispute Resolution User Fee Performance Goals, and section V.A.2., Timelines for Reviewing Formal Dispute Resolution Requests for Applications and Submissions Not Covered by PDUFA, BsUFA, or GDUFA. This guidance does not address FDR for medical devices regulated by the Center for Devices and Radiological Health.

Contains Nonbinding Recommendations

various regulatory appeal mechanisms as they relate to CDER- and CBER-regulated user fee products.

As set forth in more detail below, FDR is intended to address scientific and/or medical disputes between a sponsor and CDER or CBER as such disputes relate to the sponsor's application for a product covered by user fee goals (user fee products). As such, CDER and CBER intend to manage any formal sponsor request⁷ for appeal of a scientific and/or medical matter related to an application for a user fee product under any of the available regulatory mechanisms (21 CFR 10.75, 312.48(c), 314.103(c)), through the FDR process.⁸ Any sponsor appeal of a scientific and/or medical matter proceeds to the next management level in the center chain of command above the level at which the decision being appealed was made. However, regardless of the regulatory mechanism cited by a sponsor, if a sponsor challenges specific administrative and/or procedural decisions that arise during the course of an FDR, CDER and CBER intend to review these interim decisions as part of the review of the pending substantive scientific and/or medical dispute, and not as a separate review.

B. Formal Dispute Resolution User Fee Performance Goals

In the Prescription Drug User Fee Act of 1992 (PDUFA) and subsequent reauthorizations,⁹ CDER and CBER agreed to specific performance goals for activities associated with the development and review of human drug applications, as defined in 21 U.S.C. 379g. These performance goals contain specific time frames for resolving disputes affecting an IND, NDA, or BLA. For disputes involving human drug applications covered by PDUFA, the PDUFA goal is to respond to an appeal of a dispute above the original signatory authority within 30 calendar

⁷ As stated earlier, this guidance describes the FDR procedures for sponsors that wish to appeal a scientific and/or medical issue regarding their application regulated by CDER or CBER. The guidance and procedures do not apply to other individuals or entities that wish to appeal a scientific and/or medical issue regarding an application regulated by CDER or CBER. To the extent that 21 CFR 10.75(c) may provide a separate mechanism for nonsponsors to request internal Agency review of a CDER or CBER decision on a scientific and/or medical issue regarding an application or submission, any such review is discretionary. Except in unusual circumstances, CDER and CBER generally do not intend to accept requests by nonsponsors for internal Agency review of a scientific and/or medical issue regarding an application or submission. The Agency believes that it is highly unlikely that an individual or entity other than the sponsor would have access to the information necessary to support a request for internal Agency review of these types of decisions. The Agency also believes that it is highly unlikely that a nonsponsor would be in a position to evaluate any product development considerations that may be affected by an Agency decision for which a nonsponsor might wish to request internal Agency review.

⁸ A sponsor seeking informal resolution of a specific issue, including, but not limited to, a procedural or administrative matter regarding a product, may raise the issue with the appropriate center ombudsman (21 CFR 312.48(b), 314.103(b)). CDER and CBER ombudsmen informally investigate and facilitate resolution of such issues. Such informal contacts with the ombudsman concerning human drug applications are not subject to user fee goals. It is important to note that although sponsors may seek informal advice from the ombudsman at any time, they should not engage the ombudsman in this manner and, at the same time, pursue FDR. Moreover, such requests for ombudsman assistance are outside the scope of FDR and this guidance.

⁹ In the PDUFA performance goals and procedures letter (available at <https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm>), PDUFA performance goals for FDR are listed under Major Dispute Resolution. CDER and CBER consider FDR and major dispute resolution to be synonymous. Although CBER employs the FDR process for all of its products, outcome reporting under PDUFA performance goals includes only those issues that involve PDUFA products.

Contains Nonbinding Recommendations

days of the center's receipt of the written appeal (see section V.A.1., Timelines for Reviewing Formal Dispute Resolution Requests for Human Drug Applications Covered by PDUFA, BsUFA, or GDUFA).

In the Biosimilar User Fee Act of 2012 (BsUFA), CDER and CBER agreed to specific performance goals for the review of biosimilar biological applications.¹⁰ For disputes involving human drug applications covered by BsUFA, the BsUFA goal is to respond to an appeal of a dispute above the original signatory authority within 30 calendar days of the center's receipt of the written appeal (see section V.A.1., Timelines for Reviewing Formal Dispute Resolution Requests for Human Drug Applications Covered by PDUFA, BsUFA, or GDUFA).

In the 2017 reauthorization of the Generic Drug User Fee Amendments of 2012 (GDUFA), CDER agreed to specific performance goals for the review of generic drug applications.¹¹ For disputes involving human drug applications covered by GDUFA, the GDUFA goal is to respond to an appeal of a dispute above the original signatory authority within 30 calendar days of the center's receipt of the written appeal (see section V.A.1., Timelines for Reviewing Formal Dispute Resolution Requests for Human Drug Applications Covered by PDUFA, BsUFA, or GDUFA).

For those applications not covered by PDUFA, BsUFA, or GDUFA, and for applications or submissions for CBER-regulated medical devices (covered by the Medical Device User Fee Act), the procedures described in this guidance generally will be applied and the time frames will be met as resources permit (see section V.A.2., Timelines for Reviewing Formal Dispute Resolution Requests for Applications and Submissions Not Covered by PDUFA, BsUFA, or GDUFA).

III. CONSIDERATIONS FOR SPONSORS: BEFORE SUBMITTING A REQUEST FOR FORMAL DISPUTE RESOLUTION

A. What Is an Appropriate Matter for a Formal Dispute Resolution Request?

CDER and CBER consider a regulatory action taken by the FDA that relates to a sponsor's application for a user fee product and has scientific and/or medical significance to be a matter that could be appropriately handled through FDR. The following are a few examples of regulatory actions that would be appropriate for a request for FDR:

¹⁰ In the BsUFA performance goals and procedures letter (available at <https://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/default.htm>), BsUFA performance goals for FDR are listed under Major Dispute Resolution. CDER and CBER consider FDR and major dispute resolution to be synonymous.

¹¹ In the GDUFA performance goals and procedures letter (available at <https://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm>), GDUFA performance goals for FDR are listed under Dispute Resolution.

Contains Nonbinding Recommendations

- Complete response (CR)
- IND clinical hold (partial or full)
- Request for breakthrough therapy designation denied
- Request for proprietary name review denied
- Refuse to receive for an ANDA

B. When Is a Matter Not Appropriate for a Formal Dispute Resolution Request?

Advice communicated in meeting minutes and other correspondences is not a regulatory action taken by CDER or CBER; therefore, it would not be an appropriate subject for a formal dispute resolution request (FDRR) by a sponsor. Agency communications such as meeting minutes or other correspondences (e.g., general advice letters) typically include recommendations and/or advice made to a sponsor that generally conveys CDER's or CBER's current thinking on a particular topic raised by the sponsor. Sponsors are not bound by such recommendations and/or advice.¹² Sponsors can follow the advice in meeting minutes or other correspondences, or they can use an alternative approach, if the approach satisfies the requirements of the applicable statutes and regulations. Also, sponsors may approach the review division and/or the next highest management level to further discuss advice provided in meeting minutes or other correspondences related to their clinical development program outside of an FDRR. For example, sponsors may request a Type C guidance meeting under PDUFA, a biosimilar biological product development (BPD) Type 2 meeting under BsUFA, or a meeting under GDUFA with the review division, and request the next highest management level be present at the meeting (typically in a nondecisional capacity).

CDER and CBER recommend that before submitting an FDRR, the sponsor should ask the review division or the office that made the decision to reconsider the FDR-related issue(s). Moreover, to further ensure efficient use of Agency resources, the sponsor submitting an FDRR should not actively engage with other entities within the FDA or pursue other regulatory or legal pathways on the same matter at the same time. The following are examples of such circumstances.

- A sponsor's IND is placed on clinical hold, but the sponsor has not asked the review division to reconsider the clinical hold action, or a sponsor received a CR letter and has requested and been granted a post-action meeting with the division but has not yet participated in that post-action meeting. CDER and CBER do not intend to accept an FDRR until the sponsor has taken these steps. Under FDR, consistent with 21 CFR 10.75, 312.48, and 314.103, when a scientific and/or medical dispute arises, the sponsor should initially seek reconsideration of the matter with the original deciding official before making an appeal to the next higher management level. The FDA notes that no new information and/or new analysis of previously reviewed data should be submitted as part of a request for reconsideration.

¹² For example, 21 CFR 312.41, relating to Agency comment and advice on an IND, expressly states that FDA communications with a sponsor under this section are solely advisory and do not require any modification in the planned or ongoing clinical investigations or response to the Agency.

Contains Nonbinding Recommendations

- A sponsor anticipates receiving a CR action and submits an FDRR before receiving the CR letter. CDER and CBER do not intend to accept the FDRR until the sponsor has received the CR letter and unsuccessfully attempted to resolve the concern(s) with the review division (e.g., has submitted a request for an end-of-review meeting to discuss the matter with the review division, participated in such a meeting, and received a response from the review division indicating that its decision remains the same).
- A sponsor receives a CR action and has submitted a request for an end-of-review meeting to discuss the matter with the review division. At the same time, the sponsor submits an FDRR to the next management level. CDER and CBER do not intend to accept the appeal at that time because the sponsor has not yet attempted to resolve the concern(s) with the review division, nor received a response from the review division indicating that its decision remains the same.
- A sponsor submits an FDRR that is accepted and the deciding official¹³ on the appeal issues an interim response to the sponsor (see section V., FDA Action). The sponsor then submits an FDRR to appeal the interim response to the next management level. CDER and CBER do not intend to accept the appeal to the next management level until a final decision on the appeal has been made at the lower management level.
- A sponsor submits a Petition for Stay of Action under 21 CFR 10.35(b) and, for the same matter, several days later submits an FDRR. CDER and CBER do not intend to accept the FDRR because the sponsor is already engaged in another regulatory/legal proceeding within the Agency regarding the scientific and/or medical matter in dispute.

C. Is There New Information and/or Are There New Analyses of Previously Reviewed Data That the Sponsor Believes Is/Are Relevant?

Because internal Agency review of a decision that has been appealed by a sponsor must be based on the same information as was relied on to make the original decision (i.e., information already in the relevant administrative file; 21 CFR 10.75(d)), no new information should be submitted as part of an FDRR. If the sponsor wants to have CDER or CBER consider new information that may affect the original decision on a matter, it should submit the new information to the sponsor's application (i.e., IND, NDA, BLA, or ANDA) for review by the division and the original deciding official. CDER and CBER consider new analyses of previously reviewed data to be new information because the original deciding official might have made a different decision had he or she had the opportunity to review the new analyses.

D. Can a Sponsor Request a Meeting as Part of an FDRR?

After a sponsor has decided to submit an FDRR, as part of the appeal, it can request a meeting with the deciding official for the appeal (e.g., a Type A meeting for human drug applications covered by PDUFA, a BPD Type 1 meeting for human drug applications covered by BsUFA, or

¹³ For purposes of this guidance, the term *deciding official* refers to the person assigned to make the decision on the appeal.

Contains Nonbinding Recommendations

a meeting for a human drug application covered by GDUFA).¹⁴ This meeting is an opportunity for the sponsor to discuss the appeal issue(s) with the deciding official for the appeal.

E. Can a Sponsor Request an Advisory Committee Meeting as Part of FDR?

As part of an original appeal or at any point in the FDR process, a sponsor can request that a scientific dispute be reviewed by an appropriate advisory committee. Because it can take a significant amount of time to schedule an advisory committee meeting, if a sponsor believes that review by an advisory committee is the most appropriate venue for resolution of a scientific controversy, such a sponsor request should be made as early in the dispute resolution process as feasible.

IV. PROCEDURES FOR SUBMITTING A REQUEST FOR FORMAL DISPUTE RESOLUTION

A. How to Request Formal Dispute Resolution

The sponsor should submit an FDRR to the sponsor's application as described below. *Before submitting a request, it is strongly encouraged that the sponsor contacts CDER or CBER and provides advance notice of the sponsor's intent to submit an FDRR to ensure prompt handling of the appeal. Contact information for each Center is provided below.*

1. Requests for CDER

Requests for FDR with CDER should be submitted to the sponsor's application. The request should be submitted as an amendment to the appropriate application file (IND, NDA, BLA, or ANDA) and a copy should be submitted to the CDER Formal Dispute Resolution Project Manager (FDRPM). The contact information can be found on the CDER Formal Dispute Resolution web page.¹⁵ CDER encourages sponsors to contact the FDRPM before submitting a request for FDR.

2. Requests for CBER

Requests for FDR with CBER should be submitted to the sponsor's application when the request relates to an active submission. The request should be submitted as an amendment to the application to the appropriate review division, and a copy sent to the CBER Ombudsman. The

¹⁴ See the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* for human drug applications covered by PDUFA. (In March 2015, the FDA issued the revised draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*. When final, this guidance will represent the FDA's current thinking on this topic.) See the guidance for industry *Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants* for biosimilar biological product applications covered by BsUFA.

¹⁵ See <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ContactCDER/ucm444092.htm>.

Contains Nonbinding Recommendations

contact information can be found on the CBER Ombudsman web page.¹⁶ CBER encourages sponsors to contact the CBER Ombudsman before submitting a request for FDR. Note that the CBER Ombudsman handles both informal requests and FDRRs, so if the sponsor intends to submit an FDRR, it should be clear in its submission that the request is an FDRR.

B. Content and Format of an FDRR

To make the most efficient use of CDER or CBER and industry resources, any FDRR to either CDER or CBER should include information adequate to explain the nature of the scientific and/or medical dispute, and to allow the deciding official to determine the necessary steps needed to resolve the matter quickly and efficiently. Each request should include the following:

- Identification of the sponsor's submission as **FORMAL DISPUTE RESOLUTION REQUEST** in bold, uppercase letters
- The application number for the IND, NDA, BLA, or ANDA, if applicable
- The proprietary and/or generic name and established name for drug products; the proprietary and/or proper name for biological products
- The division or office where the application is filed
- The proposed indication(s), if applicable
- A brief, but *comprehensive* statement of each issue to be resolved, including:
 - A description of the scientific and/or medical matter to be resolved
 - A statement of the steps that have been taken to resolve the dispute, including a summary of relevant regulatory history, and any previous FDRRs
 - A statement of the sponsor's proposed possible solutions and/or outcomes
- A statement identifying the division and/or office that issued the decision on the matter being disputed and, if applicable, the deciding official on any prior FDRRs related to the same scientific and/or medical dispute
- A statement of whether the sponsor is requesting a meeting with the deciding official and what type of meeting is requested
- A statement of whether the sponsor is requesting advisory committee review

¹⁶ See

<https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm122881.htm>.

Contains Nonbinding Recommendations

- A list of documents previously submitted to the sponsor's application that are deemed necessary for resolution of the matter, with reference to submission dates so the documents can be readily located
- A statement that no new information has been submitted in support of the FDRR and, if applicable, that the last deciding official received and had the opportunity to review all of the material now being relied upon for the sponsor's FDRR
- The name, title, and contact information (i.e., mailing address, email address, telephone number, fax number) for the sponsor's contact for the appeal

V. FDA ACTION

The FDRPM or CBER Ombudsman functions as the administrative contact for all issues related to FDRRs. The FDRPM or CBER Ombudsman is responsible for communicating and explaining all regulatory processes related to FDR to the sponsor. The FDRPM or CBER Ombudsman will conduct a preliminary review of the sponsor's FDRR to evaluate whether the appeal satisfies the procedural criteria (as described in section IV., Procedures for Submitting a Request for Formal Dispute Resolution) so that the FDRR can be accepted. If the sponsor's FDRR is accepted, the FDRPM or CBER Ombudsman will forward the appeal to the appropriate CDER or CBER management level, as established under the center chain of command. The FDRPM or CBER Ombudsman will also send an acknowledgment letter to the sponsor identifying the deciding official, the due date for response to the FDRR, and the date of any meeting (if applicable). If an FDRR is not accepted, the FDRPM or CBER Ombudsman will send a letter to the sponsor on behalf of the deciding official identifying the reasons why the request was not accepted and outlining a possible path forward for acceptance of the sponsor's FDRR. Additionally, if a request for FDR is inappropriately submitted to CDER or CBER, then the FDRPM or CBER Ombudsman will re-direct the request to the appropriate entity within the FDA.

A. Responses to an Appeal

In general, the deciding official will send a written decision to a sponsor who submits an FDRR that is accepted for review. The written decision will grant or deny the appeal. If the deciding official does not agree with the sponsor's proposed outcome, he or she should provide the reasons for not agreeing with the sponsor's proposal and possibly suggest other options to achieve resolution and identify any actions that the sponsor can take to address the concerns articulated by the deciding official. Before issuing a final decision on the FDRR to the sponsor, the deciding official may also provide an *interim response*, such as a request for additional clarifying information or a request for a meeting with the sponsor, before making a decision on the appeal. An interim response should provide an explanation as to why an interim response is being issued instead of a final decision on the appeal.

Contains Nonbinding Recommendations

1. Timelines for Reviewing Formal Dispute Resolution Requests for Human Drug Applications Covered by PDUFA, BsUFA, or GDUFA

As noted earlier, if a scientific and/or medical dispute concerns a human drug application covered by PDUFA, BsUFA, or GDUFA, the deciding official should complete his or her review and provide an interim response or a decision on the appeal to the sponsor within 30 calendar days from receipt of an FDRR that has been accepted. The deciding official should respond to the sponsor within the 30-day window in writing or by telephone (i.e., *30-day response*). If the response is by telephone, the deciding official should follow up with a written confirmation within 14 calendar days of the verbal response.

If the sponsor requests a meeting as part of its appeal, CDER or CBER should treat the meeting request as a Type A meeting under PDUFA, a BPD Type 1 meeting under BsUFA, or a meeting under GDUFA. If the meeting is granted, the deciding official should provide an interim response or a decision on the FDRR to the sponsor within 30 calendar days of the meeting date. This time period allows the deciding official to consider the discussion at the meeting in his or her decision making process.

There may be instances when, to reach a decision, the deciding official needs additional clarifying information or input from other persons knowledgeable about the specific matter in dispute, or about the issue or area more generally. In such situations, the deciding official should issue an interim response to the sponsor identifying the additional information or input needed. If the product is a human drug application covered by PDUFA, BsUFA, or GDUFA, such interim responses should be made within 30 calendar days of receipt of the appeal.

- In instances when the deciding official needs clarifying information from the sponsor,¹⁷ a request for this information should be sent within 30 calendar days from receipt of the appeal. The deciding official should provide an interim response or a decision on the appeal within 30 calendar days from receipt of the clarifying information submitted to the sponsor's application.
- In instances when the deciding official decides a meeting with the sponsor is needed before a response can be issued, a meeting request should be sent within 30 calendar days from receipt of the sponsor's FDRR. CDER or CBER should schedule any meetings as quickly as the sponsor and the FDA are able to agree on a mutually acceptable date and time. After the meeting is held, the deciding official should provide an interim response or a decision on the appeal to the sponsor within 30 calendar days from the meeting date.
- In instances when the deciding official needs to discuss an FDRR with one or more members of an advisory committee or internal or external experts, CDER or CBER should inform the sponsor that the deciding official is seeking this additional input within 30 calendar days from receipt of the sponsor's FDRR. CDER or CBER should schedule

¹⁷ *Clarifying information* does not include new information or reanalysis of data that has not been reviewed by the division. As stated previously, the FDA considers new analyses of previously reviewed data to be new information because the original deciding official might have made a different decision had he or she had the opportunity to review the new analysis.

Contains Nonbinding Recommendations

such discussions with the members of an advisory committee or internal or external experts as quickly as possible. After this discussion takes place, the deciding official should provide an interim response or a decision on the appeal to the sponsor within 30 calendar days from the date of the discussion.

- In instances when the deciding official decides to seek input from an advisory committee, CDER or CBER should inform the sponsor of this request within 30 calendar days from receipt of the sponsor's FDRR. The deciding official should provide an interim response or a decision on the appeal to the sponsor within 30 calendar days after the date of the advisory committee meeting.

If the deciding official is unable to complete the review and provide either an interim response or a decision on the FDRR to the sponsor within 30 calendar days, CDER or CBER should notify the sponsor, explain the reasons for the delay, and provide the anticipated time frame for completing the review. In these cases, the PDUFA, BsUFA, or GDUFA goal for the appeal response would not be met.

2. Timelines for Reviewing Formal Dispute Resolution Requests for Applications and Submissions Not Covered by PDUFA, BsUFA, or GDUFA

For FDRRs related to applications not covered by PDUFA, BsUFA, or GDUFA, or related to applications or submissions for CBER-regulated medical devices (covered by the Medical Device User Fee Act), the timelines described in this guidance will be met as resources permit.

The FDA should provide a written or telephone response to the sponsor in a timely manner. If the response is by telephone, CDER or CBER should follow up with a written confirmation to the sponsor within 14 calendar days of the verbal notification.

B. Additional Considerations Regarding Responses to Appeals That Request Advisory Committee Review

If a sponsor seeking resolution of a scientific and/or medical dispute requests advisory committee review of the matter, CDER or CBER should determine whether such review is appropriate and would be helpful to CDER or CBER at that time in the FDR process. CDER or CBER should communicate this determination to the sponsor following the procedures described in section V.A., Responses to an Appeal.

1. Granting a Request for Advisory Committee Review

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

Contains Nonbinding Recommendations

As discussed in FDA regulations (21 CFR 14.5(b)) and the preamble to the final rule amending 21 CFR 10.75,¹⁸ the advice and recommendations of an advisory committee do not bind CDER or CBER to a particular action or policy. After receiving the advice of the advisory committee, the deciding official should provide the sponsor with an interim response or a decision within 30 calendar days.

2. Denial of a Request for Advisory Committee Review

If CDER or CBER does not grant a sponsor's request for advisory committee review, CDER or CBER should notify the sponsor in writing of such decision, including the reason(s) for the denial and any steps the sponsor may take to address CDER or CBER's concerns about the appropriate involvement of an advisory committee.

VI. REPEAT APPEALS

If a sponsor's FDRR is denied at one management level, the sponsor can appeal the same matter to the next higher management level in the center chain of command. A new FDRR should be submitted for each appeal to the next management level and should follow the process and timelines provided in this guidance. If the sponsor has exhausted the center's management levels and remains unsatisfied with CDER's or CBER's decision, the sponsor may request review of the matter by the Commissioner of Food and Drugs (Commissioner) under 21 CFR 10.75(c). Requests for review by the Commissioner should be submitted to the FDA's Ombudsman, with a copy provided to the center that denied the appeal, as described in section IV.A., How to Request Formal Dispute Resolution. Review of such matters by the Commissioner is discretionary.¹⁹

VII. 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 for a sponsor to prepare and submit a request for formal dispute resolution, 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.

¹⁸ See "Administrative Practices and Procedures; Internal Review of Decisions" (63 FR at 63980, November 18, 1998).

¹⁹ See 40 FR 40682, 40693 (September 3, 1975).

Contains Nonbinding Recommendations

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information for Form FDA 1571 have been approved under OMB control number 0910-0014 and for Form FDA 356h have been approved under OMB control number 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 02/28/2019).