

SOPP 8006: Resolution of Differences in Scientific Judgement in the Review Process

Version #2

Effective Date: January 15, 2009

1. Purpose

The purpose of this document is to describe the policies and procedures for resolving differences in scientific opinion among Center for Biologics Evaluation and Research (CBER) staff that require a formal, documented process.

2. Background

Differences in scientific opinion can occur regarding the interpretation and/or application of information pertinent to the regulatory process. Public health considerations, legislative mandates, regulations and commitments made under the user fee acts, all make it important to address such differences in a timely manner. It is equally important that the process leading to resolution of these differences be scientifically sound, well documented, and consistent with CBER's mission.

3. Policy

CBER is committed to addressing differences in scientific opinion that arise during the regulatory process through discussion of the issues, data, and the scientific principles involved. Differences in scientific opinion or perspective are an expected part of any scientific review or regulatory process and are most often addressed informally at the review team level. When internal differences of opinion cannot be resolved informally, and an individual wants to pursue a formal scientific dispute resolution (SDR) process, this SOPP is to be followed. Note: This process is for internal (CBER) use only to address differences in scientific opinion in the regulatory process. It is not intended to address other issues (e.g., issues related to personnel or work environment situations, scientific disputes that relate to non-regulatory scientific activities or disputes that challenge an established Center, Agency or Department policy).

It is CBER policy that all issues are deliberated in a scientifically sound, collegial, open, and objective fashion based on unbiased, accurate fact(s), and without retaliation.

Efforts should be made to consider and resolve scientific disagreements informally at the lowest operational level possible during the review process. Those that cannot be resolved informally can be pursued through the formal SDR process by any individual or group directly involved in the disagreement.

When the process defined in this SOPP is invoked, the discussions, decisions reached, and responses by all parties are to be documented in the appropriate Administrative File for the

submission under discussion. At the conclusion of an SDR process within an Office, a complete electronic copy of the administrative file for the formal dispute (e.g., the completed SDR template, supervisory responses and relevant associated documentation), is forwarded to the CBER Ombudsman's Office where it will be audited for completeness and compliance with this SOPP. Incomplete files will be returned to the Office/initiator for revision. If the dispute was resolved at the Office level the completed file will be archived; if not, the dispute will be submitted for Center review. For a scientific disagreement that is not associated with a specific product or file, the CBER Ombudsman's Office will maintain the file of the formal dispute resolution documentation.

Each successive response cycle (e.g., supervisor to initiator) should take no longer than three (3) weeks. When a supervisory non-concurrence is received, the initiator has one (1) week to decide whether or not to appeal the recommendation to the next supervisory level.

Note regarding timing: Because resolution cannot be predicted at any given supervisory level, it is important to move as expeditiously as possible throughout the process, especially with regard to a scientific dispute that involves an approval or clearance action. To the extent possible, the formal scientific dispute resolution process should take into account pertinent regulatory review time frames to help ensure that targets and milestones are not exceeded unnecessarily.

When an SDR request has the potential to impact the outcome of an approval or clearance action, or its timeliness, the affected Office Director (or their designee), will notify the Associate Director for Review Management of the situation.

While the scientific dispute resolution process is pending, work on the submission and a final regulatory decision will continue unless the Center Director decides that:

1. The appeal raises substantial questions involving a significant risk to the public health, and
2. Postponing the decision would not result in a negative impact on the public health.

Further, Center personnel are not expected to postpone regulatory decisions on time sensitive regulatory actions, e.g., pending investigational or marketing submissions.

It is CBER's policy that issues of scientific dispute that become formal must be presented in an accurate, concise, and clear manner. In order to accomplish a timely and effective review, disputes and responses must be documented in such a way that successive levels of managerial review can be conducted efficiently. The Scientific Differences Summary Form must be used by the initiator and supervisor and the completed forms (including supervisory responses to each issue raised), must be documented in the Administrative File for the dispute as well as in the product file. (See Appendix 1)

In the event that a formal scientific dispute involves a disagreement between scientists from two or more offices within CBER, the appropriate supervisory chain of command in each office must be engaged in the formal SDR process. The same documentation (i.e., the Scientific Differences Summary form, including a concise statement of the issue under

consideration followed by an explanation of the dissenting perspectives), must be provided for supervisory consideration to all affected offices.

Disputes that rise to the level of the Immediate Office of the Center Director, CBER, will be addressed by the Center Director, with assistance from other senior staff, as needed, within thirty (30) calendar days of receipt of the complete SDR package. If, after the Center Director issues a decision, the initiator wishes to continue to pursue the appeal, (s)he may bring the appeal to the Agency level in accordance with SMG 9010.1 Scientific Dispute Resolution at FDA (Reference 1). The initiator must document the appeal to the Agency, providing the complete documentation required by this SOPP, and must present it to the designated Agency contact within ten (10) calendar days after the CBER Center Director renders a written decision.

Note: If a situation arises where the initiator believes that the immediacy and scale of public health impact warrants immediate action, the initiator may bring the scientific dispute directly to the affected CBER Office Director to request an expedited time frame for the review within the Office. If an expedited process is followed and the initiator(s) is not satisfied with the Office level response, the initiator(s) may take the appeal directly to the CBER Center Director after receiving the Office level recommendation. As with all appeals, the appeal documentation should clearly describe the issue and opinions (i.e., initiator perspective and supervisory response), on the Scientific Differences Summary form. The appeal must be accompanied by clear and persuasive evidence of a serious and imminent public health risk. The Center Director's point of contact for such direct appeals is the CBER Ombudsman.

4. Procedure

Parties with differences in opinion on scientific issues (e.g., disagreement on interpretation of data), should attempt to discuss and resolve the issue at the review team level or other appropriate operational level informally during the review process, whenever possible. This discussion and its outcome should be documented in the administrative file for the product.

If the initiator is dissatisfied with the outcome of the informal discussions, the initiator can choose to begin the formal dispute resolution process. The initiator notifies the CBER Ombudsman in writing, for monitoring purposes, of the decision to pursue formal SDR, and then follows the remaining steps in this SOPP.

1. The initiator completes the Scientific Differences Summary form (Appendix 1) for all the issues of dispute (one form covering all issues of dispute), and presents it, along with the necessary supporting information, to the next level of supervision.
2. Upon receipt of the formal SDR request the supervisor will send email notification to the appropriate supervisory chain within the office, up to and including the Office Director, with a copy (cc) to the CBER Ombudsman and the appropriate office/division RPM (see the memo template in Appendix 2). If the supervisor determines that the SDR is incomplete, the supervisor must notify the initiator in writing no later than fourteen (14) calendar days after receipt of the package. If the SDR request is complete (as determined

by the supervisor, using the check list provided in Appendix 3), then the supervisor must respond to the initiator(s), in writing, addressing each disputed element, either concurring with the disputed element or not concurring, with justification for each determination, no later than twenty-one (21) calendar days after receipt of the complete package (or sooner depending on review timelines). The supervisor must copy the Ombudsman on the communications.

3. If the initiator does not accept the supervisor's recommendation, then the initiator has one (1) week in which to appeal the decision to the next supervisory level. The initiator must send the existing dispute documentation to the next supervisory level, accompanied by a brief (one paragraph) summary that clearly documents the disagreement with that supervisor's position. Documentation that is provided or referenced in support of a given position may be included in the dispute resolution file. However, no additional topics or issues for discussion may be added to the dispute resolution request after it has been filed. If new issues or topics arise, a new request is required and the process must start over at the first level supervisor.
4. If resolution is not achieved and the initiator wishes to continue to pursue formal SDR, the initiator must repeat Step 3 (above), typically starting from Branch/Laboratory Chief up through the Division Director, Office Director and the Center Director. Each successive supervisor must follow this SOPP, including following the specified timeframes and documenting his/her response to the initiator in accordance with Step 2.5.
5. When a formal scientific dispute resolution request is submitted to the Center Director, the CBER Ombudsman has fourteen (14) calendar days to review the documentation package to ensure that it is complete and presented in the required format and that the appeal request and the Office Director's decision clearly set forth the issue(s) for consideration by the Center Director. If the request or Office decision is unclear, or if the documentation is not adequate it will be returned to the initiator and the affected Office(s) for revision.. The thirty (30) day clock for the Center Director's review does not begin until the Ombudsman verifies that the package is complete and forwards it to the Center Director. The initiator and Office will be notified when the file is forwarded to the Center Director for review. The Center Director (and/or designee) may request to meet with the initiator, Office Director and/or other relevant parties during the Director's review.
6. If the initiator does not accept the Center Director's recommendation, then the initiator may choose to continue the SDR process in accordance with SMG9010.1. In such cases, the initiator must document the scientific disagreement and forward the dispute documentation to the Office of the Commissioner, no later than ten (10) calendar days after the Center Director renders a written decision.

5. Roles and Responsibilities:

Note: see above section for comprehensive procedures.

- 1) The initiator(s) will:

- a) Exhaust attempts to resolve the issue(s) at the review team level or other appropriate operational level during the review process, whenever possible.
- b) Document discussions relevant to the dispute and their outcome in the administrative file for the product when the dispute is associated with a specific product, or products.
- c) Notify the Ombudsman of the decision to pursue formal SDR at the time the request is submitted to their supervisor.
- d) Work with the RPM to ensure that all dispute related documents are placed in the appropriate file for the product. If the scientific dispute is not associated with a specific product or file, submit documents directly to the formal dispute resolution file maintained by the CBER Ombudsman. The initiator will provide additional documentation when it is requested in support of a supervisory review of the appeal.
- e) Complete the Scientific Differences Summary form (Appendix 1) for all the issues of dispute (one form covering all issues of dispute) and present it to the next level of supervision.
- f) Review the supervisory recommendation or response to the dispute and determine if they wish to continue to pursue formal dispute resolution.
- g) If the initiator chooses to continue to pursue formal dispute resolution he/she will send the existing dispute documentation to the next supervisory level, accompanied by a brief (one paragraph) summary that clearly documents the disagreement with that supervisor's position within one week of the issuance of the previous supervisory response.
- h) Repeat steps e and f until the dispute is resolved, or the initiator chooses to discontinue the SDR process, or Center level appeal options are exhausted.
- i) If the initiator chooses to pursue scientific dispute resolution after receiving the Center Director's recommendation, the initiator will proceed in accordance with SMG 9010.1. In such case, the initiator must forward a description of the scientific disagreement as outlined in SMG 9010.1 along with all relevant documentation generated during the Center level process to the Office of the Commissioner, no later than ten (10) calendar days after the Center Director renders a written decision.

2) The RPM will:

- a) Coordinate administrative and regulatory activities related to the SDR process when it is related to a product file to which they are assigned.
- b) Work with initiator(s) to ensure that all documentation is submitted to appropriate file for the product, where applicable.
- c) Maintain the official Office copy of the dispute resolution file until it is completed by the Office (at which time it is forwarded to the CBER Ombudsman).

- d) Forward to the CBER Ombudsman's Office a complete electronic copy of the administrative file for the formal dispute when the SDR process is concluded within the Office.

3) Supervisors will:

- a) Upon receipt of formal SDR request, verify that the request is complete and presented in the appropriate format using the checklist provided in Appendix 3. Requests that are not complete or in the correct format will be returned to the individual responsible for correcting the deficiency (i.e., the initiator or prior supervisor depending upon the nature of the deficiency), within fourteen (14) calendar days of receipt.
- b) Send email notification to the appropriate supervisory chain within the Office, up to and including the Office Director, with a courtesy copy (cc) to the CBER Ombudsman (see the memo template in Appendix 2).
- c) Respond to the initiator(s), in writing, addressing each disputed element, either concurring with the disputed element or not concurring, with justification for each determination, no later than twenty-one (21) calendar days after receipt of the complete dispute resolution request package (or sooner depending on review timelines).

4) Office Directors will:

- a) Ensure that review and supervisory staff in their Office are aware of the available formal and informal procedures available to resolve scientific disputes internally within the Office.
- b) Review requests for an expedited Office review level SDR process based on the presence of an urgent public health need and render a written decision regarding that request.
- c) Render written decisions on disputes that have advanced to them through the scientific dispute resolution processes in this SOPP, no later than twenty-one (21) calendar days after receipt of the complete dispute resolution request package (or sooner depending on review timelines).
- d) Be responsible for ensuring the Office carries out any corrective actions that the Center Director determines are necessary in response to the SDR appeal.

5) The Center Director will:

- a) Render written decisions on disputes that have advanced to them through the scientific dispute resolution processes in this SOPP no later than thirty (30) calendar days after receipt of the complete dispute resolution request package.

6) The Ombudsman will

- a) Within fourteen (14) calendar days from receipt by the Office of the Center Director of a formal SDR request addressed to the Center Director, review the SDR documentation package to ensure that it is complete and presented in the required format.
 - i) If package is complete, forward to the Center Director
 - ii) If package is not complete, return to initiator and associated Office(s) for revision.
- b) Archive a complete electronic copy of the administrative file for any formal dispute addressed entirely within a product office (e.g., the completed SDR template, supervisory responses and relevant associated documentation). As above, files received from the office RPM will be reviewed within fourteen (14) calendar days of receipt to ensure that the SDR documentation package is complete and presented in the required format.
 - i) If package is complete, the file is archived in the SDR eRoom
 - ii) If the package is not complete, it is return to the appropriate RPM for Office revision.
- c) For a scientific disagreement that is not associated with a specific product or file, maintain file of the formal dispute resolution.
- d) Serve as an information resource for CBER personnel regarding the formal scientific dispute resolution process within the Center and at the Agency level.
- e) Associate Director of Review Management will:
- f) Enable the SDR process to proceed as efficiently as possible by assisting those involved with resolving unique and timely process issues that may arise
- g) Ensure that relevant Center staff receives training on the informal and formal procedures available to them to resolve scientific disputes internally within CBER.

6. Effective Date

January 23, 2009

7. History

Written/Revised	Approved	Approval Date	Version Number	Comment
L. Wilson, S. Lard	Robert A. Yetter, PhD	Dec 11, 2008	2	Revised to be consistent with Agency procedures
		January 25, 1999	1	Original document.

8. Appendices

- [Scientific Differences Summary Form \(PDF - 28KB\)](#)

- [Memo Template for Notification of Receipt of a Formal Scientific Dispute Resolution Request \(PDF - 17KB\)](#) Appendix 2
- [Checklist for Supervisory Review of Dispute Documentation \(PDF - 36KB\)](#) Appendix 3