CENTER DIRECTOR

RESOLUTION OF DISPUTES: ROLES OF REVIEWERS, SUPERVISORS, AND MANAGEMENT DOCUMENTING VIEWS AND FINDINGS AND RESOLVING DIFFERENCES

CONTENTS

PURPOSE This MAPP provides:

- a general description of the roles of the reviewer, supervisors and team leaders, and management in arriving at institutional decisions in the drug application review process;
- guidance on how each individual involved in the scientific review process is to document his or her views or findings; and
- a procedure for resolving differences.

BACKGROUND

- As a result of the drug application review process, the Center for Drug Evaluation and Research (the Center) must reach an institutional position on the conduct of clinical trials and on the approvability of each drug application. Although easy to describe in concept, the process is complex in practice. Applications submitted to the Center for approval could be in the form of an investigational drug application (IND), a new drug application (NDA), an abbreviated new drug application (ANDA), or an abbreviated antibiotic application (AADA). Applications are reviewed by teams of scientists

consisting of primary reviewers from different disciplines. The review teams' recommendations are then reviewed by discipline-specific supervisors or team leaders, the division directors, and, if necessary, the office directors. (In the case of a reviewing medical officer, a division director or deputy director reviews the primary findings.)

- The review process ensures that each application is considered from an array of different perspectives and concerns. The process also requires that reviewers, supervisors or team leaders, and management work together. In most cases, consensus on a drug application is usually achieved through discussion as the reviews proceed. If consensus does not occur during the review process, management ultimately must resolve the differences. In all cases, it is essential that the views of all persons involved in the review process be respected and that the official administrative record of the review reflect differences of opinion if they exist.

REFERENCES

- FDA Administrative Practices Regulations: 21 CFR 10.70 and 10.75.

DEFINITIONS

- **Concurrence.** A supervisor's concurrence with a review, usually indicated by initials or a signature at the end of the review, shall be considered a personal endorsement of the review. Concurrence means (1) the supervisor finds that the review is in the required format and meets all applicable review guidelines, (2) the supervisor believes the review is complete and has considered the critical scientific and regulatory issues, and (3) the supervisor agrees with the reviewer's conclusions and recommendations.

- **Supervisor.** For purposes of this MAPP, the term *supervisor* will include supervisors, team leaders, or any other person who has oversight responsibility for the work product of a reviewer.

POLICY

- According to FDA's Administrative Practices Regulation 21 CFR 10.70 (b), FDA employees responsible for "handling a matter are responsible for insuring the completeness of the administrative file relating to it." The file must contain appropriate documentation of the bases for a decision, including relevant reviews, memoranda, opinions of consultants, letters, and minutes of meetings.

The file also must contain the recommendations and decisions of individual employees, including supervisory personnel and managers. The documentation must "reveal significant controversies or differences of opinion," if they exist, and the basis for their resolution.

- A scientific review shall be considered a reviewer's own work. In the course of completing his or her review, the reviewer may develop successive drafts or alter the primary draft with the intent of clarifying points or improving the review. Early drafts are not considered part of the administrative file of an application and can be discarded.

- Once a review is typed in final form, dated, and signed, it may not be altered, added to, or removed from the administrative files by anyone, including the reviewer. A review can be amended only by adding a new memorandum or modified review to the file.

- FDA regulations require that all documents placed in an administrative file relate to the factual, scientific, or regulatory issues under consideration. Each document must be dated and signed by the author. The full distribution of all documents must be shown. In addition, a copy of any document that records the views, analyses, recommendations, or decisions of an Agency employee other than the author must be provided to that person.

- Written reviews and minutes in an administrative file must avoid intemperate language, undocumented charges, or irrelevant remarks (e.g., personnel complaints). Caution should be exercised in including statements of legal interpretation, unless they have been concurred in by the Office of the Chief Counsel.

- The official signing the action letter is personally responsible for ensuring that the letter is scientifically accurate, consistent with Agency regulations and policy, correct in tone, and written clearly in good English.

- If a disagreement arises at any level of the review process and remains unresolved, the reviewing official who disagrees with the drafted conclusions or recommendations must prepare a separate document explaining (1) the nature of the difference in opinion, (2) the reasons for the differing opinion, and (3) the recommended changes in the findings or recommendations. This document must remain in the file with the reviewer’s documentation.

RESPONSIBILITIES AND PROCEDURES

- **Reviewers are responsible for:**

  1. consulting with their supervisors at any time during the review process, particularly if an application raises complex scientific or policy issues.

  2. the content of their review.

- **Supervisors are responsible for:**

  1. providing assistance to reviewers in evaluating application data

  2. commenting on review drafts, providing additional insights to issues, and raising points for discussion, as necessary.

  3. concurring with the review or discussing any differences with the reviewer to come to a resolution. If the difference in opinion remains unresolved, the supervisor may **not** direct the reviewer to change a review. Instead, the supervisor should draft a memorandum for the file explaining the nature of the differences in the scientific review, conclusions or recommendations, the reasons for his or her position and the resulting changes in the conclusions and recommendations. The supervisor shall then forward the file to the division director.

  4. forwarding a copy of the memorandum relating to any differences of opinion to the reviewer, division director, and, if appropriate, office director for informational purposes.

- **The Division Director is responsible for:**

  1. evaluating each review package, including all scientific reviews and recommendations, advisory committee recommendations, other memoranda, and the approvability or nonapprovability of the application.

  2. concurring with the reviewer or, if there is a disagreement, meeting with a reviewer and supervisor, if requested by either party. The division director should consider the merits of all points of view, decide the issue if consensus cannot be achieved, and place a memorandum in the file indicating how the issue was resolved or, if resolution was not achieved, stating the basis for his or her decision.

  3. forwarding appropriate review packages to the office director for

concurrence, if appropriate, or resolution of differences, if needed.

- **Office Director is responsible for:**

  1. meeting with the parties involved in the disagreement, if requested by any of the individuals. The office director should consider the merits of all points of view, decide the issue if consensus cannot be achieved, and place a memorandum in the file indicating how the issue was resolved.

  2. If the division director and the office director disagree, the previously described principles apply (the manager is always to include his or her views, if different from those of a subordinate, in a memorandum to the file). If the disagreement raises issues of general concern, they may be presented to the Deputy Center Director for Review Management or Deputy Center Director for Pharmaceutical Science, as appropriate, and they may be discussed in an appropriate policy forum.

- **Deputy Center Director for Review Management or Deputy Center Director for Pharmaceutical Science:** Unresolved scientific or regulatory issues may be brought to the Deputy Center Director for Review Management or the Deputy Center Director for Pharmaceutical Science, as appropriate, for final resolution. A memorandum indicating how the issue was resolved should be placed in the file.

EFFECTIVE DATE

This MAPP is effective upon date of publication.