POLICY AND PROCEDURES

OFFICE OF PHARMACEUTICAL SCIENCE

CLARIFICATION TELECONFERENCES BETWEEN SPONSORS, APPLICANTS, OR MASTER FILE HOLDERS AND THE ONDQA REVIEW TEAM

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PURPOSE

This MAPP establishes policies and procedures for the Office of New Drug Quality Assessment (ONDQA) within the Office of Pharmaceutical Science (OPS) to schedule, hold, and document clarification teleconferences between sponsors, applicants, or master file holders, and the ONDQA review team. This MAPP also provides a description of such teleconferences, as well as the circumstances where they can be appropriate and beneficial to the review process. The policies and procedures described in this MAPP are intended to facilitate timely and effective verbal communication between sponsors, applicants, and master file holders, and the ONDQA review team, and to increase the overall efficiency of the chemistry, manufacturing, and controls (CMC) and/or biopharmaceutics review process. These policies and procedures are also intended to provide a balance between ONDQA's resources, review workload and timelines, and the need for and benefit of such teleconferences.

The policies and procedures in this MAPP apply to:

- Clarification teleconferences between sponsors, applicants, and master file holders, and the ONDQA review team, regarding CMC and/or biophamaceutics-specific information, review issues, or concerns.

- Pre-investigational new drug applications (Pre-INDs), investigational new drug applications (INDs), new drug applications (NDAs), supplemental NDAs, and master files.

The policies and procedures in this MAPP do not apply to:

- Formal meetings between FDA and sponsors or applicants (see Background section and References).
- Communications between sponsors, applicants, or master file holders, and an ONDQA Project Manager (PM) alone.
- Communications between ONDQA staff and others on topics unrelated to a specific application or master file.
- Clinical hold teleconferences.
- Public presentations or workshops.

BACKGROUND

CDER grants and holds formal meetings with sponsors and applicants regarding the development and review of products in accordance with applicable laws and regulations (see Prescription Drug User Fee Act [PDUFA] V; 21 CFR 10.65, 312.47 and 314.102(d)). Formal meetings are described in PDUFA V, and the guidance for industry on *Formal Meetings (Type A, Type B or Type C) with Sponsors and Applicants*, as well as other FDA guidances such as *Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants* (see References). These meetings include pre-IND, end-of-phase 2, stalled clinical trial, pre-NDA, late-cycle, and end of review conferences. Such meetings are conducted, tracked, and documented in a formal manner. The format can be face-to-face, teleconference, or videoconference. Minutes of these meetings are prepared and archived in the administrative file, and copies are sent to the sponsor or applicant (see References). ONDQA participates in such formal meetings as a member of a multidisciplinary team. ONDQA also holds formal CMC- and/or biopharmaceutics-only meetings with sponsors and applicants, as appropriate.

An optional post-action feedback meeting, which focuses on lessons learned, is also available to applicants. Such a meeting is not considered a PDUFA meeting, and minutes are not required (see References).

CDER also holds teleconferences with sponsors, applicants, or master file holders for other purposes which, because of their subject matter, are not considered PDUFA meetings, and for which minutes are not required. However, all substantive teleconferences should be documented and archived (see References).

POLICY

- A clarification teleconference can be held between sponsors, applicants, or master file holders and the ONDQA review team for clarification, explanatory, and/or information-sharing purposes. Examples include teleconferences to:
    - clarify an item(s) in an FDA letter
    - discuss an alternative approach to address an item(s) in an FDA letter
    - discuss a new technology or modeling approach.
- However, a clarification teleconference is *not* appropriate if:
    - the proposed subject matter qualifies as one of the designated types of formal meetings (see Background section and References)
    - the subject matter involves, or is anticipated to involve, significant decisions, agreements, requests, or recommendations affecting a Pre-IND, IND, NDA, supplemental NDA, or master file
    - the subject matter proposed for discussion can be appropriately addressed instead by the ONDQA Project Manager (PM) alone.
- Although clarification teleconferences are conducted in a less formal manner than formal meetings, such teleconferences are official business.
- Such teleconferences should be documented and archived, as appropriate.

PROCEDURES

- Requests for clarification teleconferences may be made verbally or by email by sponsors, applicants, or master file holders, or by ONDQA staff.
- ONDQA will grant and hold clarification teleconferences requested by sponsors, applicants, or master file holders regarding CMC and/or biopharmaceutics information if the proposed purpose, subject matter, and format of such teleconference is appropriate.
- Also, ONDQA may request and hold clarification teleconferences with sponsors, applicants, or master file holders regarding CMC and/or biopharmaceutics information if the proposed purpose, subject matter, and format of such teleconference is appropriate.

- A clarification teleconference will be considered appropriate under the following circumstances:

    - The teleconference does not qualify as one of the designated types of formal meetings (see Background section and References).

    - The teleconference is for clarification, explanatory, or information sharing purposes only (see examples above).

    - The teleconference is considered to be of practical benefit to the review process, for example:

        - there is a recognized potential for a misunderstanding on a particular issue

        - a previous attempt to resolve a matter by written communication has been unsuccessful

        - verbal discussion would substantially increase understanding and/or facilitate resolution of a matter as compared to written communication alone.

    - The teleconference involves CMC- and/or biopharmaceutics-related information, issues, and/or concerns only, and not those of other disciplines.

    - The teleconference typically does not require extensive planning.

    - The teleconference is brief (generally 30 minutes or less).

- During such a teleconference, ONDQA staff members may openly discuss the scientific and/or regulatory matters at hand. However, if a subject of the type that would be more appropriately addressed in a formal meeting is presented in a clarification teleconference, ONDQA staff will refrain from addressing such matter (see References for guidance on criteria for formal meetings).

- If the teleconference only involves clarification, explanation, or information sharing, then it is documented as a note in an ongoing review. If there is no review, the teleconference is documented in a brief Memorandum of Teleconference, and archived.

- If, contrary to the original intentions of the participants, the teleconference results in any significant agreements, decisions, requests, or recommendations that affect a Pre-IND, IND, NDA, supplemental NDA, or master file, the teleconference will be documented in a Memorandum of Teleconference, and archived.

RESPONSIBILITES

The following responsibilities apply to requesting, conducting, and documenting clarification teleconferences:

- The ONDQA PM assigned to a particular application will coordinate all clarification teleconferences between sponsors, applicants, or master file holders and ONDQA staff.

- The Branch Chief (BC), or Biopharmaceutics Team Leader (BTL) for matters pertaining to biopharmaceutics, will determine whether the subject matter of a proposed teleconference is appropriate for a clarification teleconference. If so, the BC (or BTL) will determine or approve the agenda and designate the required attendees besides the assigned ONDQA PM (e.g., BC, BTL, CMC Lead, Biopharmaceutics Lead, Reviewer) and optional attendees, if any (e.g., ONDQA Division Director, Biopharmaceutics Lead). Although concurrence of this by email from the BC (or BTL) to the ONDQA PM is preferred, verbal concurrence is acceptable.

- ONDQA Reviewers, CMC Leads, and/or Biopharmaceutics Reviewers, if not designated by the BC (or BTL), will obtain clearance from their BC (or BTL) before attending the teleconference.

- The ONDQA PM will be present and take notes during all clarification teleconferences between sponsors, applicants, or master file holders and ONDQA staff.

- Preferably, the attendees will summarize the items discussed during the teleconference before conclusion of the teleconference.

- If the teleconference is relevant to an ongoing review and involves clarification, explanation, or information sharing only, then the reviewer will document the teleconference as a note in his or her review. Alternatively, if there is no ongoing review, the ONDQA PM will document it as a brief “Memorandum of Teleconference” and enter it as a “Correspondence Sent via Verbal” in the Document Archiving, Reporting, and Regulatory Tracking System (DARRTS). The correspondence will be associated with the relevant application or master file submission.

- The BC (or BTL) will determine whether the teleconference involved any significant decisions, agreements, requests, or recommendations which affect a Pre-IND, IND, NDA, supplemental NDA, or master file. If so, the ONDQA PM

will prepare a "Memorandum of Teleconference" containing a summary of the teleconference and enter it as a "Correspondence Sent via Verbal" in DARRTS. The memorandum will be signed by the ONDQA PM and additional attendees, as deemed appropriate (e.g., BC, BTL). The correspondence will be associated in DARRTS with the relevant application or master file submission.

- The BC, BTL, CMC Lead, and/or Reviewer(s) who attended the teleconference will provide input on scientific or technical issues to the ONDQA PM to aid preparation of a Memorandum of Teleconference, when requested.

- ONDQA supervisory staff can name a designee for any of the responsibilities described herein, as appropriate.

The following additional responsibilities are specific to whether the teleconference is externally or internally initiated:

<u>For Externally-Initiated Clarification Teleconferences:</u>

- The assigned ONDQA PM will discuss all requests received from sponsors, applicants, and master file holders with the BC (or BTL) for all clarification teleconferences with the review team.

- If any ONDQA staff member receives a request in error for a teleconference, he or she will direct it to the assigned ONDQA PM.

- The assigned ONDQA PM will inform the requestor whether a clarification teleconference is granted or denied.

    - If a clarification teleconference is granted, the teleconference will be scheduled to occur on the date and at the time requested or at least in as timely a manner as is practical and as resources allow. The ONDQA PM will obtain a list of the external attendees and inform the requestor of the FDA attendees.

    - If a clarification teleconference is denied, the BC (or BTL), and/or ONDQA PM will consider alternative means of communication (e.g., formal meeting, written communication, ONDQA PM-only communication), as appropriate. The ONDQA PM will then inform the requestor.

- During a clarification teleconference, if a sponsor or applicant presents a subject for discussion that would qualify as a subject for a formal meeting (see Background section and References), the ONDQA PM will recommend that the sponsor or applicant submit a written request for a formal meeting. Any ONDQA staff member attending the teleconference may advise the PM that the subject qualifies as one for a formal meeting.

For ONDQA-Initiated Clarification Teleconferences:

- An ONDQA Reviewer, CMC Lead, and/or Biopharmaceutics Lead who wants to initiate a clarification teleconference will first discuss the issue with his or her BC (or BTL) and obtain concurrence. An ONDQA PM who wants to initiate a clarification teleconference involving the ONDQA review team will first discuss the issue or concern with the assigned BC (or BTL) and obtain concurrence. Although concurrence by email from the BC (or BTL) to the assigned ONDQA PM is preferred, verbal concurrence is acceptable.

- Any request to a sponsor, applicant, or master file holder for an ONDQA-initiated clarification teleconference will be made by the assigned ONDQA PM. The ONDQA PM will also inform the sponsor, applicant, or master file holder of the proposed subject, agenda, and format of the teleconference, as well as the FDA attendees. In keeping with the conduct of a clarification teleconference being less formal than a formal meeting, the request will be made by telephone or secure email, rather than by a written letter.

- A request for a clarification teleconference will be made as far in advance as reasonable and practicable to allow the sponsor, applicant, or master file holder to adequately prepare for the teleconference. ONDQA staff will recognize that a sponsor, applicant, or master file holder may grant or refuse a requested teleconference at their discretion.

- The BC (or BTL) will lead the discussion during the teleconference.

These procedures and responsibilities are summarized in the flow chart (see Attachment).

REFERENCES

- 21 CFR 10.70 Documentation of significant decisions in the administrative file.

- FDA Guidance for Industry: *Formal Meetings Between the FDA and Sponsors or Applicants*, May 2009. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf

- CDER 21st Century Review Process Desk Reference Guide, New Drug Application and Biologics License Application Reviews (NDA/BLA Review Process), September 2012. http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/UCM218757.pdf

- PDUFA Reauthorization Performance Goals And Procedures Fiscal Years 2013 Through 2017. http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf

- FDA Draft Guidance for Industry: *Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants*, March 2013. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM345649.pdf[1]

EFFECTIVE DATE

This MAPP is effective upon date of publication.

[1] When finalized, the draft guidance will represent FDA's current thinking on the topic.

ATTACHMENT: FLOW CHART