SOPP 8002: Procedures for the Preparation, Clearance and Issuance of Guidance Documents

Version# 6

Effective Date: December 10, 2012

I. Purpose

This Standard Operating Policy and Procedure (SOPP) serves as a guide for Center for Biologics Evaluation and Research (CBER) staff for developing and issuing guidance documents.

II. Scope

This SOPP applies to all guidance documents initiated, developed and processed in CBER.

III. Background

A. FDA announced its Good Guidance Practices (GGP) Policy in 1997 (62 FR 8961, February 27, 1997). Subsequently, Congress passed the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Ref. B.1) which amends the Federal Food, Drug, and Cosmetic Act to incorporate aspects of GGP. In response to FDAMA, FDA codified its GGP in 21 CFR 10.115 (Ref. B.2).

B. Guidance documents explain how the Agency believes the statutes and regulations apply and reflect FDA's current thinking on the subject addressed in the guidance document. FDA is willing to discuss an alternative approach with applicants/sponsors to ensure that they comply with the relevant statutes and regulations, but CBER staff may depart from guidance documents only with appropriate justification and supervisory concurrence (21 CFR 10.115(d)).

IV. Definitions

A. **Concept paper** - A brief document that describes basic information about a proposed new guidance document to facilitate the Center's decision on whether to develop the proposed guidance document.

B. **Guidance Documents (21 CFR 10.115)** - Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the Agency's interpretation of or policy on a regulatory issue.

1. Guidance documents include, but are not limited to, documents that relate to:
    a. design, production, labeling, promotion, manufacturing, and testing of regulated products;

b. processing, content, and evaluation or approval of submissions; and
c. inspection and enforcement policies.

2. Guidance documents do not include:
   a. Internal FDA procedures;
   b. Agency reports;
   c. General information documents provided to consumers or health professionals;
   d. Speeches;
   e. Journal articles and editorials;
   f. Media interviews and press materials;
   g. Warning letters;
   h. Memorandum of understanding;
   i. Other communications directed to individual persons or firms.
   Note: The terms Guideline, Guidance Memoranda, Memoranda to Industry, Points to Consider, and Blood Memo were previously used to refer to guidance documents. These terms are no longer used when drafting new or revised guidance documents.

C. **Level 1 Guidance Documents (21 CFR 10.115(c)(1))**
   1. Guidance documents that:
      a. Set forth initial interpretations of statutory or regulatory requirements;
      b. Set forth changes in interpretation or policy that are of more than a minor nature;
      c. Include complex scientific issues; or,
      d. Cover highly controversial issues.

D. **Level 2 Guidance Documents** (21 CFR 10.115(c)(2))
   1. Guidance documents that:
      a. Set forth existing practices or minor changes in policy; and
      b. are not Level 1.

E. **Notice of Availability (NOA) -** a notice issued in the Federal Register that:
   1. Notifies the public of the issuance of the guidance document;
   2. Invites comment on the guidance document; and
   3. Informs the public how to obtain copies of the guidance document.

F. **Plain Language -** Plain language (also called Plain English) is communication your audience can understand the first time they read or hear it. Plain language documents have logical organization, easy-to-read design features, and use:
   - common, everyday words, except for necessary technical terms;
   - "you" and other pronouns;
   - the active voice; and
   - short sentences. (see Refs. B.3 and 4)

V. **Policy**

A. The guidance development process seeks to ensure members of the public have equal opportunity for comment and equal access to information about the Agency's interpretation of or policy on a regulatory issue. When *considering* the development of a guidance document, CBER can seek or accept early input from individuals or groups outside the Agency. For example, CBER can do this by participating in or holding public meetings and workshops.

B. Once preparation of a guidance document has been initiated, but before the document has issued, staff should not reveal the specifics of the internal draft guidance to the public when issues to be addressed in the guidance are publicly discussed. Once a guidance document has been issued, the guidance and comments received may be publicly discussed; however, the Agency's intentions regarding potential changes to the guidance in response to comments received should not be discussed until after the revised or final guidance is issued.

C. The Agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time. (21 CFR 10.115(e)). CBER staff may consult with the Associate Director for Policy (ADP) of the relevant CBER office(s) and the CBER ADP on questions they have on how to communicate with the public during the development of a guidance document.

D. FDA has adopted a two-level approach to developing guidance documents, depending on whether the guidance document is a Level 1 guidance or a Level 2 guidance.

1. Level 1 Guidance Documents
    a. Generally, FDA solicits public input on Level 1 guidances prior to implementation. The Agency posts draft Level 1 guidances on its Web site and publicizes them by issuing a NOA of the draft guidance in the Federal Register. Typically, the public has 60 to 90 days to provide comments to FDA on draft guidances. Once the comment period has closed the Agency reviews and considers the comments from the public as it prepares the final guidance. When finalized, the Agency also posts final Level 1 guidances on its Web site and publicizes them by publishing an NOA in the Federal Register.Interested persons may comment on final guidances at any time after they have been issued. FDA will review those comments and revise the guidance document when appropriate.
    b. FDA may issue a Level 1 guidance "for immediate implementation" if prior public participation is not feasible or appropriate (21 CFR 10.115(g)(2)). In this case, FDA still offers an opportunity for public comment by issuing a NOA announcing the availability of the guidance and posting the guidance on its Web site. FDA will review any public comments submitted and revise the guidance as appropriate.

2. Level 2 Guidance Documents
    a. Generally, FDA does not solicit public input on Level 2 guidances prior to issuance. At the Agency's discretion, an NOA announcing the availability of the guidance may be issued. FDA posts Level 2 guidances on its Web site. Unless otherwise stated when FDA makes the guidance available, the guidance is effective immediately. Interested persons may comment at any time after the guidance has been issued. FDA will review the comments and revise the guidance, as appropriate.

E. When a Level 1 draft guidance document is being revised in response to public comments, FDA must review all comments received and incorporate suggested changes, when appropriate. (21 CFR 10.115(g)). At the Agency's discretion, the NOA may discuss very significant comments or comments that caused significant revision to the guidance document.

F. When a Level 1 final guidance is issued, the NOA provides information for submission of public comments. Similarly, when a Level 2 guidance is issued without an NOA, the guidance cover page will provide an opportunity for public comment and information for submission of public comments. FDA will consider these comments and revise guidance documents when appropriate.

G. The Agency requests approval from the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA) of 1995 (44 U.S.C. 3501-3520) when a guidance requests the submission of information that is not already covered in an OMB approval. OMB approval is required even if FDA recommends voluntary submission of information. If you suspect that your guidance requests the submission of information that is not already covered in an existing OMB approval, consult with CBER's Regulations and Policy Staff (RPS) as early as possible.

H. Anyone may recommend to FDA that a guidance document be created, revised, or withdrawn. Drafts of proposed guidance documents may be submitted to FDA for consideration. FDA has discretion to pursue the use or development of such guidance.

I. FDA publishes a guidance agenda that includes the possible topics for future guidance development or revision. FDA is not required to issue every guidance document on the agenda and may issue guidance documents not listed on the agenda.

J. When a CBER staff member is representing CBER in a working group lead by another Center or Agency component preparing a guidance document, the CBER representative should discuss issues with appropriate peers and/or managers in CBER for comment and resolution as they occur and not wait until the final clearance process. CBER works to meet established goals for review/clearance timeframes agreed upon with other Agency components.

VI. **Responsibilities**

A. **Champion- (subject matter expert/guidance lead) -** coordinates and manages the day-to-day work on the guidance document and is most responsible for the technical quality of the document. The champion is generally the principal author and chair of the working group.

B. **Office Associate Director for Policy (office ADP)** - oversees guidance development for an office. The office ADP is often designated by the Office Director to submit consolidated, cleared office comments during the clearance process for a guidance document.

C. **Regulations and Policy Staff (RPS) -** A division located in the CBER Office of the Director that is responsible for assisting the champion in preparation of the guidance document, reviewing guidance documents, preparing clearance packages, and managing the clearance process for guidance documents.

D. **Policy Coordinating Committee (PCC) -** a CBER forum to discuss policy issues, including concept papers for proposed guidance documents, in a manner that provides for participation by all CBER offices.

E. **CBER Associate Director for Policy (CBER ADP) -** oversees guidance development for the Center.

VII. Procedures

A. Initiation and Work Planning/ Developing Concept Papers

1. Develop a concept paper, with appropriate office level supervisory concurrence. **[champion]**
    a. The concept paper should:
        i. include the champion's name and contact information;
        ii. identify affected or interested divisions/offices/centers and any other Agency components;
        iii. clearly state guidance objectives and/or concepts;
        iv. address the potential workload on the lead division/office/center and other Agency components;
        v. address how the guidance relates to the center/office programs and priorities to better inform management prioritization decisions if the guidance is approved for development;
        vi. address the potential effect of the guidance on stakeholders and anticipated stakeholder response;
        vii. include a proposed timeline for development; and
        viii. include any additional items of relevance.
2. Schedule a presentation for the Policy Coordinating Committee (PCC) by sharing the concept paper with the PCC manager and RPS Director. **[office ADP]**
3. Present the concept paper to the PCC. **[champion or office designee]**
4. Distribute the concept paper for comment and request input regarding individuals who should serve as working group members for developing the draft guidance. **[PCC manager]**
5. Revise concept paper based on comments received. **[champion]**

6. Approve concept paper. **[CBER ADP or CBER Director]**

B. Developing Draft Guidance

1. Carefully choose a champion/author to ensure that he or she has the requisite scientific expertise and writing skills and can meet established timeframes. **[Office Director, in consultation with relevant Division Director and Branch Chief]**
2. Determine whether a CBER level working group is needed. **[champion and office ADP]**
3. Solicit additional working group members, if needed. **[Office Director/office ADP].** In addition to staff from the lead CBER office, the working group may include staff from non-lead CBER Offices, other Centers, Office of Chief Counsel (OCC), and any other individual within FDA that may contribute expertise in developing the guidance document. Consult with OCC and other components of the Agency as appropriate in the preparation process as early coordination may help avoid delays in the clearance process. **[Office Director/office ADP]**
4. Manage the working group to draft the guidance document. **[champion/office ADP]** Consider the following:
    a. Encourage individual working group members to identify and resolve policy issues before the review/clearance phase so that the formal review/clearance processes are not used to address or revisit contentious issues that could have been resolved earlier;
    b. Identify cross-cutting issues early; involve any additional affected divisions/offices/centers in the drafting process prior to the review/clearance phase;
    c. Clearly delineate roles and responsibilities for each working group member to prevent duplicative efforts and to help ensure timely resolution of issues;
    d. Establish smaller core working groups that could more efficiently develop specific deliverables, such as drafting one section of the guidance, as needed;
    e. Communicate issues and their resolution with division/office/center management as appropriate on an ongoing basis so that each level of review is more predictable and streamlined; and
    f. Elevate to division/office/center managers as appropriate issues that the working group cannot resolve in a timely fashion.
5. Develop work plans with target milestones and manage guidance drafting and development consistent with those milestones. **[champion]**
6. Draft all guidance documents in "Plain Language" (Refs. B.3 and 4) using current standardized templates with pre-formatted templates (Ref. A.1). Contact RPS for additional information or help. **[champion]**
7. Ensure references used in the guidance document are relevant, appropriate, and accurately described. **[champion]**

8. Obtain concurrence with the draft from the Office Director with primary responsibility for the document. **[champion or office ADP]**
9. Email the guidance document and complete copies of the documents cited as references to the RPS Director. **[champion or office ADP]** The email should contain any background information on the issues not covered in the guidance but are important to understanding the guidance.
10. Schedule a briefing meeting that, at a minimum, includes: the champion, office ADP; RPS Director, RPS team leaders and assigned staff, CBER ADP, Special Assistants to the CBER ADP, and ADPs from affected offices. **[champion or office ADP]**
11. Present the guidance document at the briefing meeting. **[champion or office ADP]** Input is requested from all invited participants regarding:
    a. agreement on timeline/priority status, and designation as Level 1 or Level 2;
    b. agreement on clearance process, such as consideration of the appropriate entities/reviewers for clearance (including OCC, HHS, OMB);
    c. discussion of all major issues in document, including PRA analysis;
    d. name of the contact person for inquiries;
    e. Web pages where the guidance will be ultimately posted; and
    f. identification of any remaining issues, including cross-cutting issues, so that affected divisions/offices/centers are brought into the process prior to the review/clearance phase.

C. Reviewing, Clearing, and Issuing Guidance

1. Performs review of guidance documents including: **[RPS]**
    a. Develops work plans with target milestones and manages guidance review, clearance, and issuance consistent with those milestones;
    b. Tracks and updates progress of the guidance document in appropriate database;
    c. Drafts PRA analysis, if applicable, with the lead office and the PRA staff in the Office of the Commissioner;
    d. Assures appropriate use of regulatory language, correct citations, plain language, and consistency with CBER policy and practice;
    e. Checks all listed guidance references for accuracy, e.g., ensure links are active and the titles are correct;
    f. Helps to identify and resolve any remaining policy issues, including cross-cutting issues;
    g. Helps to facilitate the review process so that each level of review reflects input and consideration of appropriate office level managers and subject matter experts in order to help streamline final clearance;
    h. Helps to identify the appropriate reviewers prior to initiating clearance to avoid requesting clearance unnecessarily from certain individuals or offices, based on discussion at briefing meeting; and

i. Drafts the NOA, as applicable. (Ref. A.2

2. Coordinates CBER, OCC, and general Agency (other division/office/center) clearance of the guidance document and, as applicable, the NOA. **[RPS]** These steps include the following, not necessarily in the order stated:
    a. Circulates guidance document for initial clearance or final sign-off (or FYI) to FDA staff as appropriate, e.g., CBER, other Centers, OCC, OC;
    b. Communicates expectations that established time-frames (e.g., those agreed upon in the briefing meeting) be met and communicates obstacles to meeting established time-frames;
    c. Works to resolve obstacles, as needed, such as highlighting issues relevant to individual reviewers or facilitating targeted discussions;
    d. Receives comments from FDA staff, including consolidated, cleared comments from the Office Directors or designees (often the office ADP), other Centers, OCC, and OC;
    e. Works to facilitate a focused or limited review, so that previous decisions are not unnecessarily revisited multiple times during the review process;
    f. Works with the appropriate office ADPs to limit multi-level reviews within the same office to controversial or otherwise difficult issues; and
    g. Works with the champion and office ADP to address the comments received during the clearance process.
3. Issuance of Guidance **[RPS]**
    a. Sends a copy of the guidance document for publication and/or submits a request to CBER/Office of Communication, Outreach and Development (OCOD) to post the guidance document on the CBER Web site and to make the guidance document otherwise publicly available. (Ref. A.3)
    b. Submits the guidance document along with references to Division of Dockets Management to request that the guidance document be placed on the docket.

D. Developing Final Guidance

1. Forwards to the champion copies of comments submitted to the docket on the issued guidance document or facilitates access to these comments; works with the champion to address those comments. **[RPS]**
2. Forwards to the champion the Word version of the draft guidance in final guidance template. **[RPS]**
3. Obtains agreement of champion and office ADP on responsibility and timeframe for preparing a summary of comments submitted to the docket. **[RPS]**
4. Forms a working group, as appropriate, to evaluate, consider, and revise the guidance as needed based on the comments submitted. **[office ADP]**
5. Repeat steps from VII.B above to finalize the guidance.

E. Guidance Management

1. Submit to RPS Director and CBER ADP a list of annual office priorities. **[office ADPs]**
2. Discuss office priorities and proposed Center priorities at PCC annually. **[RPS Director]** Factors considered in determining Office and Center priorities include public health significance, Department and Agency strategic priorities, legislative mandates, input from stakeholders, modernization/clarification of regulatory requirements, resource savings (to industry, Agency, consumers), and deliverables related to guidance development in performance plans.
3. Distribute a list of Center priorities to office ADPs annually. **[CBER ADP]**
4. Assess progress on Center priorities periodically. **[RPS Director/CBER ADP]**
5. Revise the list of priorities as needed, with input from offices. **[CBER ADP]**
6. Submit CBER list to the Office of the Commissioner for FDA guidance agenda, consistent with priorities. **[RPS]**
7. Withdraw draft or final guidance when necessary. **[RPS]** On occasion, a draft or final guidance may be withdrawn. If you wish to initiate the withdrawal of a draft or final guidance, send an email to the CBER ADP explaining why the guidance should be withdrawn.

VIII. Appendix

N/A

IX. References

A. **References below are located on CBER's Intranet Web Page**

1. Templates for Drafting Guidance Documents for CBER
2. Template for the Preparation of a Notice of Availability
3. SOPP 8105: Submitting Documents for the CBER Web Sites

B. **Web links to the references below can be found in the list following the History Section**

1. The Food and Drug Administration Modernization Act (FDAMA) of 1997 https://www.fda.gov/regulatoryinformation/lawsenforcedbyfda/significantamendmentstothefdcact/fdama/default.htm
2. Administrative Practices and Procedures; Good Guidance Practices, Final Rule (65 FR 56468, September 19, 2000)
3. Presidential Memorandum on Plain Language, dated June 1, 1998 http://www.plainlanguage.gov/whatisPL/govmandates/memo.cfm
4. Website for Plain Language http://www.plainlanguage.gov/

X. **History**

Written/ Revised	Approved By	Approval Date	Version Number	Comment
PCC	Robert Yetter, Ph.D.	December 3, 2012	6	Revised to incorporate recommendations of 12/2011 FDA Report on GGPs and to update format
RPS	Robert Yetter, Ph.D.	September 21, 2009	5	Templates Revised
RPS	Robert Yetter, Ph.D.	January 15, 2004	4	Revised to include OCC change in template language; also includes technical changes
P.McKeever, RMCC	Rebecca Devine, Ph.D.	January 15, 2003	3	Addition of updated instructions and templates
S.Sensabaugh G.Hicks	Rebecca Devine, Ph.D.	June 24, 1997	2	Reissued as SOPP 8002 in August 1997. No change to Guide content
S.Ripley	Rebecca Devine, Ph.D.	December 31, 1996	1	Revisions to content pursuant to FDA Modernization Act of 1997