GENERAL MANAGEMENT AND ADMINISTRATION

Developing and Issuing Guidance

CONTENTS

PURPOSE

This MAPP describes the process for developing, finalizing, and publishing guidance on Agency and Center policy.

BACKGROUND

In February 1997, the Agency announced its Good Guidance Practices Policy (GGPs) (62 FR 8961). This policy was widely praised and later that year, in the Food and Drug Administration Modernization Act of 1997, Congress directed the FDA to codify its GGP policy. A final rule codifying the GGPs was published on September 19, 2000 (65 FR 56468). This MAPP, which reflects the requirements of 21 CFR 10.115, was first issued in April 1998; it was revised in July 2003, and again in 2005 after a 6-month, centerwide review and revision of the guidance development process.

DEFINITIONS

Guidance: A *guidance* refers to any written communication that explains an Agency or Center policy or procedure. The term *guidance* generally refers to guidance for regulated entities (e.g., the pharmaceutical industry). In some instances, CDER has developed *reviewer guidance* or *guidance for industry and reviewers.*

Guidance documents do *not* include (1) FDA reports; (2) general information provided to consumers; (3) documents relating solely to internal FDA procedures (e.g., where there is no external interaction); (4) speeches, journal articles, editorials, or media interviews; (5) warning letters; (6) other communications or actions taken by individuals at the FDA directed to individual persons or firms.

MAPP: Agency and CDER policy directed toward the performance of the daily activities of Center personnel are called MAPPs and are kept in the *CDER Manual of Policies & Procedures*, from which the name MAPP is taken. A MAPP may be issued by any CDER administrative level (center, office, division, staff, branch, or section) and can apply to Center administration and management as well as program activities. Employees are responsible for staying up to date on the directives outlined in Center MAPPs. Detailed information on how to prepare a MAPP can be found in MAPP 4000.1.

Guideline, Guidance Memoranda, Points to Consider: These terms were previously used to refer to guidance documents. This nomenclature is no longer being used.

Good Guidance Practices (GGPs): Codified into law in September 2000, GGPs define how the FDA develops and uses guidance documents (21 CFR 10.115).

Regulation, Rule: Both terms refer to legally binding and enforceable requirements that are promulgated through notice and comment rulemaking.

G^2 Web Site: The Guidance on Guidance (G^2) Web site contains a variety of information on developing guidances and MAPPs. The Reviewer Style Manual, as well as templates for guidances, notices of availability, MAPPs, and clearance sheets also are available on the G^2 Web site (http://cdernet.cder.fda.gov/guidancedoc/gsquaredindex.htm).

Documents mentioned in this MAPP that are part of the guidance development process are defined here. They are available on the G^2 Web site.

Guidance Initiation Sheet: Anyone wishing to begin development of a guidance should fill out a Guidance Initiation Sheet and submit it to her or his Senior Management Team (SMT) Member (e.g., Director of the Office of New Drugs (OND), Office of Pharmaceutical Sciences (OPS), Office of Compliance (OC)).

Flow Chart on Guidance Development Process: This flow chart graphically depicts the guidance development process, including all of its possible cycles.

Best Practices for Guidance Development: This list contains useful suggestions for organizing guidance development and working with groups.

CDER Guidance Routing Slip: The routing slip must accompany each guidance as it moves through the official clearance process.

Workplan Template: This template provides guidance developers with a framework for completing the various tasks involved with guidance development.

Instructions for Digitally Signing PDF Files: Some supervisors are signing off on documents using the Adobe Acrobat electronic signature capability. These instructions explain how to do that.

Frequently Asked Questions

DOCUMENTING CDER POLICY

- All important CDER policies will be documented in the form of (1) a regulation, (2) a guidance, or (3) a MAPP.
- A policy that is intended to be legally binding and enforceable on anyone should be promulgated under the procedures set forth in the Administrative Procedure Act (5 U.S.C. 552), usually with notice and comment rulemaking.
- Nonbinding recommendations and guidance intended primarily to assist the pharmaceutical industry or other regulated entities will be issued in the form of a guidance document.
- Policies and procedures *primarily* intended to provide direction to reviewers or other staff within the Center on how they are to do their work will be issued in a CDER MAPP. (See MAPP 4000.1 for information on preparing MAPPs.)
- Communication of new policies through informal mechanisms such as speeches or letters to firms should be avoided until a policy is appropriately formulated, documented, and cleared. This does not limit the ability of CDER officials to respond to questions as to how an established policy applies to a specific situation or to questions about areas that may lack established policy. However, repeated questions about a particular area may signal the need to develop clarifying policy and guidance for that area.
- Retroactive application of a new policy should be avoided unless there is a public health and safety reason for making the policy effective retroactively.

GUIDANCE DOCUMENTS — DESCRIPTION AND GOAL

- Guidances are prepared to establish clarity and consistency in FDA policies, regulatory activities, and inspection and enforcement procedures (see CDER compliance policy guides). They reflect FDA's current thinking on an issue. Guidances are intended to assist the pharmaceutical industry in carrying out its obligations under laws and regulations on subjects such as the processing, content, evaluation, and approval of drug product applications and the design, production, manufacturing, and testing of regulated products.
- Guidance documents are ***not legally binding*** or enforceable. However, guidance documents contain important Agency recommendations. Because guidance documents represent current Agency thinking, sponsor submissions that conform to current guidance should be considered acceptable. If an employee wishes to request that a sponsor use an alternative approach, this decision should be discussed first with his or her supervisor and then with the office or division director as appropriate. Similarly, alternative approaches proposed by sponsors may be acceptable and should be discussed with CDER supervisors before they are accepted. ***The decision to deviate from a guidance document should be clearly documented.***
- Guidance documents must be developed according to good guidance practices.
- Sometimes guidance documents raise paperwork issues. If you are developing a guidance that requests the submission of information that is not already covered in a regulation, you may have to do a Paperwork Reduction Act analysis. For more information, contact the Associate Director for Policy, or designee.

TRANSPARENCY IN GUIDANCE DEVELOPMENT

The Agency recognizes the importance of maintaining a transparent guidance development process. Therefore, the Agency has implemented various practices intended to obtain input at the earliest stages of guidance document development.

- CDER maintains a ***guidance agenda*** on its Internet site listing the guidances it intends to issue in the current year. This enables the public to see what the Center is working on. The Agency is required to publish once a year in the *Federal Register* an Agency guidance agenda with the goal of soliciting comment on Agency intentions to develop guidance.
- The Agency may solicit or accept early input on the need for a new or revised guidance, or assistance in the development of a particular guidance document, from individual governmental and/or nongovernmental groups (e.g., National Institutes of Health, consumer groups, trade associations, patient groups, public interest groups).
- The Agency may participate in meetings with these various parties to obtain each party's views on priorities for developing guidance documents.

- The Agency may hold meetings and workshops to obtain input from interested parties on the development or revision of guidance documents on a particular subject area.
- The Agency may hold a public workshop to discuss a draft and/or present a draft to an advisory committee when there are highly controversial or unusually complex new scientific issues.
- The Agency may issue a notice in the *Federal Register* soliciting public input before developing draft guidance.

THE 2-LEVEL APPROACH TO GUIDANCE DEVELOPMENT

The GGP regulation provides for a 2-level approach to the development of guidance documents with regard to public input. The procedures for developing and implementing a guidance document will depend on whether that guidance document is a *Level 1* guidance or a *Level 2* guidance.

Level 1 Guidance

Level 1 guidance documents generally include guidances directed primarily to applicants or sponsors or other members of the regulated industry that set forth any of the following.

- First interpretations of statutory or regulatory requirements
- Changes in interpretation or policy that are of more than a minor nature
- Unusually complex scientific issues
- Highly controversial issues

Level 2 Guidance

Level 2 guidance documents include all other guidance documents. For example, a guidance that reformats an old policy statement to make it consistent with GGPs would be a Level 2. The development of a guidance around a policy that has been in place and that is not controversial would probably be a Level 2 guidance. Most guidances are Level 1. If you believe your guidance is a Level 2 guidance, contact the Associate Director for Policy for confirmation.

Public Input for Level 1 Guidance Documents

For Level 1 guidance documents, the Agency will solicit public input prior to implementation, unless:

- There are public health reasons for immediate implementation.
- There is a new statutory requirement, executive order, or court order that requires immediate implementation, and guidance is needed to help effect such implementation.
- The guidance is presenting a less burdensome policy that is consistent with public health.

In these situations, the Agency will solicit public input at the time of issuance and implementation.

For Level 1 guidance documents, the Agency will, at a minimum, solicit public input through the following two actions.

1. Issue a notice of availability (NOA) announcing the availability of a draft guidance in the *Federal Register*[1] explaining the context for the development of the guidance and requesting that comments on the guidance be sent to the Division of Dockets Management to a specified docket number. A copy of the draft guidance will be placed in the docket. The Agency may use one *Federal Register* NOA to solicit public input on several different draft guidance documents.

2. Post the draft guidance on CDER's home page in the guidance document list.[2]

Comments submitted on draft Level 1 guidance documents should be sent to the Division of Dockets Management, to the docket number identified in the *Federal Register* notice. Staff should encourage anyone providing informal input on guidance documents to submit their thoughts to the docket as well. All comments received in the docket will be made available to the public for review. The Center will review all comments, but need not specifically address every comment when issuing the final guidance. The Center will revise the guidance document in response to comments, as appropriate.

[1] Templates for *Federal Register* notices to announce the availability of draft and final guidances are available on the CDERnet at the guidance on guidance (G^2) Web site.

[2] CDER maintains a complete list of all Center guidance documents on the Internet at http://www.fda.gov/cder/guidance/index.htm. Most guidance documents can be downloaded directly from the Internet. Copies also are available from the Drug Information Branch.

Public Input for Level 2 Guidance Documents

For Level 2 guidance, the Agency will provide an opportunity for public comment at the time of issuance. As with Level 1 comments, comments on Level 2 guidances should be submitted to the Division of Dockets Management. Unless otherwise indicated, Level 2 guidance will be implemented upon issuance. New guidance documents will be posted on the CDER guidance Web page as each guidance is issued. Periodically, the Agency publishes a list in the *Federal Register* of all Agency guidance documents.

Depending on the issue, CDER may decide to issue a Level 2 guidance in draft form and solicit public input. In addition, the Center may decide to announce the publication of a Level 2 guidance by placing a notice in the *Federal Register*. Changes will be made to the guidance in response to comments, as appropriate.

Comments on Guidance Documents in Use

For all final guidance documents — Levels 1 and 2 — comments will be accepted at any time. Comments on guidance documents in use should be submitted to the Division of Dockets Management or to the relevant division. Guidances will be revised in response to such comments, as appropriate.

DRAFTING A GUIDANCE — THE SPECIFICS

- All guidance documents should be complete, concise, and easy to understand (written in plain English).
- FDA guidances must abide by the following: (The template at the G^2 Web site contains all necessary boilerplate language.)

  — A disclaimer box must appear at the top of page one indicating the nonbinding nature of the guidance. It includes directions to a contact person who can respond to questions or concerns about the guidance.

  — Guidances must not include mandatory language such as *shall, must, required*, or *requirement* unless FDA is using these words to describe a statutory or regulatory requirement, and the reference includes the citation to the requirement.

  — Guidances that use the word *should* will contain the approved *should paragraph* as the last paragraph in the Introduction section of the guidance. This paragraph clarifies that in Agency guidances, the term *should* indicates that something is recommended. A header should also be included that says *Contains Nonbinding Recommendations*.

  — All guidances must include the term *guidance*.

  — Guidances must identify the center or centers or offices issuing the document.

  — Guidances must identify the intended audience of a guidance and the reason for its

development.

— Guidances must include the date of issuance.

— If a document revises a previously issued guidance it must identify the document that it replaces. Please include a statement in the introductory paragraph of the guidance explaining which guidance it replaces and why the guidance was revised.

— If it is a draft, the guidance must contain the phrase *draft — not for implementation* in the header on ***all*** pages.

— The above policy does not apply to draft ICH guidances. Any final ICH guidance must contain the elements listed here, however.

— Guidances with paperwork analyses must contain the standard paperwork language.

CLEARING A GUIDANCE

- All drafts of Level 1 guidance documents that are being made available for public comment and all final versions of Level 1 guidance documents will receive sign-off by the Associate Director for Policy and at least one member of the SMT (e.g., Director of OND, OPS, OC). For particularly significant Level 1 documents with Centerwide implications, sign-off by the Deputy Center Director or Center Director may be appropriate. Guidances developed jointly with other centers require sign-off within each center.
- The FDA Office of the Chief Counsel (OCC) will review and sign off on Level 1 guidance documents that set forth new legal interpretations and any other guidance documents that the issuing officials determine should have OCC review.
- The Office of Policy (OP) signs off on documents that are published in the *Federal Register*, including the NOAs that accompany all Level 1 guidances.
- All Level 2 guidance documents will receive sign-off of an official at the office director level or higher. Agency employees with sign-off authority should ensure that the Agency's GGPs have been followed whenever a guidance document is issued. If GGPs were not followed, the person with sign-off authority should withdraw the guidance document and reissue it in accordance with GGPs.
- We recommend that guidance clearance packages be routed electronically. Electronic routing can significantly speed the clearance process.

ROLES AND RESPONSIBILITIES

Roles (A person can serve in one or more of these roles.)

CDER Senior Management Team (SMT) Member: SMT members include the Directors of the following offices in CDER: OND, OPS, OC, OTCOM, OPASS, OIT, OIM, OMP, OM, EXOPS, OCTAP, OCPB.

Sponsor: The sponsor ensures that the right type and number of staff are devoted to development of the guidance and bears ultimate responsibility for the successful completion, clearance, and publication of the guidance.

Coordinator: This person coordinates and manages day-to-day guidance development activities.

Author: The author is the writer or the principal writer (in instances when there is a working group or multiple writers) of the guidance and the individual most responsible for the technical quality of the document.

Workgroup Chair: This is the person who runs the working group. For most guidances, the Workgroup Chair is either the sponsor or the author.

Guidance Project Manager: The project manager prepares the clearance package and manages the clearance process. In some divisions, the editor is also the Guidance Project Manager.

Editor: The editor reviews the document for format, grammar, and consistency with the GGP regulation and other Agency guidances. The editor has professional editing experience and is recognized by the Office of Regulatory Policy as qualified to perform in this capacity

Responsibilities

Among the various responsibilities of the ***CDER SMT Member (or designee)*** in the development of guidance, he or she:

- Initiates/approves guidance development
- Reviews and prioritizes ongoing guidance and policy development efforts within the Office
- Designates high-priority topics for guidance development within the Office
- Select sponsors
- Allocates resources

Among the various responsibilities of the ***Sponsor*** in the development of guidance, he or she:

- Selects the Coordinator and the Author
- Leads the selection of the working group, if one is needed
- Ensures that the appropriate subject-matter experts are consulted during the drafting process
- Oversees development of a work plan, including a timeline, for document creation and completion
- Clears the document

Among the various responsibilities of the ***Coordinator*** in the development of guidance, he or she:

- Schedules meetings and convenes the working group as needed and provides minutes of these meetings as needed
- Assists the Author in obtaining scientific and policy input from all appropriate experts
- Manages the work plan

Among the various responsibilities of the ***Author*** in the development of guidance, he or she:

- Obtains scientific and policy input from the working group and other appropriate subject-matter experts
- Uses available resources for guidance and policy document authoring, including guidance and NOA templates, the Reviewer Style Manual, and the advice of the sponsor and coordinator
- Considers the comments obtained during the preclearance and editing/clearance phases and makes appropriate revisions to the document in consultation with the coordinator, the Sponsor, the working group, and other subject-matter experts as necessary
- Keeps the coordinator and sponsor informed of the document's development

Among the various responsibilities of the ***Workgroup Chair*** in the development of guidance, he/she

- Manages the working group using identified best practices
- Runs the working group meetings
- Clarifies the roles and responsibilities of the working group members

Among the various responsibilities of the ***Guidance Project Manager*** in the development of guidance, he or she:

- Enters the document into the editing/clearance queue
- Obtains COMIS and FDRTS numbers
- Completes the CDER Guidance Routing Slip with the help of the author, and creates the clearance package
- Monitors the package as it moves through clearance
- When cleared, sends the document to the CDER webmaster for posting on the CDER guidance Web site and places the document on the CDER read-only shared area for internal access

Among the various responsibilities of the ***Editor*** in the development of guidance, he or she:

- Edits the document
- Collects comments and coordinates the changes, ensuring that any substantive changes to the document are approved by the author

STEP-BY-STEP PROCEDURES

See the Flow Chart, which depicts the Level 1 draft guidance development process.

1. Using the Guidance Initiation Sheet (available on the G^2 Web site),[3] the author will notify his or her SMT member, or designee, of the desire to develop guidance. ***Once the Super Office has agreed to proceed with the guidance, the SMT or author (depending on the procedures established in the office) will forward a copy of the Guidance Initiation Sheet to the Associate Director for Policy for tracking purposes.*** The sheet asks the author to make an initial judgment about whether the guidance will be Level 1 or 2, which centers will be involved, and who from the other centers is participating in guidance development. If there are questions, the author can confirm the level of the guidance (1 or 2) with the Associate Director for Policy, or designee.

2. Before beginning a guidance, consider the need for early public input (e.g., through a workshop, Advisory Committee, or concept paper). Consult with the Associate Director for Policy, or designee, on how best to get public input.

3. When drafting guidance documents and NOAs, use the templates provided at the Guidance G^2 Web site. This Web site is maintained by the Associate Director for Policy and is updated periodically. Templates are provided for CDER-only and joint center guidances. The Reviewer Style Manual is also available at that location.

4. If a work group is needed to develop the guidance, ensure that the appropriate members are invited and provide input. See the list of Best Practices on the G^2 Web site.

5. Once the guidance is drafted, circulate the draft guidance to affected individuals within the Center and, if appropriate, other parts of the Agency (e.g., offices that will be affected by the guidance and directors who will have to agree and sign off on the policy; we encourage the use of electronic signatures). Revise the guidance to reflect relevant comments. Some guidances may require repeated reviews. It may be necessary to meet with those who have comments. This part of guidance development often takes the longest, as it is at this time that Agency policy is developed and agreed to.

6. Obtain sign-off from the appropriate individuals overseeing the development of the guidance. SMT members have the responsibility of ensuring that the appropriate managers see the guidance before it moves into final clearance.

7. If public input is needed (e.g., for a Level 1 guidance) or desired (e.g., for a Level 2 guidance), draft a notice of availability (NOA) for publication in the *Federal Register*.

   NOTE: Level 1 guidances (both draft and final) always require publication of a notice of

[3] http://cdernet.cder.fda.gov/guidancedoc/gsquaredindex.htm.

availability in the *Federal Register*.

8. Once it is final, forward an electronic copy of the guidance and the notice of availability (if needed) to the designated Guidance Project Manager (in some cases the editor is also the Guidance Project Manager) for review and clearance.

9. The Guidance Project Manager will:
   - Ensure that the appropriate tracking numbers are assigned to the documents and that the documents have been entered into the tracking system in the Office of Regulatory Policy (ORP)
   - Create a clearance package for the guidance
   - Send both documents to an editor
   - Route the package electronically for clearance

   The Guidance Project Manager will also:
   - Maintain record copies of all guidances
   - Maintain a list of all existing guidance documents
   - Maintain a list of guidance documents under development (Guidance Agenda)
   - Coordinate the distribution of draft and final guidances to the appropriate individuals within the Center

10. The editor will review the guidance for clarity, format, and consistency with the Federal Food, Drug, and Cosmetic Act and FDA regulations and policies, and work with the author to produce and concur in a final product. This process could take as much as 1 or 2 months, depending on the shape of the document when it arrives. The editor will also review the *Federal Register* notice for clarity, format, and consistency with the requirements of the Office of the Federal Register.

11. The Guidance Project Manager will assist in obtaining clearance from the appropriate CDER SMT Directors, the Associate Director for Policy, Office of Chief Counsel (OCC), and other Agency organizations, when necessary. Note that extensive changes to the guidance resulting from the clearance process may require the document to be recirculated to obtain clearance of new material.

12. After final clearance, the Guidance Project Manager will forward a copy of the guidance to the CDER Webmaster. Generally, if a notice regarding the guidance is to be published in the *Federal Register*, the guidance document should not be posted on the Web until ***after*** the *Federal Register* notice has gone on display. (The Regulations Editorial Staff (RES) in the Office of the Commissioner will notify the Guidance Project Manager when the document is to go on display.) The Guidance Project Manager will also forward a copy of the guidance and NOA to the Division of Drug Information in the Office of Training and Communications, which will maintain hard copies of the final guidance documents and distribute copies to members of the public on request once the guidance has been posted on the Web.

13. After the draft has issued, the Division of Dockets Management will send the author the submitted comments. The author should evaluate, consider, and revise the guidance as needed based on the comments, then repeat steps 5 through 12 (above) to finalize the guidance. For final guidances, it is helpful to include in the electronic clearance package a redlined version of the document showing what has changed since the draft issued.

WITHDRAWING A GUIDANCE

On occasion, a draft or final guidance will be withdrawn. If you wish to initiate the withdrawal of a draft or final guidance, send an e-mail explaining why the guidance should be withdrawn to the Associate Director for Policy. The Associate Director for Policy, or designee, will remove the guidance from the CDER guidance page and notify the appropriate people to list the withdrawn guidance in the New/Withdrawn/Revised list, which is accessible from the CDER guidance page.

EFFECTIVE DATE

This MAPP is effective on date of publication.