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 1995, the Indiana Medical Devices Manufacturers Council, Inc., submitted a petition to the Agency requesting the development of a new policy on issuing guidance. Among other things, the petition requested the development of consistent, Agency-wide guidance documents.

The petition spurred ongoing Agency efforts to develop better guidance practices and to standardize the nomenclature used to identify guidance documents (see 61 FR 9181, March 7, 1996). This effort culminated in the publication in February 1997 of the FDA's Good Guidance Practices Policy (GGPs) (62 FR 8961).

Later in 1997, in the Food and Drug Administration Modernization Act of 1997, the FDA was directed to codify its GGP policy. A final rule codifying the GGPs was published on September 19, 2000 (65 FR 56468). This MaPP reflects the requirements of 21 CFR 10.115.

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 a few instances, CDER has developed *reviewer guidance*.

Guidances are prepared to establish clarity and consistency in FDA policies, regulatory activities, and inspection and enforcement procedures (see CDER compliance policy guides). 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. Guidances also are useful to FDA review staff as they reflect the FDA=s current thinking on an issue. Guidance documents contain recommendations about how best to do things, but do not *legally* bind the FDA or the public.

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.

Originator: This is the individual, usually a working group or office, who develops or revises a guidance and who is responsible for answering questions about the guidance.

GENERAL CDER POLICY

- All important CDER policies should be documented in the form either 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 pursuant to 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 should 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 should 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.

- 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.***

- Retroactive application of a new policy should be avoided unless there is a public health and safety reason for making the policy effective retroactively.

- All guidance documents should be complete, concise, and easy to understand (written in plain English).

- All guidance documents should be accurate and consistent with CDER and FDA policies. Because guidances are nonbinding, mandatory language (e.g., must, need) should be avoided in guidance documents (unless it is accompanied by a regulatory cite).

! Guidances that use the word *should* will contain the approved *should paragraph* as the last paragraph in the Introduction section. 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*. The guidance template contains both the header and the *should paragraph*.

! Based on 21 CFR 10.115, FDA guidances must contain the following elements. (A template has been developed and is available with other guidance-related information on CDERnet at the Guidance on Guidance (G^2) Web site.

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

— All guidances must include the term *guidance*.

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

— Guidances must identify the activity to which and the people to whom the document applies.

— 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 why the guidance was revised.

— If it is a draft, the guidance must contain the word *draft*.

— 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 includes the citation to the requirement.

— When issuing draft ICH guidances, we do not have to apply the above policy, but any final ICH guidance must contain the elements listed here.

GUIDANCE DEVELOPMENT

The Agency recognizes the importance of maintaining a transparent guidance development process. Therefore, the Agency is implementing 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. Once a year, the Agency publishes in the *Federal Register* an Agency guidance agenda and solicits public 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 nongovernmental groups such as consumer groups, trade associations, patient groups, and 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 panel when there are highly controversial or unusually complex new scientific issues.

The Two-Level Approach to Guidance Development

The GGP regulation provides for a two-tiered approach to the development of guidance documents. 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 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 documents include all other guidance documents. If a questions arises as to whether a guidance is a Level 1 or Level 2, contact the Associate Director for Policy.

A. Development of Level 1 Guidance Documents

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

1. There are public health reasons for immediate implementation.

2. There is a new statutory requirement, executive order, or court order that requires immediate implementation, and guidance is needed to help effect such implementation

.

3. 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 announcing the availability of a draft guidance in the *Federal Register*[1] explaining the context for the development of the guidance and requesting comments on the guidance be sent to the Dockets Management Branch to a specified docket number. A copy of the draft guidance will be placed in the docket. The Agency may use one *Federal Register* notice of availability 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 Dockets Management Branch, 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

[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.

guidance document in response to comments, as appropriate.

B. Development of 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 Dockets Management Branch. Unless otherwise indicated, the guidance will be implemented upon issuance. The availability of new Level 2 guidance documents will be posted on the appropriate FDA WWW home page as each guidance is issued. Periodically, the Agency will publish a list in the *Federal Register* of all new Level 2 guidance documents issued by all of the centers.

Depending on the issue, the Center 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.

C. Comments on Guidance Documents In Use

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

D. Clearance Policy

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 the sign-off of at least an *office director* (e.g., Director, ODE V; Director, Office of Compliance) in the Center and the Associate Director for Policy. For particularly significant Level 1 documents with Center-wide implications, sign-off by the Deputy Center Director or Center Director may be appropriate.

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 FDA Office of Policy (OP) will review and sign off on Level 1 guidance documents that constitute significant changes in Agency policy and any other guidance documents that the issuing officials determine should have OP review. The Office of Policy signs off on documents that are published in the *Federal Register*.

All Level 2 guidance documents will receive the 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.

RESPONSIBILITIES AND PROCEDURES

! **The originator will perform the following:**

1. Using the attached form, notify the Associate Director for Policy when *initiating* the preparation of a guidance or during the early development of a guidance. The Initiation Form should be sent to the Associate Director (or designee) and will be used for tracking purposes. The Initiation Form should include an initial judgment about whether the guidance will be a Level 1 or 2 and should designate which centers will be involved and who from the other centers is participating in guidance development. Confirm the level (1 or 2) of the guidance with the Associate Director for Policy, or designee. A Level 1 guidance always requires a *Federal Register* notice of availability.

2. When drafting guidance documents and notices of availability, use the templates provided at the 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. A style guide also is available at that location.

3. Circulate the draft guidance to affected individuals within the Center and, if appropriate, other parts of the Agency. Revise guidance to reflect relevant comments. Some guidances may require repeated reviews. It may be necessary to meet with those who have comments.

4. Obtain clearance (sign-off) from the appropriate coordinating committee chairs (and members of the senior team with oversight, if different from the coordinating committee chair) for discipline-specific guidances (e.g., chemistry, medical, compliance, research, information technology, biopharmaceutics, pharmacology/toxicology, or project management guidances).

5. If public input is needed, draft the notice of availability for publication in the *Federal Register*. NOTE: Level 1 guidances (both draft and final) always require publication of a notice of availability in the *Federal Register*.

6. Obtain clearance from the appropriate division directors and office directors for office- or division-specific guidances.

7. For draft and final Level 1 guidances, forward an electronic copy of the guidance and notice of availability to the Associate Director for Policy (or designee) for final review, clearance, and issuance.

8. For Level 2 guidances, forward an electronic copy of the guidance to the Associate Director for Policy (or designee) for issuance. (A notice of availability is optional for Level 2 guidances.)

! **The Associate Director for Policy (or designee) will perform the following:**

1. Assign the guidance document COMIS and FRDTS numbers and track it as it moves through the system.

2. 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 originator to produce and concur in a final product. This process could take as much as 1 month, depending on the shape of the document when it arrives in the office of the Associate Director for Policy. Review the *Federal Register* notice for clarity, format, and consistency with the requirements of the Office of the Federal Register.

3. Consult with the originator on the need for public input; if needed, decide how to get public input (e.g., public workshops, advisory committees).

4. Assist in obtaining clearance from the Office of Chief Counsel (OCC) and other Agency organizations, when necessary.

5. After final clearance, 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.

6. Maintain record copies of all guidances.

7. Maintain a list of all existing guidance documents.

8. Maintain a list of guidance documents under development (Guidance Agenda).

9. Coordinate the distribution of draft and final guidances to the appropriate individuals within the Center.

! The **Office of Regulatory Policy** staff will support the Associate Director for Policy in the above tasks.

- **The Drug Information Branch** (Office of Training and Communications, Division of Communications Management) will maintain hard copies of the final guidance documents and distribute copies to members of the public on request.

EFFECTIVE DATE

This MaPP is effective upon date of publication.

Guidance Initiation Form

Title of proposed guidance:

_____

Name of Center lead: _____ Tel. #: _____

Level (circle one)

Level 1 Level 2

Name of originating division or committee: _____

Participating Centers (circle one):

CDER CBER CFSAN CVM CDRH

Names of center leads, if applicable:

CBER: _____
CFSAN: _____
CVM: _____
CDRH: _____

Please return this form to:

Associate Director for Policy (HFD-5)
WOC 2, Rm 6030