The Least Burdensome Provisions of the FDA Modernization Act of 1997

Concept and Principles

A Document

Prepared by Representatives of

The Least Burdensome Industry Task Force and FDA

Draft – Not for Implementation

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Preface

Introduction:

The Food and Drug Administration Modernization Act of 1997 (FDAMA) amended the Federal Food, Drug, and Cosmetic Act by adding sections 513(a)(3)(D)(ii) and 513(i)(1)(D). These two sections of the law contain what are commonly referred to as the Least Burdensome Provisions. Since the enactment of FDAMA, the regulated industry and FDA have each been working independently to develop guidance that would capture the intent of these new statutory provisions and aid in their incorporation into the device development process. Recently, at the request of the Least Burdensome Industry Task Force (LBITF), FDA representatives have been collaborating with representatives of the LBITF to develop a common approach to the interpretation and implementation of the Least Burdensome Provisions.

The attached document represents a joint effort by these representatives to define the Least Burdensome Concept and its underlying principles. It has not previously been reviewed by all members of the LBITF, nor has it been vetted to other Agency staff. That is, this represents the draft document's first release to a wider audience. It is anticipated that this document will serve as the basis for the development of guidance on the Least Burdensome Provisions, further discussions among interested parties, and the development of training materials for use by the regulated industry and FDA. With this in mind, comments on the document are being solicited from other members of the LBITF, Agency staff, device manufacturers in general, as well as other interested parties.

Public Comment:

Comments and suggestions regarding this draft document should be submitted by May 20, 2000. They may be submitted to either the Least Burdensome Industry Task Force or the FDA representative, as indicated below:

To Submit Comments to the Least Burdensome Industry Task Force:

Comments should be submitted to Janet Trunzo by e-mail at jtrunzo@himanet.com or by telefacsimile at (202) 783-8750.

To Submit Comments to FDA:

Comments should be submitted to Joanne R. Less by e-mail at jrl@cdrh.fda.gov or by telefacsimile at (301) 594-2977.

The Least Burdensome Provisions of the FDA Modernization Act of 1997

I. What Is The Least Burdensome Concept?

The Least Burdensome Concept is defined as a successful means of addressing a premarket issue that involves the smallest investment of time, effort, and resources (e.g., money) on the part of the submitter and FDA. The Concept applies to all devices regulated by FDA (including *in vitro* diagnostics (IVDs)) and, when conscientiously applied, will help to ensure scientific integrity in the decision-making process, while affording a high degree of public health protection and expediting the availability of new device technologies. The Least Burdensome Concept should be integrated into all premarket activities as well as postmarket activities, as appropriate. These activities include:

- Simple inquiries regarding device development
- Pre-submission activities, including early collaboration meetings and the Pre-IDE process
- Premarket submissions
- Panel review and recommendations
- Post-approval studies
- Guidance document development and application
- Regulation development

II. What Basic Principles Underlie the Least Burdensome Concept?

The Food and Drug Administration Modernization Act of 1997 (FDAMA) did not change the standard for premarket clearance or approval. To continue to meet this standard, while also fulfilling the intent of the Least Burdensome Provisions of FDAMA, the following basic principles have been identified:

- The spirit and the letter of the law should be the basis for all regulatory decisions;
- Information unrelated to the regulatory decision should not be part of the decision-making process;
- Alternative approaches to all regulatory issues should be considered to optimize the time, effort, and cost of reaching proper resolution of the issue; and
- All reasonable mechanisms to lessen review times and render regulatory decisions within statutory timeframes should be used.

III. How Do The Least Burdensome Principles Apply to PMAs (Originals and Supplements)?

Manufacturers and reviewers should focus on the statutory criteria for approval of the PMA, i.e., the determination of reasonable assurance of safety and effectiveness, as defined in the

regulations (21 CFR 860.7). Information unrelated to the premarket approval decision should not be submitted to nor requested by the Agency.

Manufacturers and reviewers should consider whether pre-clinical data (well-designed bench and/or animal testing) could meet the statutory threshold for approval of the PMA, especially for "me-too" devices and modifications of approved devices. If clinical data are needed, alternatives to randomized, controlled clinical trials should always be considered. This could include:

- Reliance on non-U.S. data (where appropriate for the intended U.S. patient population),
- Paper[1] PMAs, or
- Trial designs employing controls such as literature, historical, non-active, and patient as their own control.

If clinical data are needed for PMA approval, the agency should consider the use of surrogate endpoints, as well as early submission of the application, as appropriate.

The role of postmarketing information in assuring safety and effectiveness should be considered, wherever appropriate, in deciding what type of data or information is needed for approval of a PMA.

Reviewers should evaluate a manufacturer's claims in a PMA only when the claims affect the safe and effective use of the device.

IV. How Do The Least Burdensome Principles Apply to 510(k)s?

Manufacturers and reviewers should focus their attention on those issues that can affect the substantial equivalence (SE) determination, that is, whether the device has the same intended use as the predicate device and is as safe and effective as a legally marketed device. Information unrelated to the substantial equivalence decision should not be submitted to nor requested by the Agency. For example, ensuring compliance with other regulations, such as Parts 801 and 809, should not be part of the SE determination. Labeling should only be reviewed to assure that the necessary elements (device description, intended use, and directions for use) are adequate.

In making the SE determination, the Center should reaffirm its longstanding review policy that:

(1) Substantial equivalence will normally be determined based on comparative device descriptions, and
(2) Performance testing will not normally be required unless there are important descriptive differences between the device and other devices of the same type, or when the descriptive information provided is not precise enough to assure device comparability. (If performance testing is required, summary information should normally suffice.)

[1] A "paper PMA" is one that is based solely on bench testing and/or information derived from the literature.

In the 510(k) process, reviewers should rely on a manufacturer's statement that a device will meet a recognized standard just as they rely on the device description as being representative of the description of the device that will be marketed.

Postmarket controls (e.g., compliance with the Quality Systems regulation) should be considered as a mechanism to reduce the premarket requirements.

Reviewers should not request information regarding changes observed in a new 510(k) that were previously incorporated without the need for 510(k) clearance in a legally marketed version of the device that will be marketed.

Manufacturing information should not be part of a 510(k) submission unless the information directly relates to the equivalency determination.

Reviewers should limit their analysis of claims in a 510(k) to those that present a major impact on the intended use of the device. Other claims, which do not have a major impact on intended use of the device, do not affect the substantial equivalence determination and should not affect the review process.

V. What Are Some General Applications of the Least Burdensome Principles?

FDA and industry should use all regulatory tools available through FDAMA and reengineering, such as the *de novo* risk-based classification process and *The New 510(k) Paradigm*.

Manufacturers should incorporate by reference other premarket submissions, whenever possible, rather than re-submitting duplicative information. FDA should encourage and accept this practice as a means of saving review resources.

Manufacturers should make effective use of FDA-recognized standards and submit declarations of conformity to these standards, as appropriate.

Reviewers should avoid attempting to ensure compliance with FDA statutes or regulations unrelated to the decision (such as the QS Regulation) or laws and regulations administered by other federal agencies.

When requesting additional information to resolve a regulatory issue, reviewers should:

- Identify the specific issue or question that the request is attempting to address;
- Acknowledge information submitted and why the information is deficient;
- Establish the relevance of the request to the determination that is being made, i.e., SE or S&E; and
- Remain open-minded to alternate ways to address the issue or question.

In responding to the reviewer's request for additional information, Industry should:

- State the Agency issue, and
- Provide
  - the information requested, or
  - an explanation why the issue is not relevant to substantial equivalence or safety and effectiveness, or
  - an explanation of alternative information that addresses the same issue.

Whenever possible, reviewers should attempt to resolve minor questions/issues by phone, fax, or e-mail. Reviewers should limit deficiency letters to the more complicated issues (major deficiencies) unless minor deficiencies have not been adequately addressed. Industry should promptly respond to questions regarding minor deficiencies so as to avoid requests for this information in deficiency letters.