Staff Update: The Least Burdensome Provisions of FDAMA

Presented
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References to the "Least Burdensome" Requirements

Section 205 of FDAMA amended the FD&C Act to incorporate two references to the "least burdensome" decision threshold

- Section 513(a)(3)(D)(ii)
- Section 513(i)(1)(D)

Section 513(a)(3)(D)(ii)

"Any clinical data, including one or more well-controlled investigations, … shall be specified as the result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in conjunction with the applicant, the *least burdensome* appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval."

Section 513(i)(1)(D)

"Whenever the Secretary requests information to demonstrate that devices … are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such requests, the Secretary shall consider the *least burdensome* means of demonstrating substantial equivalence and request information accordingly."

FDAMA did not change the standard

For premarket approval or clearance:

- Reasonable assurance of safety and effectiveness (PMA)
- Substantial equivalence (510(k))

Past Activities

- Public meeting - January 4, 1999
- Least Burdensome Industry Task Force Proposal - Spring 1999
- Draft FDA guidance document - Fall 1999
- LBITF requested meeting with FDA - January 2000

The Least Burdensome Provisions of the FDA Modernization Act of 1997
Concepts and Principles

- Prepared by representatives of the LBITF and FDA
- Draft - Not for Implementation
- Released on March 20, 2000
- Comment period ends May 20, 2000

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 on the part of the submitter and FDA.
- The Concept applies to all devices regulated by FDA (including *in vitro* diagnostics (IVDs))

What is the Least Burdensome Concept?

- The Concept should be integrated into all premarket as well as postmarket activities, as appropriate
- Activities such as:
  - Simple inquiries regarding device development
  - Pre-submission activities (e.g., early collaboration meetings and the Pre-IDE process)
  - Premarket submissions
  - Panel review and recommendations
  - Post-approval studies
  - Guidance development and application
  - Regulation development

What Basic Principles Underlie the Least Burdensome Concept?

1) The spirit and the letter of the law should be the basis for all regulatory decisions;
2) Information unrelated to the regulatory decision should not be part of the decision-making process;

What Basic Principles Underlie the Least Burdensome Concept?

3) Alternative approaches to all regulatory issues should be considered to optimize the time, effort, and cost of reaching proper resolution of the issue; and
4) All reasonable mechanisms to lessen review times and render regulatory decisions within statutory timeframes should be used.

How Do The Principles Apply to PMAs (Originals and Supplements)?

- Focus on the statutory criteria for approval of the PMA, i.e., reasonable assurance of safety and effectiveness
- Information unrelated to the decision should not be submitted to nor requested by the Agency.
- Consider whether pre-clinical data (well-designed bench and/or animal testing) could meet the statutory threshold for approval.

How Do The Principles Apply to PMAs (Originals and Supplements)?

- If clinical data are needed, alternatives to randomized, controlled clinical trials should always be considered.
- If clinical data are needed, the Agency should consider the use of surrogate endpoints.

How Do The Principles Apply to PMAs (Originals and Supplements)?

- The role of postmarketing information should be considered in deciding what type of premarket data or information is needed for approval of the PMA.
- Reviewers should evaluate a manufacturer's claims in a PMA only when the claims affect the safe and effective use of the device.

How Do The Principles Apply to 510(k)s?

- Manufacturers and reviewers should focus their attention on those issues that affect the substantial equivalence (SE) determination.
- Information unrelated to the SE decision should not be submitted to nor requested by the Agency.

How Do The Principles Apply to 510(k)s?

- In making SE determinations, reviewers should follow longstanding policy:
  - SE is based on comparative device descriptions
  - Performance testing will not normally be required
- Reviewers should rely on a manufacturer's statement that a device will meet a recognized standard.

How Do The Principles Apply to 510(k)s?

- 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.

How Do The Principles Apply to 510(k)s?

- 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.

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 rather than re-submitting duplicative information.

What Are Some General Applications of the Least Burdensome Principles?

- 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.

What Are Some General Applications of the Least Burdensome Principles?

- When requesting additional information to resolve a regulatory issue, reviewers should:
  - Identify the specific issue 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 (SE or S&E); and
  - Remain open-minded to alternatives to address the issue or question.

What Are Some General Applications of the Least Burdensome Principles?

- In responding to the reviewer's request for additional information, industry should state the Agency issue and provide:
    - Information requested;
    - Alternative information that addresses the issue; or
    - An explanation why the issue is not relevant to SE or S&E.

What Are Some General Applications of the Least Burdensome Principles?

- Reviewers should attempt to resolve minor questions/issues by phone, fax, or e-mail.
- Reviewers should limit deficiency letters to the more complicated issues 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.

The Bottom Line

- The spirit and letter of the law should be the basis of all regulatory decisions.
- Factor least burdensome concepts into all premarket activities (e.g., pre-submission and review activities, guidance document use and development, regulation development).
- Remain open-minded to alternative ways for satisfying all regulatory requirements.

Next Steps

- Continue collaboration with industry
- Develop a LB website
- Further illustrate LB concept by examples
- Add LB language to boilerplate letters and guidance documents
- Develop a LB thought process for industry/FDA
- Identify a working level appeals process
- LB Teleconference - Summer 2000