The CDRH Staff College

The Least Burdensome Provisions of the FDA Modernization Act of 1997

Presented by:
Linda Kahan
Joanne R. Less
Philip J. Phillips
Heather Rosecrans

AGENDA

I. References to Least Burdensome Requirements
II. FDA Implementation
III. Least Burdensome and the 510(k) Program
IV. Least Burdensome and the PMA Program
V. Key Points

I. References to "Least Burdensome" Requirements

Section 205 of FDAMA amended the FD&C Act to incorporate 2 references to "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, specified in writing by the Secretary for demonstrating reasonable assurance of device effectiveness shall be specified as the result of determinations 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 with differing technological characteristics 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."

Standard for Premarket Clearance and Approval Has Not Changed

II. FDA Implementation

- Open public meeting
  - January 4, 1999 meeting in Rockville, MD
- Dr. Henney's reference to "Most Reasonable"
- Memorandum to ODE Staff from Susan Alpert dated September 2, 1999

FDA Implementation (con't)

- Draft agency guidance document entitled, **"Evidence Models for the Least Burdensome Means to Market"**
  - Federal Register Vol. 64, No. 169, Sept.1, 1999
  - http://www.fda.gov/ohrms/dockets/98FR/090199g.pdf
  - Comment period ended Nov. 30, 1999

“Evidence Models for the Least Burdensome Means to Market” (con’t)

- A decision algorithm to determine the need for clinical data
- Focuses on two questions:
  - Does available VSE provide a basis for clearance when used as indicated in target population?
  - What is most appropriate and reasonable way to obtain these data?

FDA Implementation (con't)

"The Least Burdensome Industry Task Force Proposal"

- Task Force convened by HIMA
- Proposal dated March 11, 1999
- Incorporated in Appendix D of FDA guidance document - subject to same comment period

Least Burdensome Task Force Proposal

- **Promoters of "Least Burdensome" concept**
  - Application of appropriate risk/benefit criteria in decision-making
  - Acceptance of historical data
  - Premarket/postmarket balance, particularly when addressing long-term S&E issues
  - Acceptance of "state of the art" scientific principles and methods (including clinical study design)
  - Consistent use of guidance documents and standards

Least Burdensome Task Force Proposal (con't)

- **Promoters of "Least Burdensome" concept**
  - Consistent requirements for manual methods v. automated methods
  - Application of a hierarchical approach to least burdensome
  - Consideration of "accepted medical practice" in decision-making
  - Communication across FDA regarding least burdensome approaches

Least Burdensome Task Force Proposal (con't)

- **Deterrents to the "Least Burdensome" concept**
  - Necessity of submission in question
  - Ineffective communication leads to prolonged decisions and to delays
  - Requirements exceeding expectations in guidance documents and recognized standards

Least Burdensome Task Force Proposal (con't)

- **Deterrents to the "Least Burdensome" concept**
  - Clinical testing in 510(k)s when bench testing shows SE
  - Unclear justifications for NSE decisions
  - Lack of reviewer familiarity with new technology
  - Lack of clarity for FDA rejection of industry approach or proposal

An “Interim” FDA Definition

“Least Burdensome” - a successful means of addressing a premarket issue that involves the smallest investment of time, effort and money on the part of the submitter

Regulatory Indicators of Burden

- **Time** to market reflected in cumulative review days and number of review cycles
- **Expense ($)** associated with obtaining FDA marketing authorization
- **Effort** required to meet regulatory requirements

Least Burdensome Requires a Change in FDA Culture

- Recognize that there are **multiple approaches to satisfying regulatory requirements**
- Communicate, collaborate and compromise **in the interest of public health**
- Understand not just the letter of the law, but also **the spirit of the law**
- Factor **"time, effort and money"** as considerations in decision-making

Least Burdensome and Scientific Integrity

- All scientific endeavors are affected by the availability of resources
- Good science includes cost-effectiveness
- Compromise is a necessity for successful research
- Lessening regulatory burden may serve to enhance scientific progress and advance medicine

Pre-Submission Activities: PMA and 510(k)

Informal Activities

- Simple Inquiries (DSMA and ODE)
- Guidance Document Development Activities
- Pre-IDE Program

FDAMA Early Collaboration Activities

- Determination meetings
- Agreement meetings

Pre-IDE Program

1995 Guidance:

- Informal advice on pre-clinical testing and/or clinical protocol
- Letter, phone, fax, meeting

1999 Guidance:

- Goal is to benefit the sponsor
- Not a pre-requisite for an IDE
- Single Cycle

Pre-IDE Program (con't)

Pre-IDE is appropriate:

- During testing or protocol development
- NSR Studies

Pre-IDE is not appropriate:

- If device or Indications for Use are not well-characterized
- For complete IDEs
- For an in-depth review of data

Early Collaboration: Determination Meeting

- Section 520(g)(7)(A)
- Any PMA sponsor can request
- Determine valid scientific evidence to demonstrate effectiveness
- Focus on clinical trial design
- Document discussion/determination
- Binding -- unless contrary to public health

Early Collaboration: Agreement Meeting

- Section 513(a)(3)(D)(i)
- Class III devices and implants eligible
- Agree on Investigational Plan
- Document discussion/determination
- Binding -- unless substantial scientific issue essential to determining S or E is identified and after opportunity to meet

III. Least Burdensome and the 510(k) Program

- **Review of the 510(k) decision-making process**
- **Mechanisms to lessen burden**
  - Use of standards/guidance/special controls
  - Use of design controls
  - Use of "de novo" classification process
- **Recent clearances using least burdensome principles**
- **Areas outside the scope of 510(k) review**

Review of the 510(k) decision-making process [513(i)(1)(A)]

New device is SE if it has:

- Same intended use and same technological characteristics; **or**
- Same intended use and different technological characteristics, but:
  - It does not raise different questions of safety and effectiveness, and
  - Data demonstrates it is as safe and effective

Use of Standards/Guidance/ Special Controls

- “Recognition and Use of Consensus Standards” (Feb. 19, 1998)
- Modified guidance on the use of standards to issue soon
- “The New 510(k) Paradigm” (March 20, 1998)

Use of Design Controls

The New 510(k) Paradigm -- Special 510(k)s

- Summary of design control activities
- Declaration of conformity to design controls
- Relies in QSR requirements
- Final decisions in 30 days

Use of "de novo" Classification Process

- Section 513(f)(2)
- Risk-based classification process
- When a device cannot be found SE
- Is less burdensome than PMA or PDP

Recent Clearances Using Least Burdensome Principles

- Topical non-invasive wound closure devices
  - Appeal of request for AI
  - Use of class I exemption
  - Immediate application to new devices
- 510(k)υHDEυ510(k)
- Sterilization solutions

Areas Outside the Scope of 510(k) Review

- Verifying conformance with standards (Section 514, RCHSA, or voluntary standards)
- Ensuring adherence to quality systems requirements, e.g., *special 510(k)s*
- Claims substantiation activities (draft guidance to issue soon)

IV. Least Burdensome and The PMA Program

- Reasonable Assurance of Safety and Effectiveness
- Valid Scientific Evidence
- 45% are RCTs; 48% are not RCTs, 7% had no control

Mechanisms to Lessen Burden in PMA

- Declarations of conformity to standards
- Use of surrogate endpoints
- Reliance on non-clinical testing
  - E.g., Needle destruction devices
- Reliance on literature and/or non-active controls
  - Paper PMAs
  - IOL (historical control)
  - Lithotriptors (patient as own control)

V. Key Points

- **In general**
  - Factor least burdensome concepts into all premarket activities, e.g., guidance development
  - Discuss need for additional studies with colleagues and management before making requests of industry
  - Remain open-minded to alternative proposals for satisfying regulatory requirements

Key Points (con't)

- **In 510(k)**
  - Consider what information was envisioned by the statute to demonstrate SE
  - Learn from previous 510(k) decisions, i.e., consider whether additional studies are necessary for decision-making
  - Use the tools provided by FDAMA and reengineering, e.g., special and abbreviated 510(k)s, exemptions and other FDA guidance

Key Points (con't)

- **In PMA**
  - Factor recognized standards into the decision-making processes
  - Consider non-clinical alternatives for low risk devices or device modifications
  - If clinical data is needed, consider alternatives to RCTs
  - Make a conscious effort to factor in all relevant publicly available information to reduce regulatory burden.