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The Least Burdensome Provisions: Concept and Principles

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March 14, 2019

Agenda

This presentation will cover:

- Background
- Summary of Final Guidance
- Update on Implementation Efforts
- Questions and Answers

Objectives

After this webinar, you should know:

- Least burdensome principles apply across the total product lifecycle and enables the FDA to focus resources on the issues of highest public health concern.
- The FDA has identified guiding principles to support a least burdensome approach to device regulation
- Select examples of how the FDA and industry have used a least burdensome approach
- How the FDA is implementing these changes to the least burdensome approach
- Implementation of least burdensome upholds our stringent review standards and maintains the scientific integrity of our decision-making process.

Background

- Congress added the least burdensome provisions to the Federal Food, Drug, and Cosmetic Act (FD&C Act) in the FDA Modernization Act of 1997

- CDRH issued three final guidances on least burdensome from 2000-2002:

  – “The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles”

  – “Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA”

  – “A Suggested Approach to Resolving Least Burdensome Issues”

- Congress updated the least burdensome provisions to clarify the least burdensome standard in the FDA Safety and Innovation Act of 2012

Background

- Congress further clarified least burdensome in the 21st Century Cures Act of 2016 and expanded least burdensome, required training of FDA staff, and that the FDA document how least burdensome requirements are considered for significant decisions in substantive summaries

- The FDA issued final guidance, Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions, on September 29, 2017 that updated the 2000 guidance on premarket deficiencies

- The FDA issued draft guidance, "The Least Burdensome Provisions: Concept and Principles" on December 15, 2017

- The Government Accountability Office published a report on December 15, 2017 recommending that the FDA develop metrics to evaluate whether it consistently applies a least burdensome approach in reviews

Summary of Current Least Burdensome Provisions

- “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 request, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly.” (section 513(i)(1)(D)(i) of the (FD&C Act)

- “Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as a result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval.” (section 513(a)(3)(D)(ii) of the FD&C Act)

- In requesting additional information with respect to a premarket approval application (PMA), “the Secretary shall consider the least burdensome appropriate means necessary to demonstrate a reasonable assurance of device safety and effectiveness.” (section 515(c)(5)(A) of the FD&C Act)

Summary of Current Least Burdensome Provisions

- "[T]he Secretary shall consider the role of postmarket information in determining the least burdensome means of demonstrating a reasonable assurance of device safety and effectiveness." (section 515(c)(5)(C) of the FD&C Act)

- The term "necessary" in the least burdensome provisions means the "minimum required information" that would support a determination of substantial equivalence or a reasonable assurance of device safety and effectiveness. (sections 513(a)(3)(D)(iii), 513(i)(1)(D)(ii), and 515(c)(5)(B) of the FD&C Act)

- The least burdensome provisions do not change the standards for premarket approval or substantial equivalence. (sections 513(a)(3)(D)(iv), 513(i)(1)(D)(iii), and 515(c)(5)(D) of the FD&C Act)

Stakeholder Feedback on Draft Guidance

- The FDA received 79 comments from 13 external stakeholders:
  - Device manufacturers
  - Law firm
  - Trade associations
  - Academia and healthcare associations
  - Individuals
- Most comments were supportive of CDRH proposal
- Revisions and additions requested regarding the least burdensome definition and guiding principles
- Request for inclusion of additional examples
- Stakeholders requested more information about implementation

Definition of Least Burdensome

The minimum amount of information necessary to adequately address a relevant regulatory question or issue through the most efficient manner at the right time

Scope

- The least burdensome concept applies to all products that meet the definition of a device, including device constituent parts of combination products

- The policy in this guidance applies to all activities pertaining to the regulation of devices, including premarket and postmarket actions

- The policy maintains the FDA's "gold standard"

Guiding Principles

- The FDA has identified seven least burdensome guiding principles

- These guiding principles:
  - Represent what the FDA and industry should apply when taking a least burdensome approach
  - Explain the FDA's commitment for least burdensome review

Guiding Principles

1. The FDA intends to request the minimum information necessary to adequately address the regulatory question or issue at hand

2. Industry should submit material, including premarket submissions, to the FDA that are least burdensome for FDA to review
    - Industry should submit well-organized, clear, and concise information
    - Industry should not submit information unrelated to the regulatory decision to the FDA
    - Industry should reference applicable FDA guidance documents where FDA recommendations were considered

Guiding Principles

3. FDA intends to use the most efficient means to resolve regulatory questions and issues
    - FDA intends to use all reasonable measures to streamline processes and policies, as well as render regulatory decisions within appropriate timeframes, such as Medical Device User Fee Amendments (MDUFA) performance goals
    - FDA intends to routinely use both formal and informal interactive approaches, whenever possible, to resolve questions and issues
    - FDA intends to, and industry should, use reasonable, tailored approaches that have been adapted to individual circumstances and needs to address regulatory questions and issues
    - FDA intends to take appropriate consideration of the time and resource implications of its requests

Guiding Principles

4. The right information should be provided at the right time (just-in-time data collection) to address the right questions
    - The FDA intends to, and industry should, consider the use of postmarket data collection to reduce premarket data collection whenever appropriate and feasible

5. Regulatory approaches should be designed to fit the technology, taking into account its unique innovation cycles, evidence generation needs, and timely patient access

Guiding Principles

6. The FDA intends to leverage data from other countries and decisions by, or on behalf of, other national medical device regulatory authorities to the extent appropriate and feasible

7. The FDA intends to apply least burdensome principles in international medical device convergence and harmonization efforts
    - The FDA intends to actively engage in the development, recognition, and use of voluntary consensus standards published by international and other standards development organizations

Applications of Least Burdensome

- Final guidance includes examples to represent how least burdensome principles can be implemented

- These examples generally relate to:
  - Different sources of and reducing the burden of clinical data
  - Using nonclinical data
  - Accepting alternative approaches
  - Benefit-risk assessments
  - Reducing administrative burden
  - Smart regulation
  - Global harmonization
  - Balance premarket and postmarket
  - The use of just-in-time testing

Examples – Minimum Information Necessary

- Leveraging existing data
  - Peer reviewed literature has been used to as the pillar for:
    - Marketing authorization in De Novo requests and humanitarian device exemption applications
    - Support expanded indications for use and other labeling changes in 510(k) submissions

  - Information filed in premarket approval applications was used to reclassify stair-climbing wheelchairs and sharps needle destruction devices under the six-year rule

Examples – Most Efficient Means

- Reducing the burden of traditional clinical studies using historical control groups, non-comparative clinical outcome studies, subject as own control, adaptive study designs, and alternatives to prospective sample collection

- Global harmonization
  - Voluntary consensus standards create consistent approaches to device development, manufacturing, and evaluation
  - The Medical Device Single Audit Program minimizes the number of audits, redundant requests, and disruption of business, while still meeting the requirements of applicable jurisdictions

Examples – The Right Time

- Striking the right balance between Premarket and Postmarket data collection
  - The FDA assessed 200 product codes for Class III devices to consider whether these device types were candidates for a premarket/postmarket shift of data capture or reclassification. Three final orders to reclassify have been published thus far

- Just-in-time testing
  - Device evaluation strategies can be used to transparently establish a timeline for deferred or additional nonclinical testing as a company proceeds through subsequent clinical studies

Update on Implementation Efforts

- The FDA published the FDA Report to Congress: Least Burdensome Training Audit in June 2018

- Since the FDA Report to Congress, CDRH finished training all staff with a targeted course entitled “How to Make the Most of Least Burdensome: Case Study Practice”

- CDRH conducted a pilot on a new approach to resolving issues in 510(k) submissions called the least burdensome flag

Least Burdensome Flag Pilot

- The least burdensome flag is an opportunity for a submitter to request an informal review by upper management because they believe the FDA's request is not least burdensome or that they are being held to an inappropriate review standard

- CDRH ran a least burdensome flag pilot from February - September, 2018 in seven review Branches

- 510(k) requests for additional information for applicable Branches that did not raise a potential not substantially equivalent (NSE) issue included an attachment offering the opportunity to use the least burdensome flag

Pilot Criteria

- Submitters should discuss with Branch/Division management at least one time before being eligible
- Flag was limited to deficiency or deficiencies in two topics areas (e.g., biocompatibility and sterility)
- The least burdensome flag expires 60 days after the request for additional information was sent
- If used, least burdensome flag feedback is sent within 21 days of receipt

Summary of Pilot

- The FDA requested feedback from one third of submitters who did not use the flag and all submitters who used the flag

- Pilot sought to answer questions related to customer satisfaction, efficiency, and submission outcomes

- 132 letters received the least burdensome flag opportunity. Two (2) submitters used the flag (1.5%)

Feedback from Expired Least Burdensome Flags

- The majority of respondents understood the purpose of the least burdensome flag, its process, and appreciated the opportunity to receive feedback from senior management
- Respondents did not use the flag because the issues were resolved either with the Branch Chief or a 10-day phone call, or the deficiencies were reasonable
- A few respondents thought the pilot was too restrictive or were concerned about using official meetings
- All respondents would use the least burdensome flag if they did not agree with the FDA's request for additional information

Feedback from Least Burdensome Flags

- More likely to use the least burdensome flag over an appeal
- Timing of the least burdensome flag with a 10-day call, Submission Issue Meeting, or an appeal were not clear
- Prospectively understanding the depth of review would have helped
- 510(k) is the highest priority for this program, if made final

Summary of Pilot Data

- The least burdensome flag was used in 1.5% of submissions included in the pilot
- Flags were resolved in a straightforward manner within the 21-day deadline
- Limiting the least burdensome flag to two topic areas made resolution efficient
- Submitters appreciated the opportunity to obtain senior management feedback

Pilot Conclusions and Next Steps

- The pilot results support that the least burdensome flag is simpler than an appeal, is a useful process for our staff, and provided preliminary results that our staff are least burdensome. Industry believed that the least burdensome flag provided a valuable opportunity to raise concerns about their submissions

- CDRH is implementing the least burdensome flag as a program for 510(k) submissions to act as a performance metric for the implementation of least burdensome requirements.

Least Burdensome Flag Program

- CDRH implemented the least burdensome flag on March 4, 2019 for all 510(k) requests for additional information that are not potential not substantially equivalent decisions
- Before using flag, submitters should discuss concerns with the signatory authority or their manager
- Least burdensome flags should be within two topic areas. If more than two topic areas, contact the 510(k) Staff
- Flags should be used within 60 days of the letter or they expire. Flags do not change response due date for the submitter

How to use the Least Burdensome Flag

Email the lead reviewer, their manager, and the 510(k) Staff with the following information (1-2 pages):

- A summary of the deficiencies being flagged, including why the request is not least burdensome or the submitter is being held to a different standard
- A summary of relevant communications with the signatory authority or their manager to show that the submitter has sought management input before “throwing the flag”
- Proposed path forward

What Submitters Should Expect

- The FDA will hold an internal meeting(s) and only schedule a teleconference with the submitter if they could not resolve the least burdensome flag internally

- The least burdensome flag response will be emailed on behalf of the Director of the organizational unit in CDRH responsible for your 510(k)

- The least burdensome flag resolution is included in the administrative record

Resources

Link to final least burdensome guidance:

- The Least Burdensome Provisions: Concept and Principles

Selected links:

- Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions
- FDA Report to Congress: Least Burdensome Training Audit
- Government Accountability Office report on least burdensome medical device reviews

Questions?

510(k) Questions: 510K_Program@fda.hhs.gov

Division of Industry and Consumer Education: DICE@fda.hhs.gov

Slide Presentation, Transcript and Webinar Recording
will be available at: http://www.fda.gov/training/cdrhlearn Under the heading: How to Study and Market Your Device; Subheading: Cross-Cutting Premarket Policy

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