Regulatory Perspectives for Device Development for Inhalation Combination Products

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Outline

- Classification of Medical Devices
- Respiratory Products
  - Drug-Device development
- Device Review Considerations for OIDPs
- Case study
- Conclusions
Medical Devices

- Class I General Controls
  - Mostly exempt

- Class II General Controls and Special Controls
  - Mostly require 510(k)

- Class III General Controls and Premarket Approval
  - Require Premarket Approval (PMA)
Combination Products

Definition in 21 CFR 3.2(e):

(1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity.

*Parts (2) - (4) include definitions of other types of combination products

Typically involves multi-Center review:
- CBER
- CDER
- CDRH
How to Prepare a Pre-Request for Designation (Pre-RFD)

Guidance for Industry

Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-363), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the Federal Register.

Additional copies of this guidance are available from the Office of Combination Products website at https://www.fda.gov/CombinationProducts/default.htm.

For questions on the content of this guidance, contact the Office of Combination Products at combination@fda.gov.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0845 (expires October 31, 2020).

See additional PRA statement in Section VI of the guidance.

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Combination Products in the Office of the Commissioner

February 2018

Guidance for Industry
How to Write a Request for Designation (RFD)

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of Combination Products

April 2011
Inhalation Devices Typically Seen in OINDPs

- **Nebulizers**
  - General indications
    (cleared via 510(k) path)
  - Drug-Specific
    (approved via NDA)

- **Inhalers**
  - Drug-Specific (approved via NDA)
General Use Inhalation Device

- Examples of drug classes for general use inhalation devices:
  - Beta-agonist bronchodilators (albuterol)
  - Anti-cholinergic bronchodilators (ipratropium bromide)
  - Anti-inflammatory drugs (cromolyn sodium)
- Reviewed by CDRH via 510(k) pathway
A 510(K) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR §807.92(a)(2)) that is not subject to premarket approval.

Learn more...
Drug-Specific Inhalation Devices

The Sponsor can select the preferred pathway for seeking approval of the device component:

– Device module in NDA/IND
– File for a separate 510(k) with CDRH (drug already approved by CDER)
The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]

Guidance for Industry and Food and Drug Administration Staff

Document issued on: July 28, 2014

The draft of this document issued on December 27, 2011.


For questions for the Center for Devices and Radiological Health regarding this document, contact the Premarket Notification (510(k)) Section at 301-796-5640.

For questions for the Center for Biologics Evaluation and Research regarding this document, contact the Office of Communication, Outreach and Development at 1-800-335-4709 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Intended Use

- Indications use
- Patient population
- Environment of Use
Device Review Considerations

- Intended Use
- Device Description
- Performance Testing
- Biocompatibility
- Electrical Safety
- Electromechanical Compatibility
- Mechanical Safety
- Software
- Human factors
- Labeling
Performance Testing

- Cascade impaction with at least six stages
- Testing at minimum, nominal and maximum flow rates allowable by device
Other Considerations for Performance Testing

- Addressing variability (inter and intra sample)
  - Sufficient sample size
  - Appropriate confidence level
- Testing with add-ons
  - Spacers and holding chambers
  - Patient interface (e.g., facemasks, mouthpieces)
Biocompatibility

- Gas pathway contact is considered externally communicating
- Correctly identify contact category (Type/Duration)
Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"

Guidance for Industry and Food and Drug Administration Staff

Document issued on: June 16, 2016

The draft of this document was issued on April 23, 2013.


For questions regarding this document, contact Jennifer Goode, 301-796-6374, jennifer.goode@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

INTERNATIONAL STANDARD
ISO
18562-1

First edition
2017-03

Biocompatibility evaluation of breathing gas pathways in healthcare applications —
Part 1: Evaluation and testing within a risk management process

Évaluation de la biocompatibilité des voies de gaz respiratoires dans les applications de soins de santé —
Partie 1: Évaluation et enlèvement au sein d’un processus de gestion du risque

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Biocompatibility

- Materials certification (formulation and processing)
- Particulate matter and volatile organic compounds testing
- Chemical characterization vs. Biological Testing
- Inclusion of accessories
- Finished device testing
Basic Safety and Electromagnetic Compatibility Testing

- ANSI/AAMI ES60601-1: Medical Electrical Equipment – Part 1: General Requirements for Safety

- IEC 60601-1-2: Medical Electrical Equipment - Electromagnetic Compatibility: Requirements and Tests
Software

Guidance for Industry and FDA Staff

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices

Document issued on: May 11, 2005


For questions regarding this document concerning devices regulated by CDRH contact Linda Ricci at (301) 796-6325. For questions regarding this document concerning devices regulated by CBER contact Linda Weir at (301) 827-6136.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health
Office of Device Evaluation
Office of In Vitro Diagnostics

Center for Biologies Evaluation and Research
Office of Blood Research and Review

American National Standard

(Consolidated Text)
Medical device software—Software life cycle processes
FDA encourages early communication during development through our various interactive processes:

- CDRH: Pre-submission process
- CDER/CBER: Type A, B and C meetings
Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program

Guidance for Industry and Food and Drug Administration Staff

Document issued on May 7, 2019.

This guidance supersedes “Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff,” dated September 29, 2017.

For questions about this document regarding CDRH-regulated devices, contact ORP: Office of Regulatory Programs/DRP1: Division of Submission Support at 301-796-5640. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently OMB control number. The OMB control number for this collection is 0910-0756 (expires January 31, 2020).

See additional PRA statement in Section V of the guidance.
Conclusions

- Inhalation drug delivery is dependent on a successful interplay between drug, device and patient use
  - Review grounded by regulations, standards and risk analysis
- FDA strives to work with the manufacturers to ensure safe and effective devices are available to public
Thank you!