Regulatory Perspectives for Device Development for Inhalation Combination Products

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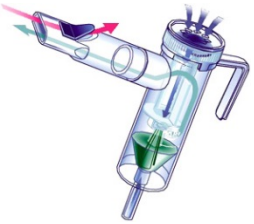
Outline

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

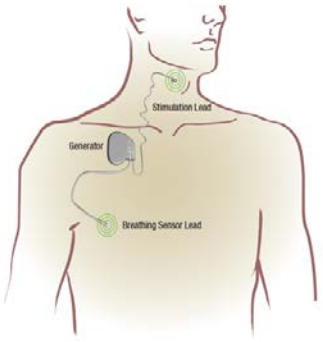
Medical Devices

- 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)



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.

This document supersedes FDA's Guidance on the CDRH Premarket Notification Review Program, 510(k) Memorandum K86-3, dated June 30, 1986.

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.

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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

Guidance for Industry

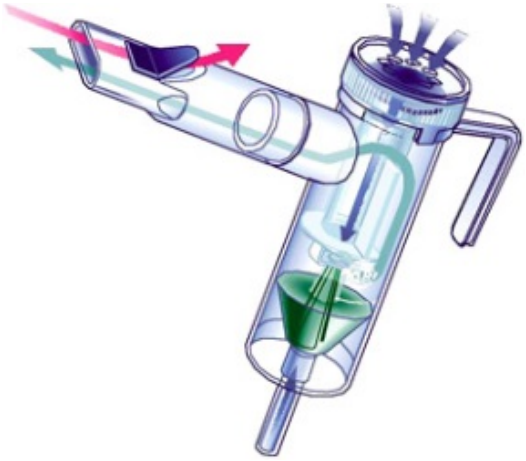
How to Write a Request for Designation (RFD)

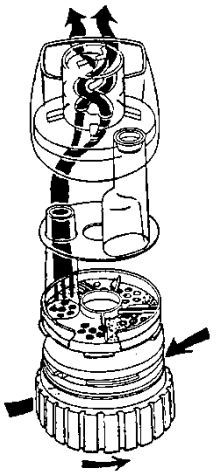
U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of Combination Products

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

510(k) Premarket Notification

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)(3)) that is not subject to premarket approval.

Learn more...

Search Database

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510K Number | Type | Product Code CAF

Center | Combination Products

Applicant Name | Cleared/Approved In Vitro Products

Device Name | Redacted FOIA 510(k)

Panel | Third Party Reviewed

Decision

Decision Date | to | Clinical Trials

Sort by: Decision Date (descending)

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Other Databases

- De Novo
- Medical Device Reports (MAUDE)
- CDRH Export Certificate Validation (CECV)
- CDRH FOIA Electronic Reading Room
- CFR Title 21
- CLIA
- Device Classification
- FDA Guidance Documents
- Humanitarian Device Exemption
- Medsun Reports
- Premarket Approvals (PMAs)
- Post-Approval Studies
- Postmarket Surveillance Studies
- Radiation-Emitting Products
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- Standards
- Total Product Life Cycle
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Page Last Updated: 06/18/2018

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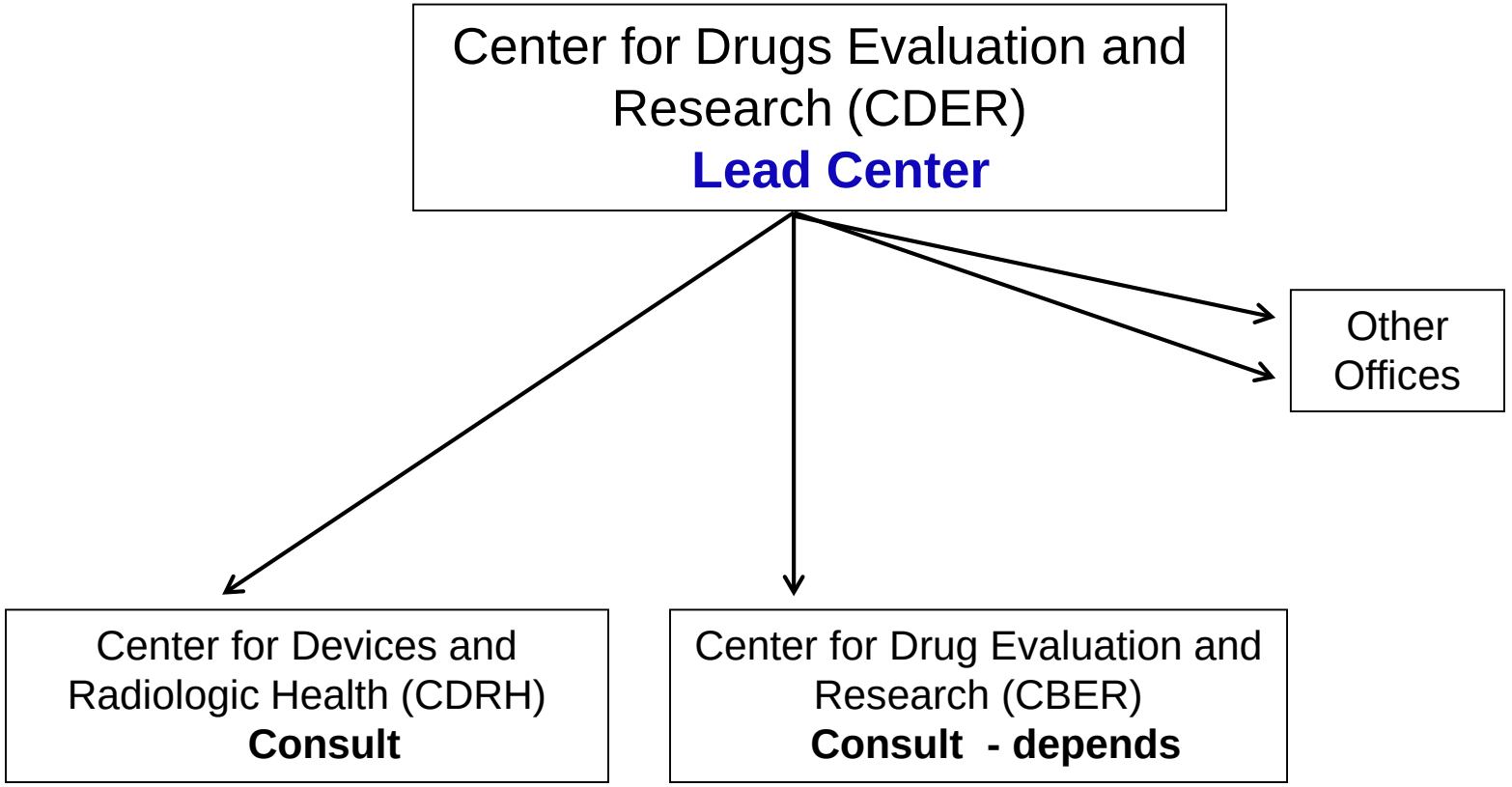
Drug-Specific Inhalation Devices

- 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)

Orally Inhaled Drug Products may involve Multi-Center Review



Device Review Considerations

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

Indications for Use

- Intended use
- Patient population
- Environment of Use

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
  - Facemasks

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.

As of September 14, 2016, this document supersedes Blue Book Memorandum #G95-1 "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing,'" dated May 1, 1995.

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

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Biocompatibility

- Materials certification

  (formulation *and* processing)
- Particulate matter and volatile organic compounds testing vs. biological testing
- Dry vs. heated/humidified gas pathway
- Inclusion of accessories
- Finished device testing

Electrical Safety and Electromechanical 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

This document supersedes Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, issued May 29, 1998, and Reviewer Guidance for a Premarket Notification Submission for Blood Establishment Computer Software, issued January 13, 1997.

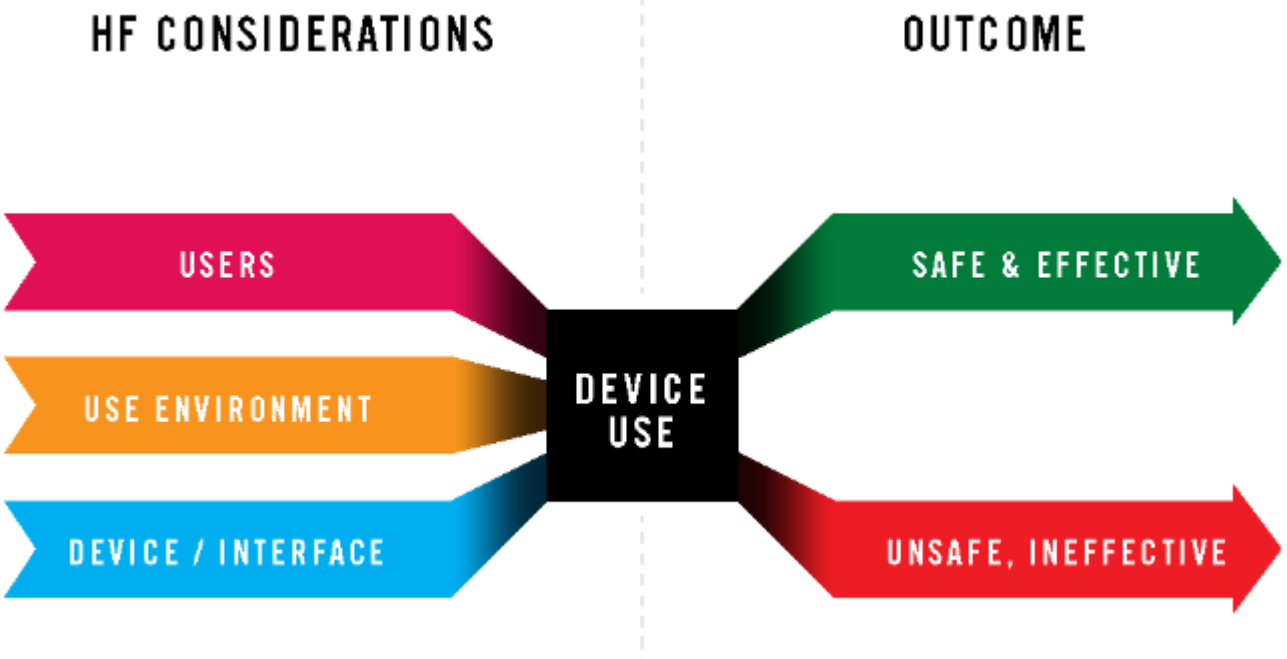
For questions regarding this document concerning devices regulated by CDRH contact Linda Ricci at (301) 796-6325. For questions regarding this document concerning devices regulated by CBER contact Linda Weir at (301) 827-6136.

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 Biologics Evaluation and Research
Office of Blood Research and Review

Human Factors



- 10% medication 90% patient interface

Case Study
Nebulizer-Drug Combination

- New nebulizer technology for delivery intended for delivery of *only* this drug.
- Sponsor proposed 510(k) clearance for the new nebulizer.
- CDRH was able to communicate to the Sponsor that a 510(k) clearance is *not* required as the proposed device is developed for delivery of this drug. Device data can be submitted in the NDA.

- 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 on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff

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Guidance for Industry and Food and Drug Administration Staff

Document issued on: February 18, 2014

This document supersedes Pre-IDE Program: Issues and Answers - Blue Book Memo D99-1, dated March 25, 1999

The draft of this document was issued on: July 13, 2012

For questions regarding this document, contact the CDRH Program Operations Staff (POS) at 301-796-5640. For questions regarding submissions to the Center for Biologics Evaluation and Research (CBER), contact CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

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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!