Regulatory Perspectives for Device Development for Inhalation Combination Products

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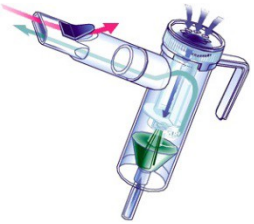
Outline

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

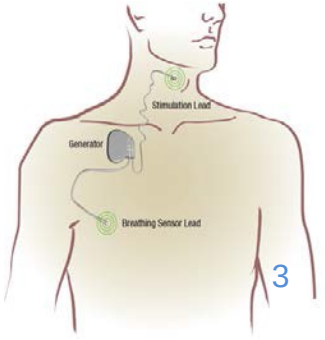
Medical Devices

- 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)



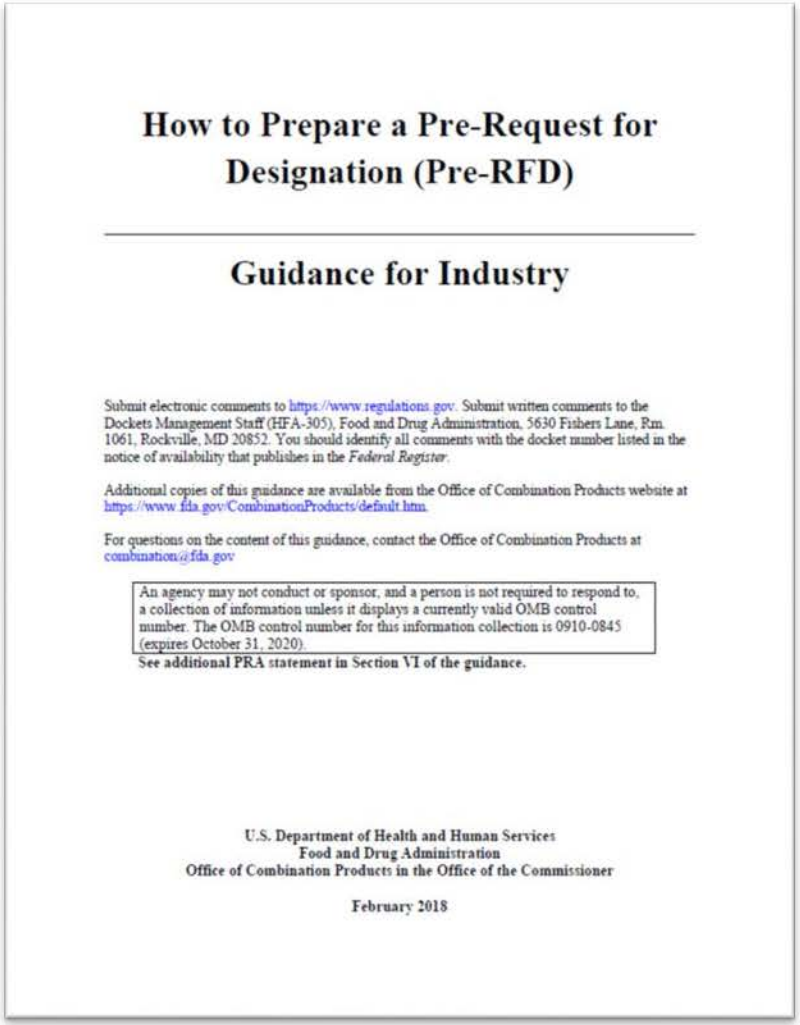
Combination Products

- 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-305), 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.

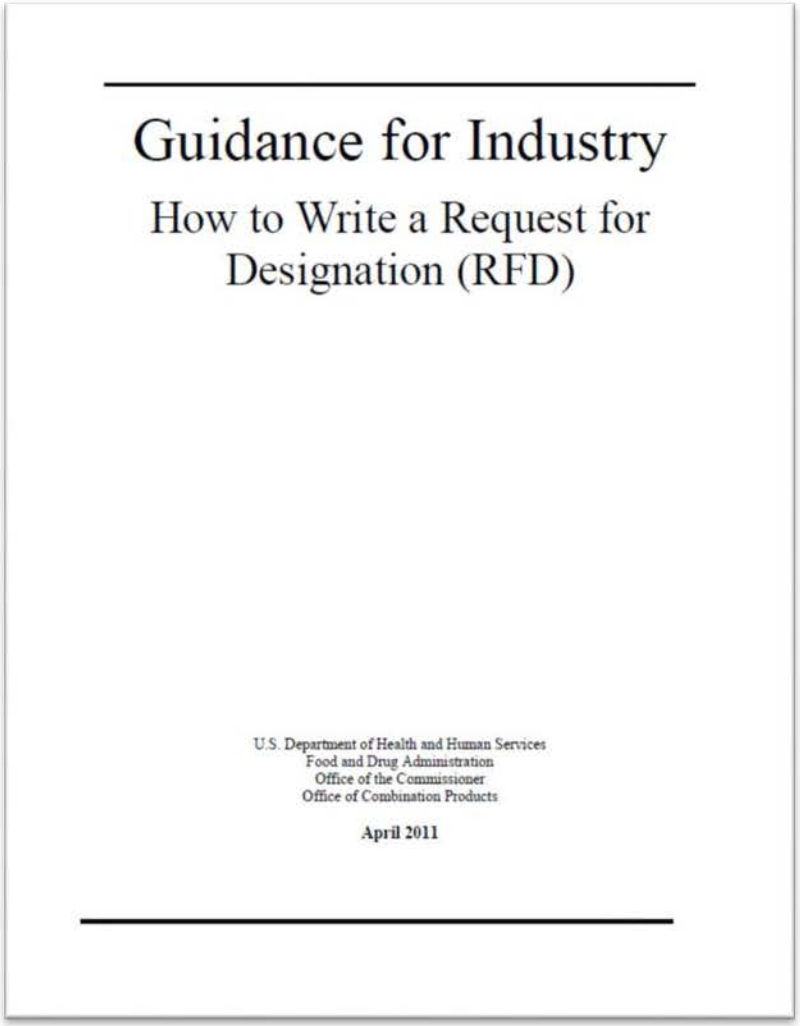
For questions on the content of this guidance, contact the Office of Combination Products at combination@fda.gov

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

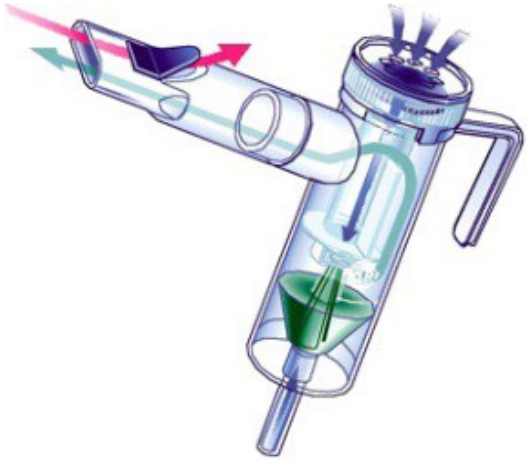
How to Write a Request for Designation (RFD)

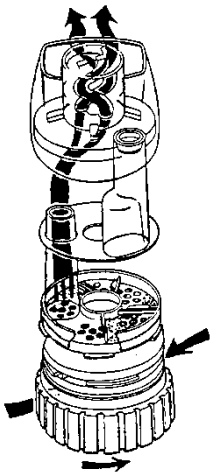
U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner
Office of Combination Products

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

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)

Quick Search | Clear Form | Search

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
- Radiation-Emitting Electronic Products Corrective Actions
- Recalls
- Registration & Listing
- Standards
- Total Product Life Cycle
- X-Ray Assembler

Page Last Updated: 06/18/2018

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Language Assistance Available: Español | 繁體中文 | Tiếng Việt | 한국어 | Tagalog | Русский | العربية | Kreyòl Ayisyen | Français | Polski | Português | Italiano | Deutsch | 日本語 | فارسی | English

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.

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.

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

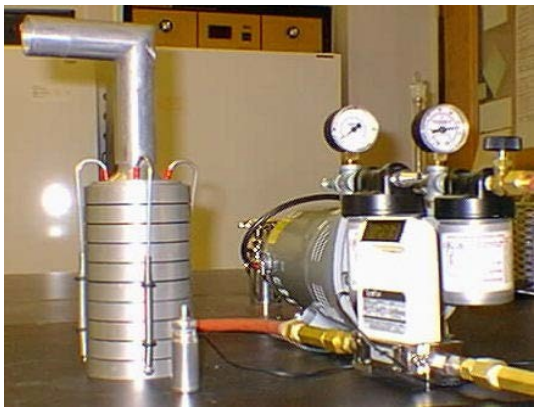
- Indications use
- Patient population
- Environment of Use

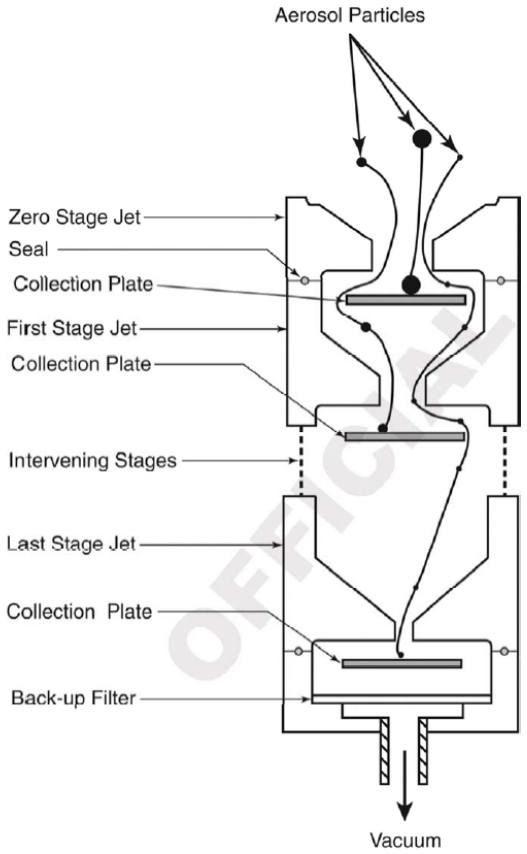
Device Review Considerations

- 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.

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.

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 essais au sein d'un processus de gestion du risque

Reference number
ISO 18562-1:2017(E)

Biocompatibility

- Materials certification

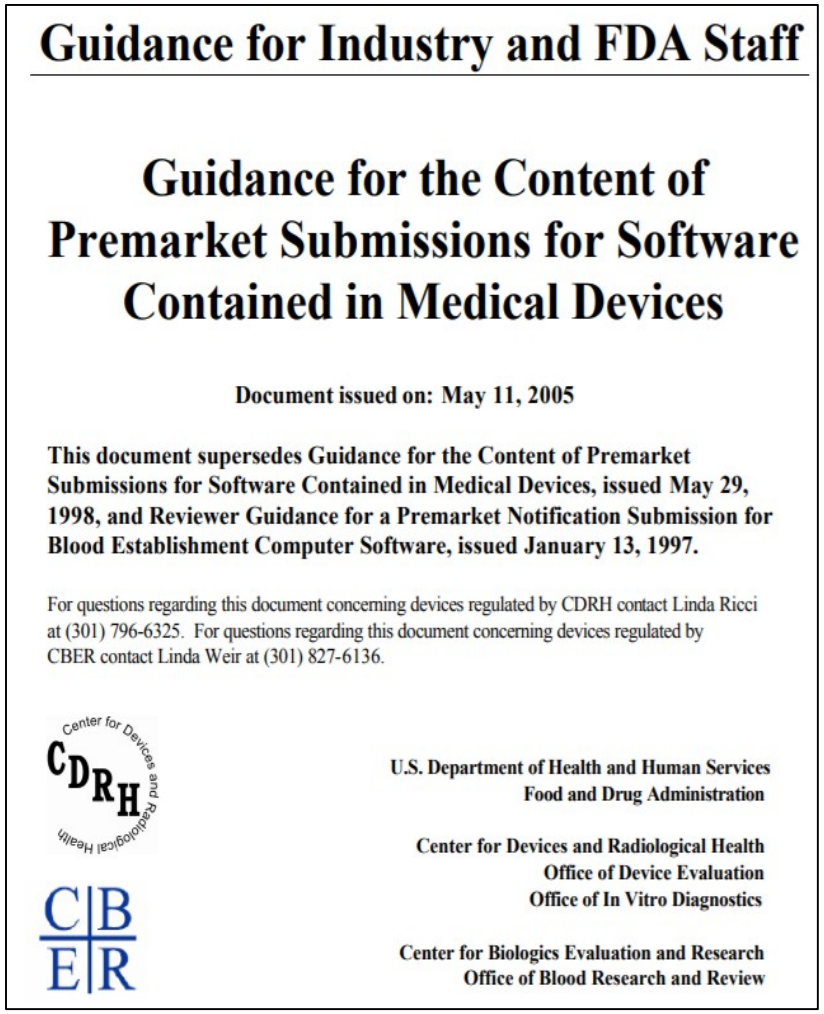
  (formulation *and* processing)
- Particulate matter and volatile organic compounds testing
- Chemical characterization vs. Biological Testing
- Inclusion of accessories
- Finished device testing

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

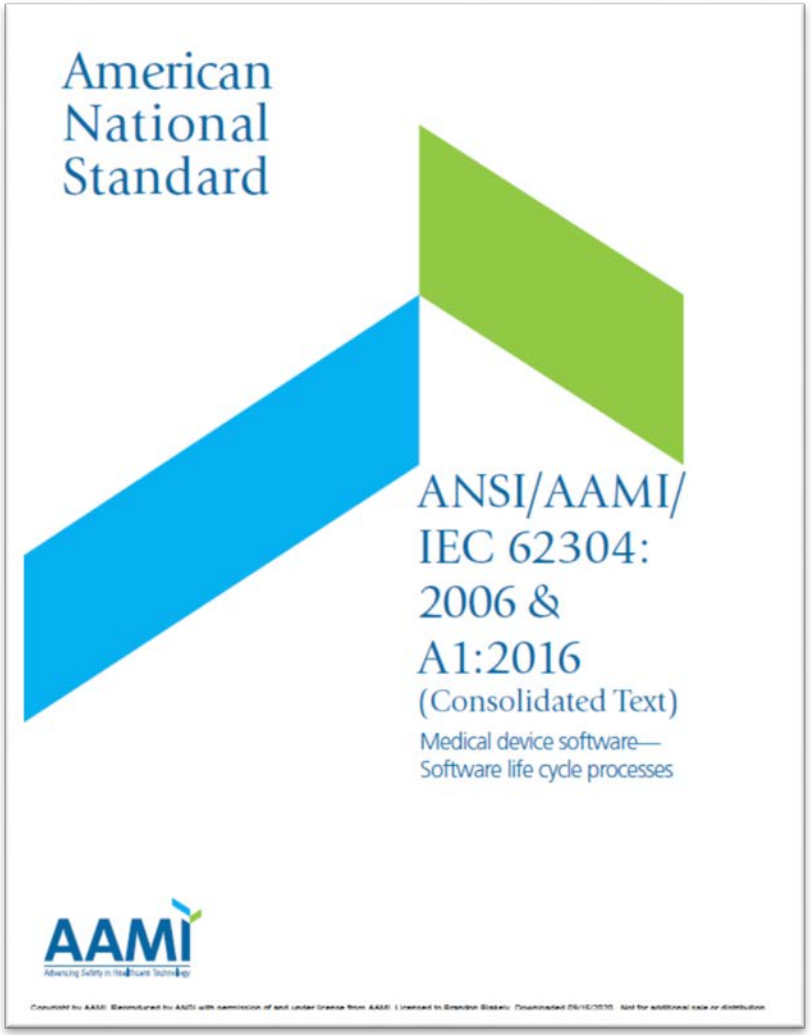
This document supersedes Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, issued May 29, 1998, and Reviewer Guidance for a Premarket Notification Submission for Blood Establishment Computer Software, issued January 13, 1997.

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



American National Standard

ANSI/AAMI/ IEC 62304: 2006 & A1:2016

(Consolidated Text)

Medical device software— Software life cycle processes

AAMI

- FDA encourages early communication during development through our various interactive processes:
  - CDRH: Pre-submission process
  - CDER/CBER: Type A, B and C meetings

Contains Nonbinding Recommendations

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.

See additional PRA statement in Section V of the guidance.

FDA U.S. FOOD & DRUG ADMINISTRATION

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

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!