

Regulation of Medical Device Clinical Trials and Innovation in Clinical Evidence Generation

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Christina Savisaar, PhD

Policy Analyst

Policy and Operations Team 1

Division of Clinical Policy and Quality

Office of Clinical Evidence and Analysis

Office of Product Evaluation and Quality

Center for Devices and Radiological Health

U.S. Food and Drug Administration



Learning Objectives

- Describe the different levels of applicability of Investigational Device Exemption (IDE) regulations
- Discuss Real-World Evidence for clinical evidence generation
- Identify the role of Early Feasibility Studies
- Describe the purpose of the Breakthrough Devices Program and the Safer Technologies Program (STeP)

Applicability of the IDE regulations

Good Clinical Practice Regulations



- Help provide assurance of:
 - Data quality and integrity
 - Protection of rights, safety, and well-being of participants

Investigational Device Exemptions



*The purpose of this part is to encourage, to the extent consistent with the **protection of public health and safety**, ... the **discovery and development of useful devices** intended for human use....*

21 CFR 812.1



Approved IDEs are exempt from certain provisions of the FD&C Act, including those related to:

- Misbranding
- Registration
- Performance Standards
- 510(k)
- PMA
- HDE
- Good Manufacturing Practice (GMP) requirements except Design Controls
- Color Additive requirements
- Banned Devices
- Restricted Device requirements

When is an IDE needed?

Device Study

Exempt

Non-Significant Risk

Significant Risk



General Applicability of IDE Regulations

*21 CFR 812.2(a) General. This part applies to **all clinical investigations** of devices to determine safety and effectiveness, except as provided in paragraph (c) of this section.*

“Investigation” means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. 21 CFR 812.3(h)

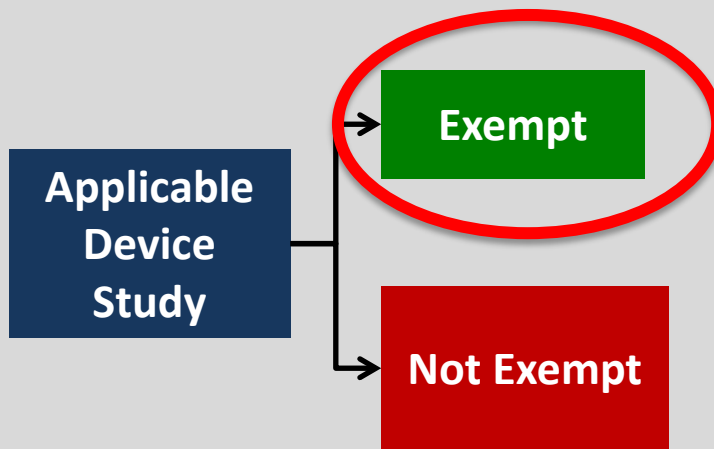
“Practice of Medicine”

“Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship....”

From Section 1006 of the FD&C Act



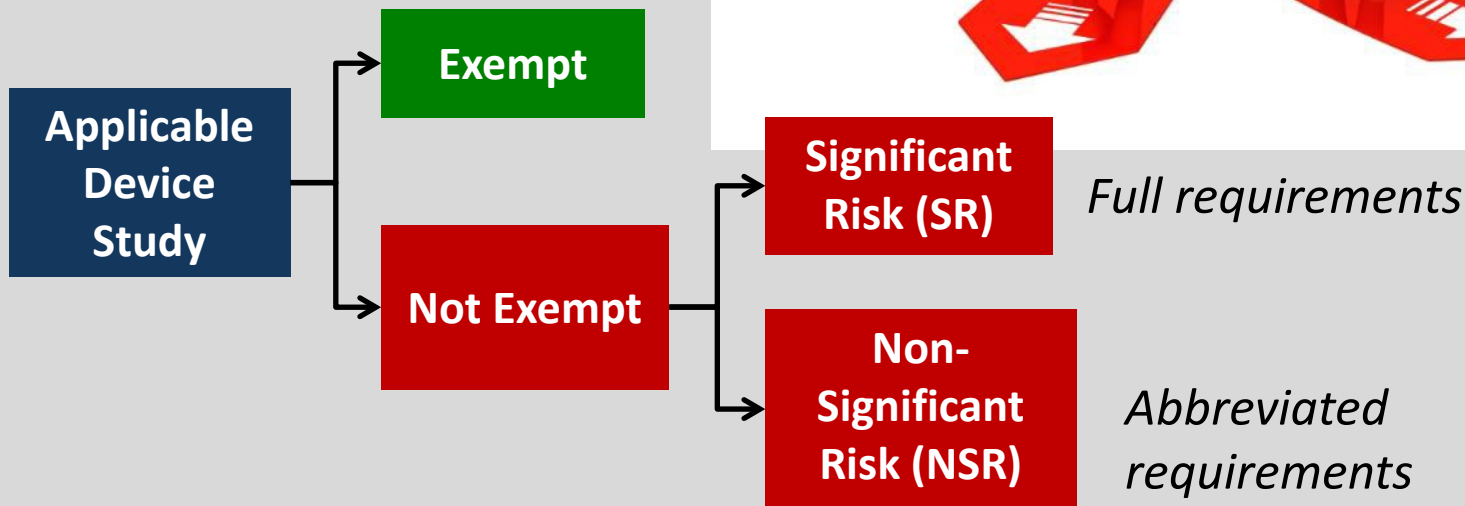
When is an IDE needed?



Exempted Studies

- Types of exempted studies given in [21 CFR 812.2\(c\)](#).
Examples:
 - Legally marketed devices used in accordance with labeling
 - Certain types of diagnostic device studies
- Do not require submission of an IDE application to FDA
- May be subject to Parts 50 (Informed Consent) and 56 (IRB Review)

When is an IDE needed?



Significant Risk Study

- A significant risk ***device*** presents a **potential for serious risk to the health, safety, and welfare of a subject** and is:
 - An implant; or
 - Used in supporting or sustaining human life; or
 - Of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health; or
 - Otherwise poses such a risk
- ***Study*** risk based on **proposed use** of a device in an investigation, **NOT the device alone**

Significant Risk Studies



- Full IDE requirements apply
- Sponsor submits IDE application to FDA
- FDA renders decision within 30 calendar days
- If approved, sponsor obtains IRB approval
- Study may begin after both FDA and IRB approve the investigation

Non-Significant Risk (NSR) Studies



- Do not meet definition of significant risk study
- IRB serves as FDA's surrogate for review
- Abbreviated requirements apply
 - Labeling
 - IRB Approval
 - Informed Consent
 - Monitoring
 - Subset of Records and Reports Requirements
 - Prohibition on promotion

Knowledge Check

What action should a sponsor take after concluding their device investigation is exempt under IDE regulations?

- 1. Initiate the study**
- 2. Submit an IDE application to FDA**
- 3. Consult the IRB**

Real-World Evidence for clinical evidence generation

RWD vs RWE

Real-World Data (RWD)

Data relating to patient health status and/or the delivery of health care ***routinely collected*** from a variety of sources

Real-World Evidence (RWE)

Clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD

Collection



Analysis



Use



Real-World Evidence

- Learn from available clinical information
- RWE may allow efficient evaluation as devices iteratively and rapidly improve
- Increased opportunities for RWE use



Real-World Evidence Draft Guidance



Contains Nonbinding Recommendations

Draft – Not for Implementation

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on December 19, 2023.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852-1740. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact the Office of Clinical Evidence and Analysis at CDRH.ClinicalEvidence@fda.hhs.gov. 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, or by email at ocod@fda.hhs.gov.

When final, this guidance will supersede “Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices,” issued August 2017.

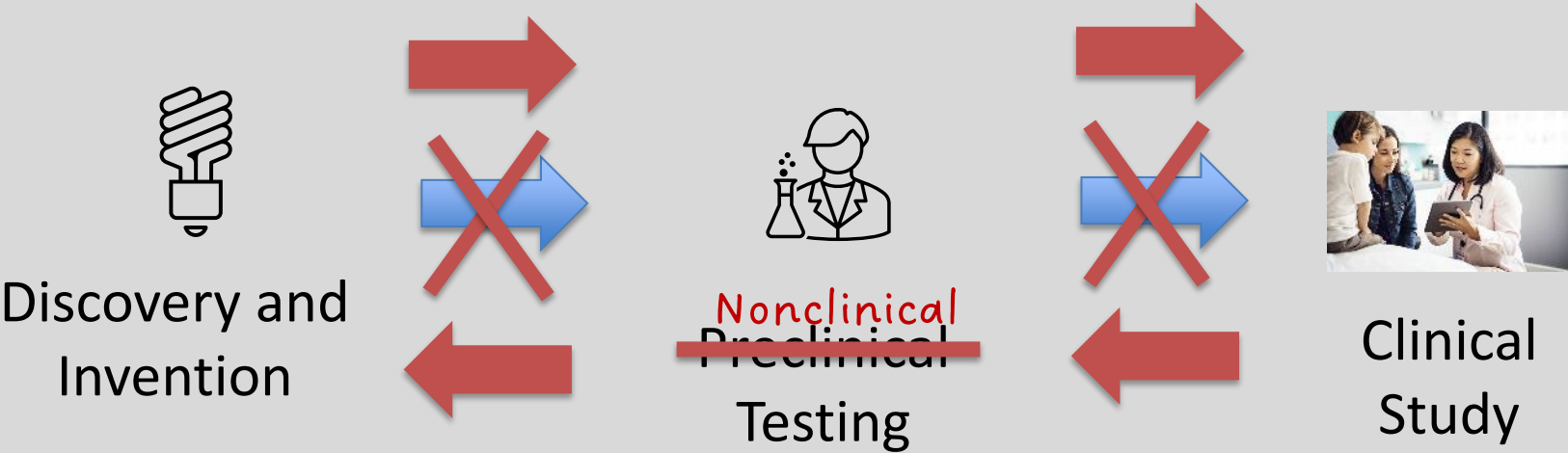


U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- [Draft guidance](#) proposes to update [2017 final guidance](#)
 - 2017 final guidance remains in effect until draft guidance is finalized
 - Comment period closed on February 20, 2024
- Draft guidance is intended to:
 - Clarify how FDA evaluates RWD quality to determine if data can serve as RWE in regulatory decision-making
 - Provide expanded recommendations to sponsors considering using RWD

Role of Early Feasibility Studies

Device Development to Clinical Studies



Early Feasibility Studies (EFS)

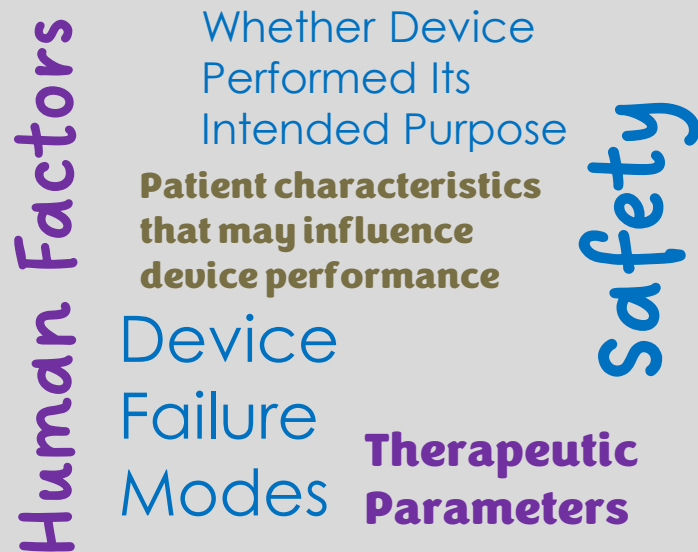
- A limited clinical investigation of a device early in development, typically before the device design has been finalized for a specific indication
- Enroll a small number of subjects (generally < 10-15)
- Do not necessarily involve the first clinical use

EFS may be used when information to advance device development cannot practically be provided via additional nonclinical assessments or appropriate nonclinical tests are unavailable

EFS Opportunities

- Provides initial insights into device proof of principle and safety
- Provides the basis for device iteration/product improvement and clinical study modifications
- Enhances collaboration among developers, industry, regulators, and investigators
- Earlier patient access to potentially beneficial devices

Operator Technique Challenges



[EFS Program Webpage](#)

Breakthrough Devices Program and Safer Technologies Program (STeP)

Breakthrough Devices Program and Safer Technologies Program (STeP)



- Intended to provide patients and health care providers with timely access to innovative devices
- Expedite the development, assessment, and review of certain devices that meet the program eligibility criteria

[Breakthrough Devices Program Guidance](#)
[STeP Guidance](#)

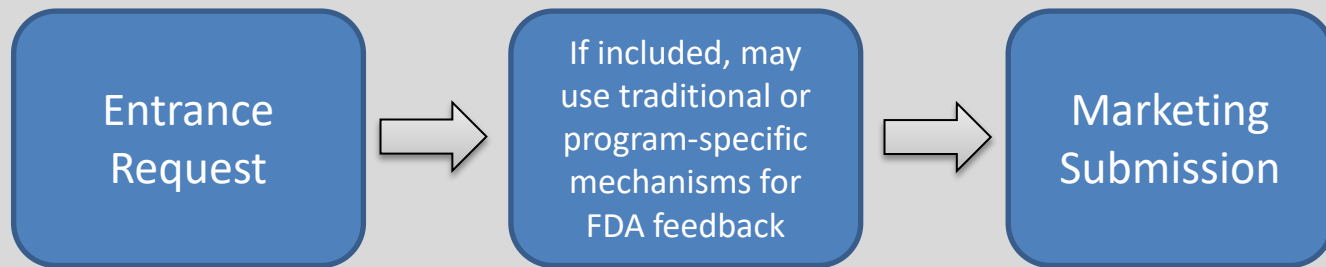


Breakthrough and STeP

Breakthrough Devices Program	STeP
For devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions	For devices reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target an underlying disease or condition associated with morbidities and mortalities less serious than those eligible for Breakthrough Devices Program

Principles and Benefits

- Interactive and timely communication
- Prioritized review of submissions
- Enhanced opportunity for pre/postmarket balance
- Efficient and flexible clinical study design



Statutory standard for marketing authorization unchanged

Program Features

- Sprint discussion
- Data Development Plan
- Traditional pre-submissions
- Status updates
- Clinical Protocol Agreements (Breakthrough only)

Knowledge Check

I must participate in the Breakthrough Devices Program if developing a clinical trial.

- 1. True**
- 2. False**
- 3. It depends**

Resources

Slide Number	Cited Resource	URL
13	21 CFR 812.2(c)	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-812#:~:text=January%2019%2C%201981.-,(c),812.30%20of%20an%20IDE%20application%20for%20the%20in,vestigation%20of%20the%20device.,-%5B45%20FR
21	Draft Guidance (Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices)	www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-use-real-world-evidence-support-regulatory-decision-making-medical-devices
21	2017 Guidance (Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices)	www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices

Resources (continued)



Slide Number	Cited Resource	URL
25	EFS Program webpage	www.fda.gov/medical-devices/investigational-device-exemption-ide/early-feasibility-studies-efs-program
27	Breakthrough Devices Program guidance	www.fda.gov/regulatory-information/search-fda-guidance-documents/breakthrough-devices-program
27	STeP guidance	www.fda.gov/regulatory-information/search-fda-guidance-documents/safer-technologies-program-medical-devices

Summary

- IDE regulations balance the need to promote innovation and provide access to novel products with protecting patient safety
- There are opportunities for innovation in clinical trials and clinical evidence generation within the regulatory framework
- There are regulatory programs for enhanced sponsor engagement with FDA during device development for innovative products

Questions



Your Call to Action

- Know there are a lot of resources available for sponsors of clinical trials
- Download, review, and use the links in this presentation to help
- Understand the requirements that will apply to your investigation
- Engage early with FDA when thinking about clinical evidence generation