

INTRODUCTION & OVERVIEW

Investigational Device Exemptions

(IDEs) are required to gather safety and effectiveness data for the support of medical device premarket submissions. They are needed for most Class II and all Class III devices used in clinical studies. Some clinical studies are exempt from IDE regulations, including ones for many diagnostics. Non-exempt device studies must meet all applicable IDE requirements before they begin. They are broken down into two types:

- Significant risk device (SRD) studies: require FDA IDE approval
- Non-significant risk device (NSRD) studies: do not require FDA IDE approval – “deemed approved”

SRD and NSRD studies must also be approved by the Institutional Review Board (IRB) at each facility participating in an IDE study. Individual IRBs may have their own processes and requirements, sometimes requiring approval for an exempt study.

Once an IDE is approved, investigational devices are exempt from many FDA regulations, including ones that pertain to premarket submissions, device registration and listing, and most aspects of Good Manufacturing Practices (GMPs). Patient informed consent is required for all clinical studies; all human subjects must agree to participate. There are a few exceptions to this rule, found in Title 21 Part 812 of the Code of Federal Regulations.

IDE Application Contents (for SRD studies)

- ✓ Name and address of company sponsor
- ✓ Report of prior investigations (if any)
- ✓ Investigational plan (must include a risk analysis and trial monitoring procedures)
- ✓ Description of all manufacturing methods
- ✓ Investigator agreement and list of the names and addresses of all investigators (if known at the time of the initial application)
- ✓ Names, addresses and chairpersons for IRBs that will review the application (if known at the time of the initial application)
- ✓ Device labeling
- ✓ A copy of all proposed informed consent forms

Types of Clinical Studies

Early Feasibility studies (EFS) may occur in the initial or later stages of product development and involve only a small number of participants.

First in Human (FIH) studies mark the first time that an investigational device is used on human subjects. FIH studies may also be EFS.

Pivotal studies gather safety and effectiveness data to provide evidence for premarket submissions (i.e., 510(k)s and PMAs).

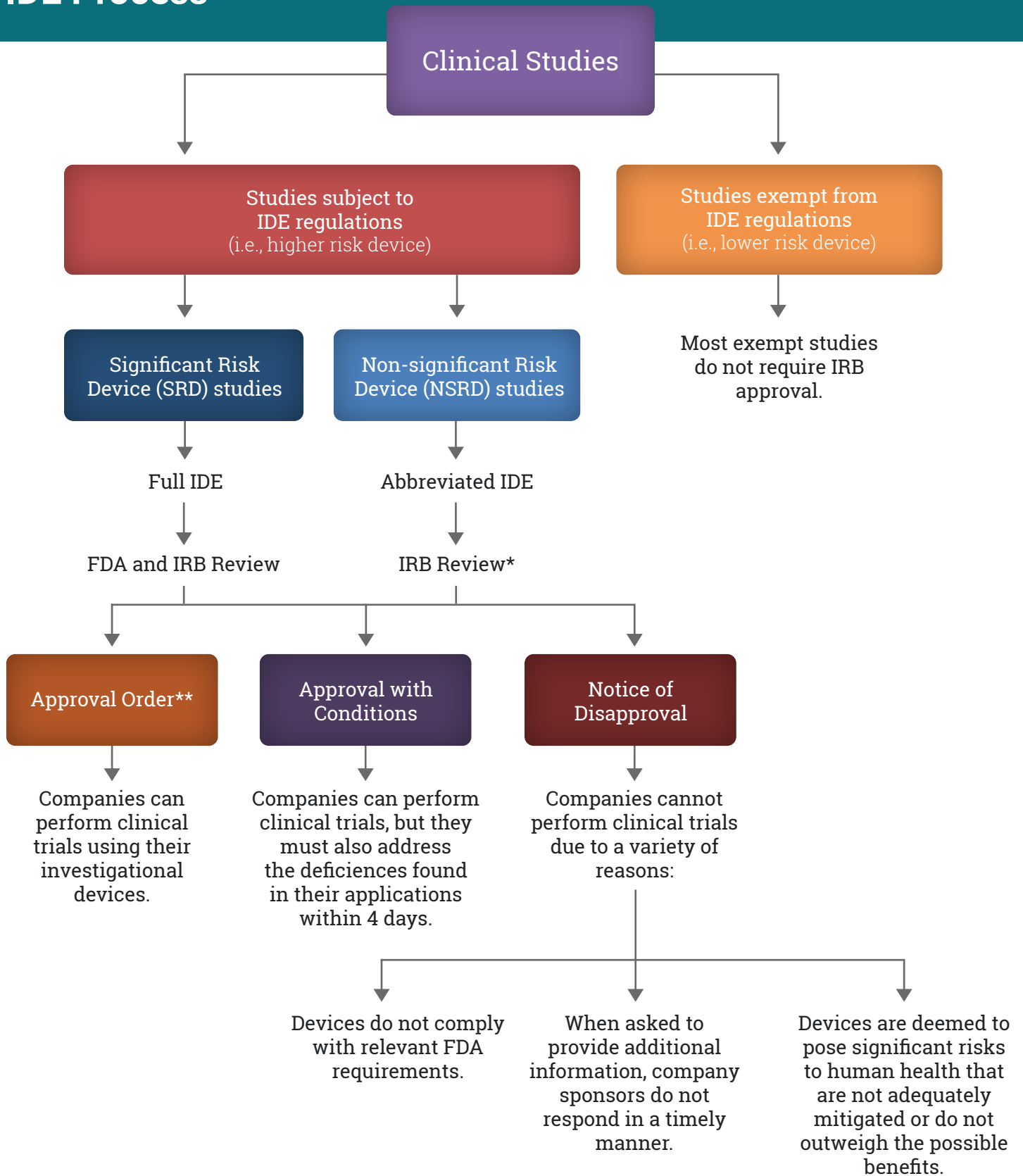
Institutional Review Boards (IRBs)

IRBs review biomedical research involving human subjects at clinical research sites/facilities. IRBs have the authority to disapprove clinical studies if they believe patient rights are not adequately protected or if other FDA or local requirements are not met. The IRB process was standardized in Title 21 Part 812 of the Code of Federal Regulations, and most recently, the **21st Century Cures Act**, implemented in late 2016, removed the requirement that restricted companies to “local” IRBs only.

Bioresearch Monitoring (BIMO)

BIMO, similar to IRBs, was implemented to protect the rights and welfare of human subjects. It permits FDA to inspect company sponsors and clinical sites by examining study data and protocols. Inspections are typically done for studies supporting PMAs under review but they may be applied to any situation where human clinical data is recorded.

IDE Process



*If any IRB finds an NSRD study to be significant risk, this information must be reported to FDA. In this case, a full IDE is required.

**There is a 30-day review period for IDEs submitted to the FDA. If companies do not receive a response from the Agency within this time frame, they may proceed with their investigations.

Additional IDE Requirements



Labeling: Companies must state that their devices are for investigational use only. **“CAUTION Investigational Device. Limited by Federal (or United States) law to investigational use.”**



Informed Consent: All human subjects are required to sign a consent form before participating in a clinical study (with limited exceptions, including a study being performed with a marketed product in accordance with its FDA sanctioned intended use).



Monitoring: All studies are monitored to ensure they comply with human protection regulations and follow the study protocol.



Prohibitions: Commercialization, promotion, misbranding, and study prolongation are not permitted.

SRD studies ONLY

- **Distribution:** Devices must only be distributed to investigational sites.
- **Records and Reports:** Sponsors and investigators must record all specified information during their clinical studies. They are required to provide periodic updates and written reports to investigators, IRBs, and FDA.
- **IDE Amendments:** Any additional information submitted to FDA prior to an IDE approval.
- **IDE Supplements:** Any information submitted to FDA after an IDE is approved.

NSRD studies ONLY

- **IRB Approval:** Clinical studies are required to maintain IRB approval and NSRD status throughout the investigation.
- **Records and Reports:** Specific information from the investigation must be recorded, but reports are sent to IRBs ONLY. FDA does NOT review reports from NSRD studies.
- **Investigator Records and Reports:** Sponsors must ensure they receive detailed reports from investigators, including recorded information from the investigation.



Tips from the Experts

1. **Use an IDE application checklist** to ensure that all required subsections are present. If any item is not included, provide an explanation.
2. **Make sure any submission to FDA is complete, concise and high quality.**
3. **Take advantage of the Pre-Submission Program to request feedback about planned IDEs and clinical trials and discuss test plans/clinical protocols before they begin.** Note that this is an important step in building a working relationship and line of communication with the FDA review team.
4. **Include a statistician in Pre-Submission meetings** who is focused on the clinical protocol.
5. **Save all data and records once tests have been completed.** The company sponsor must assure that all investigational sites maintain records, and they should be retained as long as the device is on the market, for both FDA and liability purposes.
6. **FDA does not act as a consultant to the industry;** companies should always present a proposal to which FDA can react. Questions cannot be open-ended.
7. **If multiple device generations exist, save test results from each generation** as long as the device is marketed.

FDA GUIDANCE DOCUMENTS

[Clinical Trials Guidance Documents](#)

[FDA Decisions for Investigational Device Exemption Clinical Investigations](#)

[Investigational Device Exemptions \(IDEs\) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human \(FIH\) Studies](#)

[Design Considerations for Pivotal Clinical Investigations for Medical Devices](#)

[Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions](#)

[Live Case Presentations During Investigational Device Exemption \(IDE\) Clinical Trials](#)

Additional Resources

[FDA Presentation: How to Put Together an IDE Application \(November 14, 2013\)](#)

[CDRH Learn – Multimedia Industry Education](#)

[FDA Fact Sheets: Investigational Device Exemption \(IDE\) – AdvaMed Resource](#)

AdvaMed Working Groups

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