What happens after risk determination?

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If your study is exempt…

- You may begin your study
  - Informed consent and IRB approval may be required.

If your study is NSR…

- You do need to follow the abbreviated requirements.
  - Labeling (812.5)
  - IRB approval
  - Informed consent (part 50)
  - Monitoring (812.46)
  - Records (812.140) and reporting (812.150) (sponsor and investigator)
    - Annual and Final Progress Reports are not required
  - Prohibition against promotion and other practices (812.7.)

- An IDE submission is not required.

- You *have* an IDE by virtue of being NSR and complying with the abbreviated requirements.

If your study is SR…

- You must comply with the abbreviated requirements, and
  - Receive approval of an IDE submission from FDA
  - Submit Annual and Final Progress Reports

Significant Risk vs. Non-Significant Risk Requirements

Significant Risk	Nonsignificant Risk
Must Follow 21 CFR 812	Must follow abbreviated requirements in s 812.2(b)**
Must have an approved IDE submission	Do not need an approved IDE submission
Must file annual reports to FDA	Do not have to file reports to FDA, except for serious adverse events/MDRs
Must tell investigators that it is a SR study and obtain agreement to comply with regulations for these studies*	

*812.43(c)(4)(i) and 21 CFR parts 50, 56, 812

**Includes: labeling, IRB approval, informed consent, monitoring, records, report, and prohibition against promotion

IDE Submission – Basic Elements

- *Background of medical issue, purpose and goals of the study, and why this study will further the science.*
  - This should be a summary, and not a detailed description.
- *Detailed description of the device under study*
  - Components, technology, how does it work, procedure for use, other relevant detail
  - Pictures and diagrams are helpful
- *Previous studies (preclinical and clinical) relevant for the study conducted under the IDE.*
  - Summary of available data. For IVDs, this will include analytical validation data.
  - Why is a clinical study needed at this stage?
  - What evidence supports the safety of this study/device and the potential for the study data to be meaningful?
- *Sufficient analytical validation and clinical information on fully specified device*

IDE Submission – Basic Elements

- *Risk analysis*
  - What are the potential risks to the patient?
  - Does the study mitigate the risks where possible?
  - Are the risks outweighed by the potential for benefit and/or value of the study
- *Patient monitoring and follow-up plan*
- *Inclusion and exclusion criteria*
- *Informed consent document*
- *Sample size and number of investigational centers, with justification*

Administrative Tips

- DCC Address:

  Food and Drug Administration
  Center for Devices and Radiological Health
  Document Mail Center - WO66-G609
  10903 New Hampshire Avenue
  Silver Spring, Maryland 20993-0002

- Number ALL pages, including attachments
- E-copy:
  http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/ucm370879.htm
- Be ready to respond to e-mails/calls during the 30 day review cycle.
  - Designate an alternate contact.
- Provide red-lined copies of documents when appropriate

Formatting an IDE

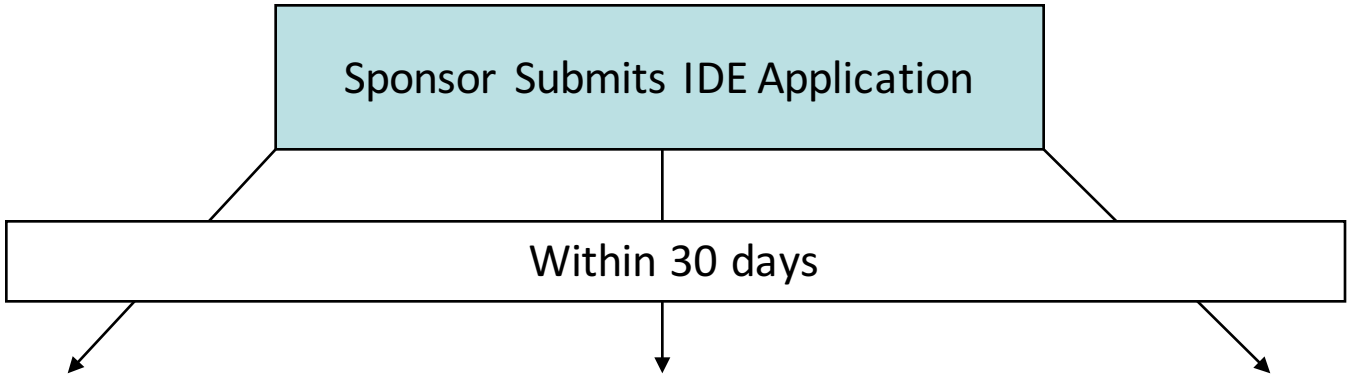
- Cover letter
- No specific format
- Make it readable! A well-organized submission, with logical sections and sub-sections, is easier to review.
- Annotate tables and describe figure legends
- Table of contents (with hyperlinks), or a well-bookmarked pdf
- Describe and interpret experiments and data included in the submission. Provide line data if necessary.
- Have someone unrelated to the project read the submission.

Don’t let the perfect be the enemy of the good

- We will ask for information we need but don’t have (interactive review)

- If in doubt, ask.

FDA Actions on an IDE



Approve, subject enrollment can begin once IRB approval is obtained

Approve with conditions, Sponsor may begin study once IRB approval is obtained on the condition that **within 45 days of the FDA letter, the Sponsor submits information to the FDA addressing the issues identified in the FDA's letter**

Disapprove, sponsor may not initiate clinical investigation until the identified deficiencies are resolved

After you have an IDE…

- Annual reports
- Final report
- Amendments
- Supplements
- Modifications

Modifications

- IDE **supplement** and approval required before implementing changes in the investigational plan, *except* for changes that can be reported under a 5-day notice or in the annual report.

5 Day Notice

The sponsor must provide notice to FDA within 5-working days of making the following changes.

- Developmental changes in the device that do not constitute a significant change in design or basic principles of operation and that are made in response to information gathered during the course of an investigation. This determination is made by the sponsor and must be based on credible information.
- Changes in clinical protocol that do not affect:
  - The validity of the data or information in the approved protocol, or the patient risk to benefit relationship relied upon to approve the protocol
  - The scientific soundness of the investigational plan
  - The rights, safety, or welfare of the human subjects involved in the investigation.

Annual Report

- Applies to minor changes in the following areas:
  - the purpose of the study
  - risk analysis
  - monitoring procedures
  - labeling
  - informed consent materials
  - IRB information
- These changes may be reported in the annual progress report for the IDE if they do not affect:
  - the validity of the data or information resulting from the completion of the approved protocol or the relationship of likely patient risk to benefit relied upon to approve the protocol
  - the scientific soundness of the investigational plan
  - the rights, safety, or welfare of the human subjects involved in the investigation

Remember…

- Take advantage of resources at **FDA** – we want to help!
  - Utilize the pre-submission process
  - Call or e-mail us if you don't understand any aspect of our letters

Interacting with FDA…for Sponsors

PRESUBMISSION

- You can meet with the FDA for nonbinding discussions and advice:
  - *before* conducting studies, including clinical trials
  - *before* submitting a marketing application
- This is an opportunity to address new scientific and regulatory issues.
- Particularly important when developing new technologies.
- Guidance on the pre-submission process http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf\

DURING REVIEW OF A SUBMISSION

- Acceptance Review Communication
- Substantive Interaction
- Interactive Review

Resources

- Medical Device Databases
  - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm
- Guidance
  - IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM328855.pdf
  - FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279107.pdf
  - Significant Risk and Nonsignificant Risk Medical Device Studies. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf
  - Others at www.fda.gov
- Device Advice
  - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm
- CDRH Learn (including information about sponsor responsibilities, investigator responsibilities, IRBs, and the Bioresearch Monitoring Program)
  - http://www.fda.gov/Training/CDRHLearn/default.htm