



Institutional Review Board (IRB)

Site Initiation to Implementation

IRB

■ Sources of Regulatory Information

- 21 CFR (Code of Federal Regulations) Parts 50 and 56
- 45 CFR Part 46
- FDA Information Sheet Guidances
- Good Clinical Practice: A Question & Answer Reference Guide (May 2006)

IRB

- Purpose is to protect the rights and welfare of human subjects.
- IRBs are subject to FDA regulations when studies of FDA-regulated products are reviewed and approved.
- Must review the research at least once per year.
- Report findings to the investigator, institution, and other agencies as required.

IRB

■ Membership Requirements

- Five members, both male and female, with varying backgrounds, professionals and nonprofessionals, including a representative for vulnerable subjects (if applicable).
- Cannot all be affiliated with the institution: 21 CFR 56.107.

Regulations

- FDA regulations apply to research involving articles that require an investigational new drug application (IND) or investigational device exemption (IDE).
- NIH regulations apply to research funded by NIH.
- If the research involves a product under an IND or IDE and is funded by the NIH, both the FDA and NIH requirements must be followed.

Assurance

- Written document by which an institution commits to comply with Health and Human Services (HHS) and all other applicable requirements set forth in 45 CFR Part 46.
- Institutions engaging in human-subject research not exempt from regulations must be covered by an Office for Human Research Protections (OHRP) assurance of compliance.
- Federal-wide assurance (FWA) is now the only new type approved by OHRP.
- Link:
http://www.hhs.gov/ohrp/assurances/assurances_index.html

Assurance

- Sponsors should verify that investigators participating in research are using IRBs in compliance with the CFR.
 - Current assurance can be used as evidence that the IRB is appropriately constituted.
 - IRB rosters can also provide evidence of compliance.

Assurance

- Participating investigators should not vote, and abstention from voting can be verified by:
 - IRB rosters or assurance numbers (per institutional policy).
 - Assurance numbers only in combination with abstention letters.

IRBs – Local vs. Central

- FDA released final guidance on use of centralized IRBs in March 2006.
- Must comply with institution's policy and procedures for using central IRBs.
- Institutions with a local IRB, who want to use a central IRB to conduct research, must obtain and document authorization from their local IRB.
- Link: <http://www.fda.gov/cder/guidance>.

Safety Reporting

- The investigator is obligated to report serious adverse events (SAEs) per the protocol and unexpected adverse events per IRB requirements.

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Start-up

- Create a temporary regulatory binder before receiving study binder.
- Use FDA Form 1572 template (IND studies).
- Keep current CVs of PI and subinvestigators on file —valid for two years only.
- Keep a listing of lab normals and lab certifications on file.
- Maintain a study authorization and signature log; record changes in staff as they occur (with signatures, start and end dates).

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Provide required regulatory documents as requested by sponsor or designee (ARO/CRO). The following documents are required for both INDs and IDEs:

- Confidentiality or Secrecy Agreement
- PI/Subinvestigator CVs
- IRB Approval Letters (Protocol/Amendments/ICF)
- IRB/EC Approved ICF/HIPAA Authorization
- IRB/EC Membership or Assurance (Abstention Letter if applicable)
- Financial Disclosure Forms
- Protocol Signature Page
- FDA 1572 Form
- Laboratory Reference Normals
- Laboratory Certifications
- Clinical Trial Site Contact Information Sheet
- Investigator Agreement

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- You must have IRB approval for the study, the informed consent form/HIPAA authorization, and advertisements or scripts that will be used in the study before initiation or use.
 - Check your local IRB regulations and follow SOPs for submitting initial, continuing, safety, and final reports.
 - Ensure that essential elements are included on the informed consent form.
 - Submit the required materials (at a minimum, investigator information, investigator's drug brochure [if applicable], protocol, consent form/authorization, and advertisements).
- HIPAA compliance is the responsibility of the investigator and everyone involved in the study.

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Points to remember for IRB submission

- PI and site staff should discuss protocol-required procedures and data expectations vs. standard of care.
- Remember an executed contract may be needed before IRB approval, so work out budget issues early.
- Use templates (regulatory packet) provided by sponsor or designee (ARO/CRO) and start preparing early.
- Send informed consent form for review prior to submission to sponsor or designee (ARO/CRO).

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Points to remember for IRB submission

- IRB approvals take about 1 to 3 months and may have to go through several committees.
- Submission deadlines can be up to 1 month in advance of meetings.
- Regular communication with contracts, IRB, and sponsor or designee (ARO/CRO) is important to successful completion of regulatory start-up.

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IRB—continuing review and reporting

- Investigator must notify the IRB in writing of any interruption of the study and when the study is completed.
- The investigator must submit study status reports to the reviewing IRB at least annually (more frequently if required by IRB policy).
- Submit for continuing renewal before its due date—do not want enrollment to lapse due to late renewal.

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IRB—continuing review and reporting

- Submit SAE (or required events) reports to IRB as the SAEs occur.
- Keep all IRB study-related documents organized in regulatory binder and forward copy as requested to the sponsor or designee (ARO/CRO).
- Submit protocol violations as recommended or per IRB requirements.

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Patient Safety

- Know your institutional and IRB processes, e.g., reporting requirements, screening, enrollment and informed consent procedures.
- Plan training sessions for all appropriate staff (subinvestigators, data entry personnel, and other hospital staff not on FDA Form 1572, e.g., ICU or pharmacy staff), and maintain study personnel training documentation.
- Document enrollment plan and procedures.
- Document in medical chart/source how and when informed consent was obtained.

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Patient Safety

- Use clinical study helpline or medical monitor for inclusion/exclusion criteria questions and significant questions or deviations.
- Assess adverse and serious events as they occur and consult with and obtain PI documentation assessing the event.
- Use proper reporting study procedures and IRB policies for adverse and serious adverse events.
- Obtain necessary source documentation (e.g., ECGs, x-ray reports, consults, progress notes) when endpoints or events occur.

Links

- **FDA: Information for Health Professionals**
<http://www.fda.gov/oc/oha/>
- **FDA: Information Sheet Guidances**
<http://www.fda.gov/oc/ohrt/irbs/default.htm>
- **FDA: IRB Frequently-Asked Questions**
<http://www.fda.gov/oc/ohrt/irbs/faqs.html>
- **OHRP**
http://www.hhs.gov/ohrp/assurances/assurances_index.html