

Regulatory Binder Instructions

Center for Clinical Research (CCR)





Applicable Regulatory Binder Tabs

Protocol/Amendments

Requirements:

- All versions of IRB-approved protocols
- Signed principal investigator (PI) protocol signature page(s)

Guidance/Recommendations:

- ✓ Maintain a log of protocol changes
- ✓ Protocol Versions should be dated and/or numbered

Federal Regulations/Good Clinical Practice:

[ICH GCP 8.2.2](#), [ICH GCP 8.3.2](#)

Consent/HIPAA

Requirements:

- All versions of IRB-approved Informed Consent Documents (i.e. Written, Assent, Online, Verbal)
- Copy of foreign language consent materials

Guidance/Recommendations:

- ✓ Maintain log of IRB-approved informed consent document versions

Federal Regulations/Good Clinical Practice:

[45 CFR 46](#), [21 CFR 50](#), [21 CFR 56](#), [GCP ICH 8.2.3](#), [GCP ICH 8.3.2](#), [GCP ICH 8.3.12](#)

1572

Requirements:

- ❑ Current and previous signed Form FDA 1572 Investigator Statement

Guidance/Recommendations:

- ✓ Form FDA 1572 is required for FDA-regulated investigational drug studies
- ✓ Update the 1572 each time there is a change to any of the information originally provided
- ✓ Maintain a log of 1572 changes
- ✓ If sponsored study, notify the sponsor of any updates

Federal Regulations/Good Clinical Practice:

[21 CFR 312.53](#)

IRB/xIRB (External IRB*)

Requirements:

- Federal-wide Assurance (FWA) number
- IRB registration
- Current IRB Membership List/Roster (required for FDA-regulated & industry-sponsored studies)^
- Initial IRB Approval Letter
- Original IRB application/submission
- Notifications of IRB disapproval, deferral, modifications required to secure approval and Investigator responses
- Email correspondence with the IRB
- IRB Approval letters for modification requests (e.g., protocol amendment, consent forms) IRB Approval letters for continuing review requests
- Reportable New Information (RNI) acknowledgment letters
- IRB suspension or termination notifications
- External IRB documentation, including IRB submissions IRB Approvals/notifications, and significant correspondence between IRB and investigator
- External IRB Initial NU IRB Acknowledgment Letter and study update modifications
- Fully executed Institutional Authorization Agreement Forms
- Approved Data Security Plans
- Inspection Reports (ex. FDA Form 483)
- Interim/annual progress reports to the IRB

IRB/xIRB (External IRB*) continued

Requirements (continued)

- Documents related to sIRB review
- For international research, a copy of the reviewed and approved proposal within the country's ethics review/approval infrastructure
- Completed NU IRB-requested Post Approval Monitoring Checklists (PAM) relevant correspondence & responses

Recommendations:

- ✓ Log of IRB submissions/changes
- ✓ Log/copies of all Corrective Action Plans (CAPs) implemented during the course of study
- ✓ IRB submission documents (e.g., IRB submission forms, local protocol addendum)
- ✓ ICH Compliance Letter

Guidance/References:

- File documents in reverse chronological order.
- *External IRB refers to third-party, including commercial & non-commercial, review boards utilized for research study
- ^For NU IRB studies, file all NU IRB Rosters current from the date of the initial study submission/approval;
- ^ For external IRB studies, file all external IRB Rosters current from the date of the initial external IRB study submission as well as the NU IRB Roster current from the date of the initial NU IRB acknowledgment submission/approval

Training

Requirements:

- Training Log
- Investigator and staff GCP training certifications
- Investigator and staff applicable HSR training certifications
- Additional training certification of study staff, (e.g., phlebotomy, vital signs)
- Sponsor training (e.g., EDC trainings, study initiation visits, use of device, GCP)

Guidance/Recommendations:

- ✓ Update training log in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferably on the same day.
- ✓ Do not remove expired training documents as they demonstrate qualification for the entire duration of the study
- ✓ CITI or equivalent training should be filed for all personnel listed on the NU IRB submission
- ✓ If Clinical Trial, GCP training should also be filed for all personnel listed on the NU IRB submission in accordance with Northwestern University and Feinberg School of Medicine Policy

Data Collection Forms

Requirements:

- Most recent Data Collection Sheet template(s)
- Most recent of Case Report Form templates(s)

Guidance/Recommendations:

- ✓ The difference between data collection sheets and case report forms is that data collection sheets typically act as source documentation. That is, during study visits, information is written directly onto the worksheets. An industry sponsor usually provides CRFs; all protocol-required information is transferred to CRFs from data collection sheets. Some studies do not use CRFs. All studies should use some type of data collection sheet.

Federal Regulations/Good Clinical Practice:

[GCP ICH 8.3.14](#), [GCP ICH 8.3.154.9.3](#), [21 CFR 312.62](#)

Lab

Recommendations:

- Lab director's CV
- Copy of the most current Lab Manual
- Record of retained body fluids/tissue samples

Federal Regulations/Good Clinical Practice:

[GCP ICH 8.2.12](#), [GCP ICH 8.2.14](#), [GCP ICH 8.3.6](#), [GCP ICH 8.3.7](#)

Recruitment

Requirements:

- ❑ All versions of IRB-approved recruitment material (advertisements, flyers, recruitment script, etc.)

Guidance/Recommendations:

- ✓ Approved/validated recruitment materials and additional study information distributed to participants should include version dates and/or numbers

Federal Regulations/Good Clinical Practice:

[GCP ICH 8.2](#), [GCP ICH 8.3](#)

CV/Medical Licenses

Requirements:

- ❑ Valid and current licenses/certification for all professional study staff (e.g., medical or nursing license)
- ❑ CVs for all investigators signed, dated, & updated at least biannually

Guidance/Recommendations:

- ✓ Medical licenses should document qualifications & eligibility to conduct trial and/or provide medical supervision of study participants
- ✓ Professional certification information should be included on individual CVs.
- ✓ CVs & medical licenses should be kept for all investigators listed on 1572, DOA log and/or IRB personnel list.
- ✓ CVs may be updated if an investigator's qualifications increase or change during course of study
- ✓ Do not remove expired CVs as they demonstrate qualification for the entire duration of study
- ✓ The investigators must be actively licensed in the state in which the study is conducted.
- ✓ The name on license must correspond to the name on the investigator's CV & 1572, if applicable.
- ✓ NU IRB Compliance Office recommends but does not require CVs & licenses to be on file for personnel other than investigators (e.g. APNs) with a significant role in the study's conduct, as PI deems appropriate
- ✓ **Federal Regulations/Good Clinical Practice:**

[GCP ICH 4.1.1](#), [GCP ICH 8.2.10](#), [GCP ICH 8.3.5](#)

Participant Materials

Requirements:

- IRB-approved information provided to participants (i.e. handouts, brochures, survey tools)

Federal Regulations/Good Clinical Practice:

[21 CFR 312.62](#)

Delegation Log

Requirements:

- Delegation of Authority Log
- Staff Signature Log

Guidance/Recommendations:

- ✓ Delegation of authority log details research staff responsibilities and length of time on study
- ✓ Staff signature log should list all study staff & be used for clinical trials
- ✓ Update logs in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferably on the same day

Screening/Enrollment Log

Requirements:

- Pre-Screening/ Enrollment Log
- A log without identifying information that lists all screened & enrolled subjects
- Subject Identification Code list (subject identifiers should be kept separately)

Guidance/Recommendations:

- ✓ Update logs in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferable on the same day
- ✓ Consider adding eligibility checklist and documentation to support participant received signed copy of consent form, or note about why not, such as participant declined copy participant declined copy

Federal Regulations/Good Clinical Practice:

[21 CFR 8.3.20](#), [21 CFR 8.3.21](#), [21 CFR 8.3.22](#)

Investigator's Brochure/Package Insert

Requirements:

- All versions of clinical investigator's brochure
- Clinical investigator's acknowledgement of receipt signature page
- Package Insert/Prescribing Information for marketed products

Guidance/Recommendations:

- ✓ If the investigational product is marketed and its pharmacology is widely understood, a basic product information brochure or package insert may be an appropriate alternative.

Federal Regulations/Good Clinical Practice:

[21 CFR 312.55](#), [GCP ICH 8.2.1](#), [GCP ICH 8.3.1](#)

Miscellaneous

Requirements:

- Data and Safety Monitoring Documents
- Memos or emails to/from site staff
- Grant application/letter
- Grant progress reports
- Copy of all audit reports (internal and external)
- Interim findings (including reports & publications related to study)
- Documents pertaining to scientific review
- Data Protection Documents (i.e. Data Security Plan, Data Use Agreements, etc.)
- Signed agreements between parties ((Examples may include; sub-contracts for an NIH grant, consulting contracts, confidentiality agreements, etc.)
- Scientific Review Committee (SRC) Cancer Center documents (including SRC submissions, correspondence & approval letters)
- Other study-related docs not pertaining to another section of binder

Miscellaneous (continued)

Guidance/Recommendations:

- ✓ Any additional correspondence (e.g. e-mails, letters, meeting minutes) with the DSMB and its members
- ✓ If your study has a DSMB, ensure all DSMB reports/documentation previously not submitted via a Northwestern IRB MOD or RNI submission are submitted at the time of continuing review

Federal Regulations/Good Clinical Practice:

[GCP ICH 8.3.10](#), [GCP ICH 5.19.3](#)

HIPAA Privacy Rule and Security Rule (as amended): [45 CFR 160](#), [45 CFR 162](#), [45 CFR 164 \(Subparts A and C\)](#), [21 CFR Part 11](#)

Financial Disclosure

Requirements:

- ❑ Signed Financial Disclosure Forms for the PI and co-investigators

Guidance/Recommendations:

- ✓ If financial disclosure information changes during the course of the study, ensure updated Financial Disclosure Forms are filed and that updates are reported to the IRB of Record

Federal Regulations/Good Clinical Practice:

[21 CFR 54](#), [21 CFR 812.43\(c\)](#)

Study Shipment Supplies

Guidance/Recommendations:

- File documentation pertaining to receipt and shipment of study supplies (i.e. shipping orders, packing slips)

Federal Regulations/Good Clinical Practice:

[21 CFR 812.140](#)

Monitor Log & Letters

Requirements:

- Site visit log
- Site Initiation report/visit documentation
- Site visit reports
- Site visit correspondence
- Site close-out report/visit documentation

Guidance/Recommendations:

- ✓ Log required for FDA-regulated protocols
- ✓ Log recommended for non-industry sponsored cancer center studies monitored by an internal Quality Assurance (QA) team
- ✓ Update logs in a timely manner
- ✓ To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferably on the same day

Federal Regulations/Good Clinical Practice:

[GCP ICH 8.3.10](#)

CLIA/CAP/Lab Certificates

Requirements:

- A copy of certifications or accreditations (i.e. Clinical Laboratory Improvement Amendments [CLIA] and College of American Pathologists [CAP])
- Updated normal-range values for each reference laboratory

Guidance/Recommendations:

- ✓ Research labs typically do not have lab certifications, e.g., CLIA, CAP, and may not have “normal” lab values. If research labs are used, ensure research lab references values are on file

Federal Regulations/Good Clinical Practice:

[ICH GCP 8.2.11](#), [ICH GCP 8.2.12](#), [ICH GCP 8.3.6](#), [ICH GCP 8.3.7](#)

FDA Submissions

Requirements:

- Initial IND/IDE or Application
- Amendments/supplements to the application
- Relevant IND/IDE FDA submission forms (i.e. 1571, 3674, 3455 or 3454, etc.)
- Correspondence to/from FDA
- Safety Reports
- Annual Progress Reports
- Guidance/Recommendations:
- Required for clinical studies regulated by the FDA under investigational new drug (IND) & investigation device exemption (IDE) procedures

Federal Regulations/Good Clinical Practice:

[21 CFR 312.30](#), [21 CFR 312.32](#), [21 CFR 312.33](#), [21 CFR 812.150\(b\)\(1\)](#), [21 CFR 812.150\(b\)\(5\)](#), [21 CFR 812.35](#)

Investigational Product Shipment Supplies

Requirements:

- ❑ Documentation showing investigational product shipment and receipt

Guidance/Recommendations:

- ✓ Update logs in a timely manner.
- ✓ To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferably on the same day

Federal Regulations/Good Clinical Practice:

[21 CFR 812.140](#)

Investigational Product Accountability Log*

Requirements:

- ❑ Investigational product Accountability/Dispensing Log (i.e. Temperature Log)
- ❑ Documentation of IP (e.g., botanicals, probiotics, or other natural products) disposition and accountability, or memo as to where records are located (e.g., research pharmacy) and who is maintaining accountability logs

Guidance/Recommendations:

- ✓ Update logs in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferable on the same day.
- ✓ File documentation pertaining to receipt & shipment of IP (i.e. shipping orders, packing slips)
- ✓ The storage area should be locked/secure with access limited to approved study staff only
- ✓ IP should not be stored with standard clinical inventory

*Investigational Product refers to investigational drug or device. If both drug or device is used for a research study, both drug and device shipment and accountability tabs may be added to the regulatory binder

If using investigational drug and using the Northwestern Memorial Hospital Investigational Pharmacy, the Investigational Product Shipment and Accountability sections may be omitted and all investigational drug, supplies and corresponding documentation may be stored with the pharmacy

Investigational Product Accountability Log (continued)

The PI is responsible for the following with respect to investigational product:

- ✓ Maintain records of IP delivery to the study site. Include dates, quantities received, batch/serial numbers, and expiration dates.
- ✓ Maintain an inventory of the IP at any site. Inventory control records should be updated, signed, and dated by the PI in a timely manner.
- ✓ Record/track use of the IP by each participant. Documentation should verify that drug dosing/device use was in accordance with the approved protocol.
- ✓ Maintain an accountability log that records when the participant(s) received the IP and the specific drug dosage/device the participant(s) received.
- ✓ Return/dispose of unused IP as specified by the sponsor.
- ✓ Maintain documentation of return/disposal.
- ✓ Store the IP

Federal Regulations/Good Clinical Practice:

[21 CFR 812.140](#)

SAE Reports (non-UPIRSO)

Requirements:

- Protocol Deviation/Exception Tracking Log
- SAE Reports
- Adverse Event Tracking Log

Guidance/Recommendations:

- ✓ Update logs in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferable on the same day

Federal Regulations/Good Clinical Practice:

[GCP ICH 4.11](#), [GCP ICH 5.16.2](#), [GCP ICH 5.17.1](#), [GCP ICH 8.3.16](#), [GCP ICH 8.3.17](#), [GCP ICH 8.3.18](#), [GCP ICH 8.3.19](#)

SAE/IND Worksheets (non-UPIRSO)

Requirements:

- SAE Report Forms
- Unanticipated Problem Forms
- IND Safety Reports
- Sponsor-issued forms for adverse event, pregnancy, etc.

Guidance/Recommendations:

- ✓ Update logs in a timely manner. To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferable on the same day

Federal Regulations/Good Clinical Practice:

[GCP ICH 4.11](#), [GCP ICH 5.16.2](#), [GCP ICH 5.17.1](#), [GCP ICH 8.3.16](#), [GCP ICH 8.3.17](#), [GCP ICH 8.3.18](#), [GCP ICH 8.3.19](#)

Investigator Agreement

Requirements:

- ❑ Copies of all versions of Investigator Agreement/Statement

Federal Regulations/Good Clinical Practice:

[ISO 14155:2011](#)

Instructions for Use (IFU)

Requirements:

- Instructions for Use/Device Manual or Report of Prior Investigations, ROPI, (for investigational devices)
- Instructions for handling of investigational product(s) and trial-related materials (if not in protocol or investigator's brochure)

Guidance/Recommendations:

- ✓ If the investigational product is marketed and its pharmacology is widely understood, a basic product information brochure or package insert may be an appropriate alternative.

Federal Regulations/Good Clinical Practice:

[ISO 14155:2011](#)

Sponsor Newsletter

Guidance/Recommendations:

- ✓ If clinical trial, file and maintain newsletters from sponsor

Sponsor Contact

Guidance/Recommendations:

- ✓ Maintain contact information of study sponsor

Correspondence/Sponsor Correspondence

Requirements:

- Correspondence related to the study (e.g. e-mails, faxes)
- Correspondence to & from funding agency (e.g. letters, meeting notes, & notes of telephone calls- required for FDA-regulated protocols)
- Important decisions regarding study conduct, such as notes to the study file
- Notes to file not pertaining to any other section of the regulatory binder

Questions?

Contact NUCATS at: 312-503-1709