This Regulatory Binder is based on content developed by the Partners Human Research Quality Improvement Program.

**Human Research Quality Improvement Unit**

**Regulatory Binder**

**Purpose:** The QI Regulatory Binder assists research sites in achieving and maintaining regulatory compliance and ensuring the highest standard of human subject research. The binder also provides:

* Guidance for organizing and record keeping.
* Assistance with proper study documentation and successful study management.
* Readily accessible links to on-line resources (QI Tools Tab) such as WFH IRB policies, guidelines, and forms.

**Do I Need A Regulatory Binder?** All research protocols approved by the WFH IRB should have a corresponding Regulatory Binder. The QI’s Regulatory Binder is available to assist investigator-initiated study sites who are creating their own binder.

Each binder section outlines the regulatory documents, institutional policies, and GCP guidelines for organization and record keeping. The bottom of each tab includes QI tips, links to QI tools, and references for applicable documents.

**How to use Binder:** The Regulatory Binder is comprised of sections that apply to the range of human subject studies. Each binder section outlines the regulatory requirements, institutional policies and GCP guidelines for organization and recordkeeping. At the bottom of each section are QIU tips and links to additional resources.

For additional guidance on establishing a regulatory binder contact QIU Staff.

**QI Tips/Additional Information**

* Label the outside of the binder with the PI name, study title, and WFH IRB assigned number.
* The Regulatory Binder should be established at the beginning of the study, prior to enrollment.
* Keep the Regulatory Binder current and up-to-date.
* Identify individual(s) responsible for maintaining the binder. Ensure that this person is on file with the IRB as a member of the study team to ensure that all IRB correspondence and documents are received/filed in a timely manner.
* Store binder in a safe and secure location, but accessible to study staff at all times. If sections of the binder are stored in a separate location, write a signed and dated note-to-file indicating the location and who maintains them. File the note behind the tab to which it applies.
* Subject-specific documentation and information, e.g., signed consent forms, test results, and completed case report forms should be maintained separately within the subject-specific file.
* Customize the binder to meet the needs of your protocol. This Regulatory Binder is a template. Include only sections pertinent to your protocol. Omit unused sections and add sections as needed. See “applicable sections” below for more information. If unsure of what sections to include/exclude, contact the QI Program to clarify.
* Financial Documents must be stored in a separate location from the Regulatory Binder, e.g. budget and billing statements.
* Documents should be filed in reverse chronological order under the appropriate tab (most recent on top).
* Use ink on all documents.
* When creating forms, include a version number or date on all documents.
* Any change or correction to a form must have a single line drawn through it, be dated, initialed, and should not obscure the original entry. Correction fluid or “white out” must not be used on study related documents.

**Applicable Sections:**

Depending on the nature of the research, some tabs may not be required. Use the list below to ensure that the applicable sections are maintained. Contact QIU staff with any questions.

All Studies:

1. Protocol
2. Staff CVs
3. Staff Licensures
4. Logs
5. IRB Documents
6. Consent Forms (unless waiver granted)
7. Data Collection/CRFs

Study Specific:

1. Lab Documents
2. NIH Funded Research
3. Sponsored Research
4. Drug/Device Accountability
5. FDA Regulated Research
6. Financial Disclosure
7. Data and Safety Monitoring

**Protocol**

**Contents**

* Current Protocol and all previously approved versions
* When applicable, a copy of the fully executed protocol signature page for original protocol and all approved versions

**QI Tips/Additional Information**

* Outdated protocol versions may be kept either in a separate location. If so, write a signed and dated note-to-file indicating where previous versions are maintained.
* All versions should be dated and/or numbered
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 8.2.2, 8.3.2
* Applicable [WFH IRB Manual: Chapter IV.H Principal Investigator Responsibilities](http://www.wfhealthcare.org/app/files/public/1822/IRB-Manual-C4-PI-Responsibilities.pdf)

**Curriculum Vitae**

**Contents**

* Signed and dated CVs for IRB approved PI and members of the study team

**QI Tips/Additional Information**

* CVs should be signed, dated, and updated every 2 years to verify that information is accurate and current
* If CVs are filed electronically for the departments, write a signed and dated note-to-file and indicate the location
* QI Tool created for tracking purposes may be completed and can be found under the QI Tools:
	+ Study Team Tracking Log
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 4.1.1, 8.2.10, 8.3.5
* Applicable [WFH IRB Manual: Chapter VI.A Operational Review Procedures: Full Board Review](http://www.wfhealthcare.org/app/files/public/1810/IRB-Manual-C6-Full-Board-Review.pdf)

**Licensure/Certification**

**Contents**

* Valid medial licenses/professional certifications for all IRB approved study staff
* Documentation of Human Subject Training for all members of the study team
* Protocol specific required training documentation

**QI Tips/Additional Information**

* Monitor licensure expiration dates and add updated copies upon receipt
* Do not remove the previous versions of licensure
* If licensure/certification documentation is maintained in another location, generate a note-to-file
* Applicable [GCP sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 4.1.1, 8.2.10
* Applicable [WFH IRB Manual: Chapter V.A Investigator and Research Staff Education](http://www.wfhealthcare.org/app/files/public/1814/IRB-Manual-C5-PI-Research-Staff-Edu.pdf)

**Logs**

**Contents**

* **Enrollment Log:** Captures all subjects who sign a consent form.
* **Participant ID Log:** Cumulative list of enrolled subjects and contact information.
* **Site Signature and Delegation Log:** Documents the study-related procedures delegeted to staff. The PI should initial, date, and sign this list, and update it as new staff or study procedures are added to the protocol.
* **Adverse Event Log:** Tracks and ensures timely reporting of all applicable adverse events to the IRB.
* **Protocol Deviation Log:** provides a record of all minor deviations and facilitates reporting at continuing review.
* **Site visit/monitoring log** (sponsored studies): Documentation of monitoring visit dates.

**QI Tips/Additional Information**

* To ensure accuracy, logs should be updated as soon as possible after a recordable event occurs, preferably on the same day.
* Deviation/Minor Noncompliance Tracking Log may be requested by the IRB at time of continuing review
* QI Tools have been created for tracking purposes and can be found under QI Tools:
	+ Enrollment Log
	+ Participant Log
	+ Site Signature and Delegation Log
	+ Adverse Event Log
	+ Deviation/Minor Noncompliance Tracking Log
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf):4.1.5, 8.3.20- 8.3.25
* Applicable WFH IRB Manual: C[hapter VI.E Planned Exceptions and Unplanned Deviations;](http://www.wfhealthcare.org/app/files/public/1811/IRB-Manual-C6-Planned-Exceptions.pdf) [Chapter VII.B Reportable Events: Safety Information and Unanticipated Problems Involving Risks to Subjects or Others](http://www.wfhealthcare.org/app/files/public/1799/IRB-Manual-C7-Reportable-Events.pdf)

**IRB Documents**

**Contents**

* Signed and dated submissions:
	+ Application
	+ Continuing Review
	+ Amendments
	+ Adverse events
	+ Violations/Deviations
	+ Close out Information
	+ Approval letters and/or notification of IRB decision
	+ Investigator response to IRB notification (if applicable)
	+ Approved recruitment materials
	+ Approved education materials/additional study information distributed to subjects
* IRB Membership Roster
* IRB Meeting Calendar
* Documentation Federal Wide Assurance number

**QI Tips/Additional Information**

* Copies of all signed and dated IRB submissions and correspondences between the study site and IRB should be kept on file.
* QI Tools have been created for tracking purposes and can be found under QI Tools:
	+ IRB Document Tracking Log
	+ Informed Consent Tracking Log
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 4.4, 8.2.7-8.2.9, 8.3.2-8.3.4
* Applicable [WFH IRB Manual: Chapter IV.H Principal Investigator Responsibilities](http://www.wfhealthcare.org/app/files/public/1822/IRB-Manual-C4-PI-Responsibilities.pdf)

**Consent Forms**

**Contents**

* Current IRB approved consent form version (s) with the IRB approval stamp
* Previous IRB approved consent forms
* Consent Templates

**QI Tips/Additional Information**

* As soon as the IRB approves a new version of the consent form, the previous version expires. Previously approved versions can be kept in the IRB section of the Regulatory Binder
* The Research Consent Note assists sites with properly documenting informed consent according to federal regulations, institutional policies, and good clinical practices.
* QI Tools have been created for tracking purposes and can be found under QI Tools:
	+ Research Consent Note
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf)**:** 4.8, 8.2.3
* Applicable Regulations: [45 CFR 46](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html), [21 CFR 50](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50), [21 CFR 56](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56)
* Applicable [WFH IRB Manual: Chapter IV.H Principal Investigator Responsibilities](http://www.wfhealthcare.org/app/files/public/1822/IRB-Manual-C4-PI-Responsibilities.pdf)

**FDA Financial Disclosure**

**Contents**

* Signed and dated Financial Disclosure Forms for all individuals listed on 1572 (drug) or IRB Application (device)

**QI Tips/Additional Information**

* If FDA Financial Disclosures are filed separately, write a signed and dated note indicating the location
* Any applicant (usually a pharmaceutical/device company) who submits a marketing application for a human drug, biological product, or device is required to submit a completed Form FDA 3455 to the FDA for each clinical investigator who participates in a covered study. This form attests to the absence of financial interests, or discloses the nature of any financial arrangements.
* Everyone listed on the Form FDA 1572 (drug) or IRB application (device) shall provide to the sponsor sufficient accurate financial information on Form FDA 3455. The investigator should promptly update this information if any relevant changes occur in the course of the study, or for one year following completion of the study.
* A copy of Form FDA 3455 can be found at: http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3455.doc
* Some studies may also require a Partners Financial Disclosure form. For Guidance see the PHRC Financial Conflicts of Interest in Human-Subjects Research policy:
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 8.2.4
* Applicable Regulations: FDA: 21 CFR 54.1; 21 CFR 54.2; 21 CFR 54.4; 21 CFR 312.64(d); 21 CFR 812.110(d)
* Applicable WFH IRB Manual: [Chapter XII Disclosure, Management and Reporting Financial Conflicts of Interest in Research](http://www.wfhealthcare.org/app/files/public/1832/IRB-Manual-C12-Disclosure-Mngt-Reporting-Financial.pdf)

**Lab Documents**

**Contents**

* Current Lab Certification (CLIA, CAP)
* Normal Lab/Reference Values
* CV of Lab director
* IATA certification for packaging and shipping human subject substance
* Reference Manual

**QI Tips/Additional Information**

* Keep updated lab documents to document the competency of all lab facilities being utilized and to support the reliability of test results
* If lab documents re filed separately, write an signed and dated note-to-file indicating the location
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 8.2.11, 8.2.12, 8.2.14, 8.3, 8.6

**Drug/Device Accountability**

**Contents**

* Drug/Device shipment and receipt records
* Drug/Device Accountability Log
* Drug/Device Inventory logs
* Drug/Device Dispensing Logs
* Drug/Device Disposal Records
* Temperature Logs
* Most recent version of the Investigator’s Brochure or Device Manual
* Package inserts and updates
* Sealed Unbinding Envelopes (or location)
* Individual Treatment Codes (or location)

**QI Tips/Additional Information**

* If the drug/device shipment, receipt, and accountability are managed by research pharmacy, indicate this in a note-to-file.
* The Investigator’s Brochure or Device Manual provides clinical and nonclinical data on an investigational new drug or device. Updated versions must be submitted to the IRB.
* If the drug is marketed, a package insert is an appropriate alternative for the Investigator Brochure. For marketed devices, basic product information is an appropriate alternative for the Device Manual.
* Refer to the QI website (tools) for the following forms:
	+ Drug Accountability Log
	+ Drug Dispensing Log
	+ Device Accountability Log
	+ Device Dispensing Log
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf):4.6, 8.2.2, 8.3.2
* Applicable WFH IRB Manual: [Chapter IX.G Drugs, Biologics, and Dietary Supplements](http://www.wfhealthcare.org/app/files/public/1769/IRB-Manual-C9-Drugs-Biologics.pdf); [Chapter IX.H investigational Devices](http://www.wfhealthcare.org/app/files/public/1772/IRB-Manual-C9-Investigational-Devices.pdf)

**Data Collection**

**Contents**

* Blank set of CRF’s
* Data collection sheets and/or diaries
* IRB approved study questionnaires
* Add in source subject file when complete

**QI Tips/Additional Information**

* Source documents are original recordings of subject or study data
* Data collection sheets can act as source documentation. For instance, during study visits, subject information is written directly onto worksheets
* An industry sponsor will usually provide CRFs to sites
* Refer to the QI website (tools) for the following forms:
	+ **Source documentation/Subject study files**
* Applicable[GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf):8.3.14, 8.3.15, 4.9
* Applicable Regulations: 21CFR312
* Applicable [WFH IRB Manual: Chapter IV.H Principal Investigator Responsibilities](http://www.wfhealthcare.org/app/files/public/1822/IRB-Manual-C4-PI-Responsibilities.pdf)

**FDA Regulated Research**

**Contents**

* FDA Form 1572 (drug)
* Investigator Agreement
* Serious Adverse event reports submitted to sponsor
* IND application (if applicable)
* IDE application (if applicable)
* Amendments to application
* Adverse event reports

**QI Tips/Additional Information**

**Regulations/Guidance**

**GCP Sections:**

* Applicable WFH IRB Manual: [Chapter IX.G Drugs, Biologics, and Dietary Supplements](http://www.wfhealthcare.org/app/files/public/1769/IRB-Manual-C9-Drugs-Biologics.pdf); [Chapter IX.H investigational Devices](http://www.wfhealthcare.org/app/files/public/1772/IRB-Manual-C9-Investigational-Devices.pdf)

**NIH Funded Research**

**Contents**

* Copy of the NIH grant application and progress reports

**QI Tips/Additional Information**

* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 8.3.14, 8.3.15, 4.9.3
* Applicable WFH IRB Manual: [WFH IRB Manual: Chapter VI.A Operational Review Procedures: Full Board Review](http://www.wfhealthcare.org/app/files/public/1810/IRB-Manual-C6-Full-Board-Review.pdf); [Chapter VI.C Expedited Reviews](http://www.wfhealthcare.org/app/files/public/1808/IRB-Manual-C6-Expedited-Review.pdf); [Chapter VI.F Continuing Reviews](http://www.wfhealthcare.org/app/files/public/1804/IRB-Manual-C6-Continuing-Review.pdf)

**Sponsored Research**

**Contents**

* Copy of all significant correspondence to and from the study sponsor
	+ letters
	+ emails
	+ meeting notes
	+ Documentation of telephone calls
	+ Newsletters
	+ Monitoring Reports

**QI Tips/Additional Information**

* Documents received from the monitor via email (i.e. monitoring reports) must be printed and maintained in the binder
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 8.3.11

**Data and Safety Monitoring Board (DSMB)**

**Contents**

* Copy of all Data and Safety Monitoring Board (DSMB Reports)
* Additional correspondence with DSMB (meeting minutes, information provided to DSMB, emails)

**QI Tips/Additional Information**

* Submit a copy of the most recent DSMB report to the IRB at the time of continuing review
* Applicable [GCP Sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf): 5.19.3, 8.3.10
* Applicable WFH IRB Manual**:** [Chapter VII.B Reportable Events: Safety Information and Unanticipated Problems Involving Risks to Subjects or Others](http://www.wfhealthcare.org/app/files/public/1799/IRB-Manual-C7-Reportable-Events.pdf)

**Other**

**Contents**

* Queries
* Notes to File
* Telephone Logs
* Study Closure Documents
* Publications, Manuscripts, Articles, Etc.

**QI Tips/Additional Information**

* QI Tools have been created for tracking purposes and can be found under QI Tools:
	+ Note-to-File Template
	+ Telephone Log Template
* Applicable [GCP sections](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf) 8.3.15