Regulatory Binders and Compliance: A Tactical Approach

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Learning Objectives

• Describe the purpose and components of the clinical research regulatory binder.

• Illustrate best practices for organizing the components, corresponding sections and contents of a regulatory binder.

• Demonstrate use of regulatory forms.

NOTE: Contents of the regulatory binder will vary depending on the type of study and the study sponsor’s requirements.
What is a regulatory binder?

• Stores and organizes required or useful study documents and correspondence

• **Common names**: Study Binder, Investigator Binder, Administrative Binder, Regulatory Files, Investigator's Study Files¹

• It is the responsibility of the investigator to ensure compliance with good clinical practice (GCP), IRB, and applicable regulatory requirements.
Why keep one?

- Federal and state regulations, institutional policy, and good clinical and research practices require investigators to maintain documents related to human subjects research.
- An up-to-date regulatory binder facilitates the effective and efficient management of studies and may decrease procedural errors.
- Used by internal and external auditors to check the quality of the data to ensure the study was run well and the data collected is valid.
Regulatory Binder Sections*

1. Monitoring
2. Protocol and Amendments
4. Investigator Brochure/Drug Insert
5. SAEs, UPs, Violations and IND Safety Reports
6. Adverse Events/Deviations
7. Consent/Assent and Parental Permission Forms
8. Participant-Viewed Materials
Sections*

9. IRB Composition/FWA
10. IRB Approvals
11. IRB Correspondence
12. Other Correspondence
13. DSMP/DSMB
14. 1571/1572/IDE Documentation
15. CV/Licensure
16. Training Documentation
Sections*

17. Delegation of Authority/Site Signature Log
18. COI/Financial Disclosure
19. Lab Certifications/Reference Ranges
20. Investigational Product Accountability
21. Screening/Enrollment Logs
22. CRFs/Source Document Listing
23. Contracts and Budget

* Contents of regulatory binder will vary depending on study type and study sponsor
• Study Initiation Visit (SIV)

• Study Monitoring Visits (SMV)

• QA Reviews (internal auditing)*

* internal audit reports should not be stored in the regulatory binder but the location should be referenced in this section—should be stored in a secure and confidential location
• Currently approved protocol should always be on file
  – Recommend keeping the most recent copy on top of outdated protocol versions
  – Separate past versions with colored paper
• Notify all research staff of updated research procedures and changes as outlined in the new amendment and file in regulatory binder

Regulations and Guidelines:
  GCP Section 8.2.2
  GCP Section 8.3.2

• **Manual of Operations (MOO):** reference document that outlines the details of how to operationalize the protocol and conduct all study-specific procedures

• **Standard Operating Procedures (SOP):** detailed, written instructions for the management of clinical trials\(^2\)
  - ensures that all the functions and activities of a trial are carried out consistently and efficiently
  - may be department or study-specific
Documents in this section should include:
- Investigator Brochure (IB)
- Drug Package Insert

IB provides documentation that the investigator has been informed of relevant information
- Contains both clinical and non-clinical data
  - **Phase I**: IB must contain preclinical information about the pharmacological and toxicological effects and the pharmacokinetics and biological disposition in animals
  - **Phase II and III**: IB must contain information about safety and efficacy in humans obtained from prior clinical studies

Drug insert\textsuperscript{11}: Contains information related to safety and efficacy of FDA-approved drugs
Examples of IB and Package Insert
SAEs, UPs, Violations & IND Safety Reports

- SAE’s must be reported to the IRB and sponsor within **24 hours** of the staff becoming aware of the event.
- Recommended to file documents by specific event with the most recent report on top.
- Recommended to keep a log of all events.

**Serious Adverse Event (SAE)**: Any untoward medical occurrence that at any dose:
  - Results in death,
  - Is life-threatening,
  - Requires inpatient hospitalization or prolongation of existing hospitalization,
  - Results in persistent or significant disability/incapacity, or
  - Is a congenital anomaly/birth defect.

**Unanticipated Problem (UP)**: An event that is both unexpected and related.

**Protocol Violation**: A deviation from the protocol resulting from error, fraud or misconduct. Such an event could cause or has caused harm.

**IND Safety Reports**: Sponsor must submit IND safety reports to inform the FDA and all participating investigators of any adverse event (AE) experience that is associated with the use of the product and that is both serious and unexpected.
• Report AE within **10 calendar days**\(^6\) of staff becoming aware of the event*

• Typically tracked on a spreadsheet form indicating:
  – Date of report
  – Date of event
  – Name of event
  – PI causality (unrelated, unlikely, possible, probable, definite)\(^8\) related to study investigational agent or intervention
  – Outcome of event

• Any updates received should be filed with the most recent report on top

• **Adverse Event (AE)**\(^7\): Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

• **Deviation**: An accidental or unintentional change to the IRB-approved protocol.

* Reporting timelines may vary based on sponsor’s requirements
## Attribution Table

<table>
<thead>
<tr>
<th>RELATIONSHIP</th>
<th>ATTRIBUTION</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrelated to investigational agent/intervention</td>
<td>Unrelated</td>
<td>The AE is clearly <strong>NOT related</strong> to the intervention</td>
</tr>
<tr>
<td>Unlikely</td>
<td>Unrelated</td>
<td>The AE is <strong>doubtfully related</strong> to the intervention</td>
</tr>
<tr>
<td>Related to investigational agent/intervention</td>
<td>Possible</td>
<td>The AE <strong>may be related</strong> to the intervention</td>
</tr>
<tr>
<td>Probable</td>
<td>Possible</td>
<td>The AE is <strong>likely related</strong> to the intervention</td>
</tr>
<tr>
<td>Definite</td>
<td>Possible</td>
<td>The AE is <strong>clearly related</strong> to the intervention</td>
</tr>
</tbody>
</table>
# AE Tracking Table Example

## Adverse Event Tracking Log

<table>
<thead>
<tr>
<th>Adverse Event (Medical Terminology)</th>
<th>Serious Adverse Event</th>
<th>Start Date</th>
<th>End Date</th>
<th>Severity</th>
<th>Relatedness</th>
<th>Action Taken with Study Intervention</th>
<th>Action Taken with Investigational Product</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>1/120</td>
<td>1/120</td>
<td>Mild</td>
<td>Unrelated</td>
<td>None</td>
<td>None</td>
<td>Not Recovered/Not Resolved</td>
</tr>
<tr>
<td></td>
<td>Yes *</td>
<td></td>
<td></td>
<td>Moderate</td>
<td>Unlikely</td>
<td>Study Intervention Interrupted</td>
<td>IP temporarily interrupted</td>
<td>Recovered/Resolved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Severe</td>
<td>Probable</td>
<td>Study Intervention Discontinued</td>
<td>IP permanently stopped</td>
<td>Recovered/Resolved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Life-threatening/Disabling</td>
<td>Possible</td>
<td>Study Intervention Modified</td>
<td>IP modified</td>
<td>Recovered/Resolved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Death</td>
<td>Definite</td>
<td>Study Intervention Modified</td>
<td>IP modified</td>
<td>Fatal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
</tbody>
</table>

|                                   | No                   | 1/120      | 1/120    | Mild     | Unrelated  | None                                 | None                                     | Not Recovered/Not Resolved                |
|                                   | Yes *                |            |          | Moderate  | Unlikely   | Study Intervention Interrupted        | IP temporarily interrupted               | Recovered/Resolved                        |
|                                   |                      |            |          | Severe    | Probable   | Study Intervention Discontinued       | IP permanently stopped                   | Recovered/Resolved                        |
|                                   |                      |            |          | Life-threatening/Disabling | Possible | Study Intervention Modified           | IP modified                              | Recovered/Resolved                        |
|                                   |                      |            |          | Death     | Definite   | Study Intervention Modified           | IP modified                              | Fatal                                      |
|                                   |                      |            |          |           |           |                                      |                                          | Unknown                                   |

|                                   | No                   | 1/120      | 1/120    | Mild     | Unrelated  | None                                 | None                                     | Not Recovered/Not Resolved                |
|                                   | Yes *                |            |          | Moderate  | Unlikely   | Study Intervention Interrupted        | IP temporarily interrupted               | Recovered/Resolved                        |
|                                   |                      |            |          | Severe    | Probable   | Study Intervention Discontinued       | IP permanently stopped                   | Recovered/Resolved                        |
|                                   |                      |            |          | Life-threatening/Disabling | Possible | Study Intervention Modified           | IP modified                              | Recovered/Resolved                        |
|                                   |                      |            |          | Death     | Definite   | Study Intervention Modified           | IP modified                              | Fatal                                      |
|                                   |                      |            |          |           |           |                                      |                                          | Unknown                                   |

* Yes should be answered when the adverse event results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
• The original Informed Consent Form (ICF) approved by the IRB as well as currently approved versions of the Assent 12-18* and Parental Permission Form* filed in this section.

• All expired and past versions of these forms are filed below the current approved documents.

  – **Informed Consent**\(^4\): A person’s voluntary agreement, based upon adequate knowledge of relevant information, to participate in research or to undergo a diagnostic, therapeutic or preventative procedure.

  – **Assent**\(^5\): Child's affirmative agreement to participate in a clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent.

  – **Permission**\(^5\): Agreement of parent(s) or guardian to the participation of their child or ward in a clinical investigation.

* Depending on the nature of the study, these may not be required.

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**Regulations and Guidelines:**

- 45 CFR 46 21 CFR 50
- 21 CFR 56
- GCP Section 8.2.7
- GCP Section 8.2.3
- GCP Section 8.3.2
- GCP Section 8.3.12
Consent, assent and parental permission form templates can be found in IRBear (www.irbear.org) or on the CNMC intranet:

Forms  ->  Research  ->  Human Research Protection Program (OPHS-IRB)
• Materials that participants will be given for the purpose of the study:
  – Recruitment/Advertising Materials
  – Scripts (used for phone screening/consenting)
  – Diaries/Journals/Tracking Logs
• Materials that are no longer used or are outdated must be retained in the regulatory binder
• Currently approved and used materials are kept in front of outdated/expired versions
Key CNMC OPHS-IRB Contacts:

- Nynesh Kamani, MD – IRB Chair, OPHS Medical Director
- Adriana Brigatti, JD, MPH, LLM, CIP – Director, Research Regulatory Affairs
- Maryann Rossi, PhD, CIM, CIP – Accreditation and Education Manager
- Kay Ayers – IRB Project Coordinator, General IRB Inquiries, IRBear Training
- Jan Martinez, BA, CIM, CIP – IRB "B" Meeting Analyst
- Michele McGee-Guthrie, CIP – IRB "A" Meeting Analyst
- Austin Grace, BS – Minimal Risk Continuing Review Protocol Transactions
**FWA**\textsuperscript{4}: A formal, written binding commitment submitted to a federal agency where an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures to be used to achieve compliance.

* A copy of this letter can be found on the CNMC intranet: Departments -> Research -> Human Research Protection Program (OPHS-IRB) -> IRB Letter of Compliance
Anything the subject will see, hear or touch may require IRB approval

This section may contain:
- Protocol approval letters
- Amendment approval letters
- Continuing review approval letters
- ICF approvals
- Approval of other written materials provided to subjects (subject diaries, subject questionnaires, study information brochures)
- Approval of advertisements/scripts

The most current approvals will be filed in front of prior versions/approvals
IRB Approval Examples

• NOTE: Anything the subject or family will see, touch or hear may require IRB approval
  ▪ Pre-screening script
  ▪ Subject diaries
  ▪ Subject questionnaires
  ▪ Study information brochure
  ▪ Study advertisements
• This section will contain all other correspondence sent and received with the IRB and other institutions (FDA, NIH, etc.).

**Examples:**
- Notification and response pertaining to adverse events
- Interim or annual reports
- IRB copy of Final Study Report
- Closeout notification
- Changes to forms
• All other uncategorized correspondence

**Examples:**
- E-mail correspondence with sponsor
- Correspondence with other sites
• Unless integrated into the protocol, this section will contain the Data and Safety Monitoring Plan (DSMP)

• **DSMP:** A written plan that describes how the investigator plans to oversee the participant’s safety and welfare and how AEs will be characterized and reported

**Regulations and Guidelines:**
GCP Section 8.3.10
GCP Section 5.19.3
DSMP/DSMB, cont.

• If a Data Safety Monitoring Board (DSMB) is specified in the DSMP, the following should be included in this section:
  – DSMB Charter
  – DSMB Members and Affiliations
  – DSMB Reports
  – DSMB Correspondence
• DSMB Reports should be submitted to the IRB
• PI acknowledgement of DSMB reports should also be documented
• **FDA Form 1572 – Statement of Investigator**
  – The PI must maintain a copy of the 1572 for themselves and all sub-investigators listed on the protocol as submitted to the sponsor
  – Must be updated with the study sponsor each time there is a change to the information originally provided – the PI must maintain copies of all versions

• **FDA Form 1571 – Investigational New Drug (IND) Application**
  – If the PI is also the sponsor (IND holder), the PI must maintain a copy of the 1571 in addition to the Form 1572, as submitted to the FDA
• **IDE – Investigational Drug Exemption**
  
  – The PI should maintain a statement of the investigator’s commitment as outlined in 21 CFR 812.43

• The FDA Forms 1571 and 1572 and the IDE should be maintained as a front-to-back (2-sided) copy, with the most current versions in front

• Forms 1571 and 1572 can be downloaded from: [http://www.fda.gov/AboutFDA/ReportsManualsFor ms/Forms/default.htm](http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm)
This section will document the suitability and credibility of the study staff. For each member of the study staff, the following should be maintained:

- Current CV (signed and dated within past 12 months)
- Current medical licensure
- Current DEA licensure

**NOTE:** Since most of this information is common across studies, some maintain it centrally and refer to that central storage location.

**Regulations and Guidelines:**
- GCP Section 4.1.1
- GCP Section 8.2.10
- GCP Section 8.3.5
This section contributes to documenting the suitability and credibility of the study staff. For each member of the study team, the following should be maintained:

- CITI training
- Protocol-specific training requirements as applicable

**NOTE:** Since CITI training requirements are common across studies, this information can be maintained centrally and referred to in the Regulatory Binder.
• Documents who can do what for the study
• Not all tasks can be delegated – those that can must be documented
• PI indicated who will perform specific tasks
  – The PI and person task was delegated to signs the form to acknowledge agreement
  – People not properly delegated tasks cannot perform them (ex: conduct/obtain informed consent)
• Form should identify the time period (start and termination authority) for each delegation

Regulations and Guidelines:
GCP Section 8.3.20
GCP Section 8.3.25
Delegation of Authority Log Example

Site Signature Log/Delegation of Authority Log

STUDY NAME

The purpose of this form is to: (a) serve as the site signature log and (b) ensure that the individuals performing study-related tasks and procedures are appropriately trained and authorized by the principal investigator to perform them. This form should be completed prior to the initiation of any study-related tasks and procedures. The original form should be maintained at your site in the regulatory/study binder. This form should be updated during the course of the study as needed.

<table>
<thead>
<tr>
<th>Please Print</th>
<th>Obtain Informed Consent</th>
<th>Source Document Completion</th>
<th>Case Report Form (CRF) Completion</th>
<th>Medical History</th>
<th>Mediation History/Concomitant Medication</th>
<th>Physical Examination</th>
<th>Review Alleles and Drug Interaction</th>
<th>Other (specify):</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAME:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other (specify):</td>
</tr>
<tr>
<td>STUDY ROLE:</td>
<td>SIGNATURE:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other (specify):</td>
</tr>
<tr>
<td>INITIALS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other (specify):</td>
</tr>
<tr>
<td>DATES OF STUDY INVOLVEMENT:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I certify that the above individuals are appropriately trained, have read the protocol and pertinent sections of 21 Code of Federal Regulations Parts 50 and 56 (21 CFR Parts 50, 56) and the International Conference on Harmonisation and Good Clinical Practice (ICH GCP) Guidance, and are authorized to perform the above study-related tasks and procedures. Although I have delegated significant trial-related duties, as the principal investigator, I still maintain full responsibility for this trial.

Investigator Signature: _________________________________ Date: ________________

(Note: If this CRF is used as a source document, it must be signed and dated by study personnel.)

Site Signature Log/Delegation of Authority Log

Version 1.0

Children’s National Medical Center

Clinical and Translational Science Institute at Children’s National

Washington, DC
• CNMC requires conflict of interest (COI) / financial disclosure forms completed and filed by all individuals involved in the design, conduct, or reporting of research in addition to all key proposal as identified in the study proposal

  – **Examples**: PI, Sub-investigator, research nurse, clinical research assistant/coordinator

Regulations and Guidelines: 21 CFR 54
Children's National Medical Center / Children's Research Institute

STUDY SPECIFIC CONFLICT OF INTEREST DISCLOSURE FORM

This form is to be completed and filed by all individuals involved in the design, conduct, or reporting of research (investigator) in addition to all KEY PERSONNEL as identified in the study proposal. This form is required to be completed when (1) submitting proposals to federal agencies requiring disclosures, (2) entering into a contract agreement with an industry sponsor, (3) requesting funding support from all other non-federal and non-industry sources (e.g., local government, foundations, non-profit). Once an award has been made or a contract has been executed and the study is ready to be initiated, all individuals involved in the design, conduct, or reporting of research are required to provide evidence to IRB or IACUC that they have completed and filed this form.

Name of Investigator:
Department/Center:
Telephone/Email:
Sponsor:
Project/Grant Title:

### Definitions:
- **Immediate Family** means spouse and dependent children.
- **Financial Interest Related to the Research** means financial interest in the sponsor, product, or service being tested, or competitor of the sponsor or product or service being tested.

### Do you or your immediate family have any of the following?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ownership interest, stock options, or other financial interest related to the research unless it meets one or more of the following four tests:</td>
<td></td>
</tr>
<tr>
<td>1. Does not exceed $10,000 when aggregated for the immediate family.</td>
<td></td>
</tr>
<tr>
<td>2. Is not publicly traded on a stock exchange.</td>
<td></td>
</tr>
<tr>
<td>3. No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research.</td>
<td></td>
</tr>
<tr>
<td>4. Does not exceed 5% interest in any one single entry when aggregated for the immediate family.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compensation related to the research unless it meets one or more of the following two tests:</td>
<td></td>
</tr>
<tr>
<td>1. Does not exceed $10,000 in the past year when aggregated for the immediate family.</td>
<td></td>
</tr>
<tr>
<td>2. No arrangement has been entered into where the amount of compensation will be affected by the outcome of the research.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement.</td>
<td></td>
</tr>
</tbody>
</table>

### Grants and Contracts Administration

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you or a member of your immediate family serve as an officer, director, trustee, partner (limited or general), employee (limited or part-time), or retained as a consultant (limited or part-time) for the sponsor/funding agency? If yes, explain your role or position.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. If this is a clinical trial, are you proposing to investigate your own invention/product or the sponsor’s product?</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>3. Is the research being conducted for regulatory (such as FDA) approval?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Does the research being conducted use a licensed technology or product? Licensed technology includes patent, trademark, or copyright. If so, who has ownership of the license?</td>
<td></td>
</tr>
</tbody>
</table>

Last Updated: January 6, 2016 CTSI
• Lab reference ranges if the reference range is not included on the lab form
• A copy of certifications or accreditations
  – College of American Pathologists (CAP)
  – Clinical Laboratory Improvement Amendments (CLIA)
CLIA and JCAHO Certificates

Children's National Medical Center
Washington, DC

has been Accredited by

The Joint Commission
Which has surveyed this organization and found it to meet the requirements for the Laboratory Accreditation Program

March 26, 2011

Accreditation is customarily valid for up to 24 months.

The Joint Commission is an independent, not-for-profit, national body that oversees the safety and quality of health care and other services provided in accredited organizations. Information about accredited organizations may be provided directly to The Joint Commission at 1-800-994-6610. Information regarding accreditation and the accreditation performances of individual organizations can be obtained through The Joint Commission's website at www.jointcommission.org.

This reproduction of the original accreditation certificate has been issued for use in regulatory/payor agency verification of accreditation by The Joint Commission. Please consult Quality Check on The Joint Commission's website to confirm the organization's current accreditation status and for a listing of the organization's locations of care.

Children's National Medical Center.
Any clinical trial involving investigational drugs must utilize the CNMC Investigational Drug Service (IDS) Pharmacy for shipment, receipt and accountability

- Indicate IDS’s role in the regulatory binder in a note-to-file

The IDS will maintain and keep study IP records in the pharmacy. CRA/CRCs can work closely with the IDS team to ensure accuracy of IP accountability records
• A log without identifying information that lists all subjects that have signed informed consent forms who were screened, including screen failures, and enrolled in the study

• Each subject enrolled in the study will be assigned a clinical trial number – the enrollment log will document chronological enrollment of subjects by trial number
## Screening Log Example

<table>
<thead>
<tr>
<th>Screening ID</th>
<th>Date of Birth</th>
<th>Sex</th>
<th>Screening Date</th>
<th>Screening Status</th>
<th>If Not Eligible, Primary Reason</th>
<th>Consent Obtained</th>
<th>Enrolled</th>
<th>If Not Enrolled, Primary Reason</th>
<th>Date Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>M</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Eligible</td>
<td></td>
<td>No</td>
<td>Yes</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>F</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Eligible but declined</td>
<td>Inclusion #</td>
<td>Yes</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>M</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Not Eligible</td>
<td>Exclusion #</td>
<td>No</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>F</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Other:</td>
<td>Other:</td>
<td>Yes</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>M</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Eligible</td>
<td></td>
<td></td>
<td>No</td>
<td>No</td>
<td>Consent Withdrawn</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>F</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Eligible but declined</td>
<td>Inclusion #</td>
<td></td>
<td></td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>M</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Not Eligible</td>
<td>Exclusion #</td>
<td>Yes</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
<tr>
<td>/ / /   (mm/dd/yyyy)</td>
<td>F</td>
<td></td>
<td>/ / /20 (mm/dd/yyyy)</td>
<td>Other:</td>
<td>Other:</td>
<td>No</td>
<td>Study ID:</td>
<td>Consent Withdrawn</td>
<td>/ / /20 (mm/dd/yyyy)</td>
</tr>
</tbody>
</table>

Core Version 3.0
• Original Case Report Forms (CRF) that will be used to capture information necessary to support the study
  – Used to standardize the collection of study data

• Source documents are original records used to capture study data.
  – Laboratory reports
  – Physician notes
  – Participant surveys and questionnaires
  – Inclusion/exclusion checklist
  – Study visit checklist

**Regulations and Guidelines:**
21 CFR 312
GCP Section 8.3.15
GCP Section 8.3.14
GCP Section 4.9.3
Budget and any financial aspect of the study should not be kept in the regulatory binder due to their confidentiality.

Documentation of location of budgets and payment schedules should be documented here.

Section contains any correspondence and/or agreements relating to the financial aspects of the study.

Regulations and Guidelines:
- GCP Section 8.2.4
- GCP Section 8.2.6
General Rules & Best Practices

• Make sure patient confidentiality is maintained
  – Black out patient names and use subject numbers in reports (e.g. expedited AE reports)
• Binder contents/organization need to be easily understood by someone who is not familiar with the study
• Keep binders in a secure location – preferably locked cabinet
• Keep in mind the purpose of the binder: to document compliance with GCP and regulatory requirements
• Store items in reverse chronological order
References

1. Center for Cancer Research, National Cancer Institute
2. CenterWatch
3. Children’s Hospital Boston
4. Cincinnati Children’s Hospital Medical Center
9. National Institutes of Health (NIH)
10. U.S. Food and Drug Administration
12. www.docstoc.com