# REGULATORY BINDER SELF-AUDIT TOOL

## PROTOCOL INFORMATION

Protocol Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

IRB Number:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Principal Investigator:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## REGULATORY REV IEW

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| **Study Contacts** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are Study Contacts up to date (including Sponsor, CRO, Medical Monitor, key local staff, and other sites, if applicable)? |  |  |  |  | *ICH GCP E6(R2) 4.1.5, 4.2.5, 4.2.6* |

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| **IRB Approved Protocol** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are all approved versions of the protocol, amendments, admin changes, and/or Protocol Clarification Letters present? |  |  |  |  | *ICH GCP E6(R2) 1.44, 1.45, 2.6, 4.5.1, 4.9.4, 8.2.2, 8.3.2*  *FDA 21 CFR 56.103, 56.109, 56.110, 56.111, 312.30, 312.66, 812.110(a), 812.140(b)(1)*  *Common Rule 45 CFR 46.109, 46.110*  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.3* |
| Are all copies of the protocol and protocol amendment signature pages present and signed? |  |  |  |  |

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| **IRB Approved Informed Consent/Assent & Authorization Documents** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Is the Informed Consent (and Assent if applicable) Tracking Log up to date?  *While not required, tracking/version logs are often used to track revisions, approvals, expirations (if applicable), and any need to reconsent for revised consent/assent documents.* |  |  |  |  | *ICH GCP E6(R2) 4.8.1, 4.8.2, 4.9.4, 8.2.3, 8.3.2, 8.3.3*  *FDA 21 CFR 56.109, 56.110, 56.111, 312.66, 812.60*  *Common Rule 45 CFR 46.109, 46.110*  *IU HRPP Policies: Informed Consent 2.3, 3.1; Research Data Management 2.0; Research Personnel Responsibilities 2.3; Use of PHI in Research 2.1 and 3.1* |
| Are all versions of the IRB approved informed consent statements (and assents, if applicable) present and filed? |  |  |  |  |
| Are all versions of the IRB approved HIPAA Authorization(s) present and filed? |  |  |  |  |

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| **Investigational Product Information & Safety**  **(Can be stored in a separate binder)** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are all versions of the Investigator’s Brochure and addenda, package inserts, and/or Instructions For Use present?  *If any included updated risks (new or increasing in frequency/severity), were they submitted to the IRB via amendment within 60 days of receipt?* |  |  |  |  | *ICH GCP E6(R2) 4.4.2, 8.2.1, 8.3.1*  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.3* |
| Are all Investigational Product Labeling and Shipping / Inventory / Storage / Dispensation / Destruction Records present? |  |  |  |  | *See Investigational Product Self-Audit Tool* |
| Have Safety Reports been reviewed and reported as appropriate? |  |  |  |  | *FDA 21 CRF 312.50, 312.55 (b), 312.64(b), 312.66, 812.40, 812.150(a)(1), 812.150(b)(1)*  *IU HRPP Policies: Reportable Events 2.1* |
| If IU serves as the lead site for a multi-site study, have additional investigative sites been properly notified of relevant safety information? |  |  |  |  | *ICH GCP E6(R2) 8.3.18*  *FDA 21 CFR 312.55(b), 812.45 and 812.46 (b)*  *IU HRPP Policies: Research Personnel Responsibilities 2.7* |

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| **Study Personnel** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| *TIP: Industry monitors/auditors and FDA inspectors use the items below (CVs, licenses, and training records) to determine whether individuals delegated to a particular role (according to the signature/delegation log) are “qualified” for that role.* | | | | | |
| Is a staff signature / delegation log present? |  |  |  |  | *ICH GCP E6(R2) 2.7, 2.8, 3.1.2, 4.1.1, 4.1.5, 4.2.4, 4.3.1, 8.2.10, 8.3.5, 8.3.24*  *FDA 21 CFR 312.50, 312.53(a), (c)(1)(vi)(g) and (c)(1)(viii), 312.53(c)(2), 812.40, 812.43(c)(1)*  *IU HRPP Policies: Research Personnel Responsibilities 2.1*  *IU HRPP Guidance – Required Human Subjects Training* [*https://research.iu.edu/training/required/human-subjects.html*](https://research.iu.edu/training/required/human-subjects.html)  *HIPAA Privacy Rule 45 CFR 164.530(b)(1)* |
| Is a curriculum vitae (CV) present for each member of the study team?  *TIP:* *Industry standard is to update CVs or have staff resign & date every 2 years to indicate that the provided CV is still current.* |  |  |  |  |
| Are current licenses present for each study team member as applicable? |  |  |  |  |
| Have all members of the study team completed the required human subjects protection training (CITI and GCP if applicable) and HIPAA training?  *TIP: Industry standard is to maintain/file all training certificates, however these can be stored in a central location rather than duplicated in each study’s regulatory binder.* |  |  |  |  |

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| **Study Personnel (continued)** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are all members of the study team considered qualified by education, training, and experience? |  |  |  |  | *Declaration of Helsinki, General Principles (12): “Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.”* |
| Are all staff working on the study listed in the IRB application? |  |  |  |  | *IU HRPP Policies: Research Personnel Responsibilities 3.1, 3.2* |
| Have changes in staff been documented appropriately? (e.g. has new staff been added to the Delegation of Authority / Signature Log, the IRB application, the 1572 if applicable, etc.) |  |  |  |  | *ICH GCP E6(R2) 4.1.5, 8.3.5*  *FDA 21 CFR 312.30(2)(c), 312.66*  *IU HRPP Policies: Research Personnel Responsibilities 3.1* |
| Is there documentation that all study team members have been trained on the protocol?  Upon protocol amendments or revisions, were staff notified of (and retrained in, if applicable) applicable changes to their assigned roles? |  |  |  |  | *ICH GCP E6(R2) 4.2.4, 4.2.6*  *IU HRPP Policies: Research Personnel Responsibilities 2.1* |

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| **IRB Communication and Correspondence** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Has documentation of IRB correspondence (submission information, responses to provisions / tabling, etc.) been maintained and filed? |  |  |  |  | *ICH GCP E6(R2) 1.5, 1.31, 4.4.1, 4.4.3, 4.9.4, 4.10, 4.11, 4.13, 8.2.7, 8.3.2-3*  *Common Rule 45 CFR 46.102 (g and h), 46.103(b)*  *FDA 21 CFR 50.50, 56.103, 312.66, 812.62, 812.140(a)(1), 812.140(b)(1)*  *IU HRPP Policies: Research Data Management 2.0* |
| Are IRB approvals present and filed for all IRB submissions? |  |  |  |  |
| Was initial IRB approval granted prior to enrollment of the first subject? |  |  |  |  | *ICH GCP E6(R2) 3.3.6, 4.4.1*  *FDA 21 CFR 56.103 (a), 312.66, 812.110(a)*  *IU HRPP Policies: Research Personnel Responsibilities 2.3* |
| Are copies of IRB continuing review approvals contained in the file?   * Were the continuing reviews filed promptly with the IRB without a lapse in approval? * If a lapse in IRB approval did occur, did any prohibited activities occur during lapse? |  |  |  |  | *ICH GCP E6(R2) 3.1.4, 4.9.4, 4.10.1, 5.18.4(l), 8.3.3*  *FDA 21 CFR 56.103, 56.109 (f), 312.66, 812.64, 812.150(a)(3)*  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.3* |

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| **IRB Communication and Correspondence, continued** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Were changes made to the protocol approved by the sponsor (if applicable) and IRB before they were implemented? |  |  |  |  | *ICH GCP E6(R2) 4.5.2, 4.5.4*  *FDA 21 CFR 312.53(vi)(a), 312.66, 812.150 (a)(4)*  *IU HRPP Policies: Research Personnel Responsibilities 2.3* |
| Have advertisements or other forms of subject recruitment been approved by the IRB and filed appropriately? |  |  |  |  | *ICH GCP E6(R2) 3.1.2, 4.4.1, 4.9.4, 8.2.3, 8.2.7, 8.3.2, 8.3.3*  *FDA BIMO Clinical Investigator Guidance Manual, Part III (Inspectional), B.5*  <https://www.fda.gov/media/75927/download>  *IU HRPP Policies: Recruitment of Human Subjects 2.1; Research Personnel Responsibilities 3.1* |
| Have other written materials provided to research subjects (e.g. diaries, questionnaires, visit schedules) been approved by the IRB and filed appropriately? |  |  |  |  | *ICH GCP E6(R2) 3.1.2, 4.9.4, 8.2.3, 8.2.7, 8.3.2,* *8.3.3*  *IU HRPP Policies: IRB Review Process 3.1; Research Personnel Responsibilities 2.3* |
| Were all protocol deviations documented and reported appropriately? |  |  |  |  | *ICH GCP E6(R2) 4.5.3, 5.18.4(q)*  *FDA 21 CFR 812.150(a)(4)*  *IU HRPP Policies: IRB Review Process 3.6, 3.8; Reportable Events 2.1, 2.2; Research Personnel Responsibilities 2.3* |
| Were applicable reportable events (or new information that may adversely affect subject safety or the conduct of the trial) submitted to the IRB and applicable authority(ies) promptly with copies present in the regulatory binder (unanticipated problems including major protocol deviations/violations, noncompliance, AEs/SAEs, etc.)? |  |  |  |  | *ICH GCP E6(R2) 3.3.8(c and d), 4.5.3, 4.5.4, 4.10.2, 4.11, 5.17, 5.18.4(o and q)*  *FDA 21 CFR, 312.32, 312.64(b), 312.66, 812.46(b), 812.140, 812.150*  *IU HRPP Policies: Reportable Events 2.1, 2.2, 2.3; Research Personnel Responsibilities 2.3, 2.5. 2.7* |
| Has a final protocol closure report been submitted to the IRB (and to other regulatory authorities, if applicable) and filed appropriately? |  |  |  |  | *ICH GCP E6(R2) 4.13, 8.4.7*  *FDA 21 CFR 312.64(c), 812.150(a)(6)*  *IU HRPP Policies: IRB Review Process 2.8, 3.8; Research Personnel Responsibilities 2.3* |
| If the IRB of record publishes its IRB member roster, is it available and up to date?  (e.g. independent review boards such as the National Cancer Institute Central IRB (NCI CIRB), the Western Institutional Review Board (WIRB) or another academic institution) |  |  |  |  | *ICH GCP E6(R2) 8.2.8*  *FDA 21 CFR 56.107, 312.66, 812.60*  *Common Rule 45 CFR 46.103 and 46.107*  *Of note, although IRBs are required to provide a membership roster to the Office of Human Research Protections (OHRP), IRBs at academic medical centers such as Indiana University are not routinely asked/required to provide these rosters to sponsor monitors or inspectors in the course of site visits or audits. Typically, a statement of compliance which indicates that the IRB composition meets the federal requirements is provided instead:*  <https://research.iu.edu/doc/compliance/human-subjects/iu-hso-irb-statement-of-compliance.pdf> |
| Is an FWA present and up to date? |  |  |  |  | *FDA 21 CFR 56.106*  *To provide evidence that the institutional FWA(s) are present and up to date, Indiana University and affiliated researchers should refer to the IU HRPP website to identify the appropriate FWA number:*  <https://research.iu.edu/compliance/human-subjects/sponsored/federalwide-assurance.html>  *The FWA can then be located in the Office of Human Research Protections (OHRP) maintained FWA database which includes expiration dates and a list of IRBs linked to the assurance.*  <https://ohrp.cit.nih.gov/search/fwasearch.aspx?styp=bsc> |

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| **Laboratory Aspects of Trial** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are current copies of laboratory accreditation(s) and certification(s) present (e.g. CLIA, CAP)? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.2.12, 8.3.7*  *FDA BIMO Clinical Investigator Guidance Manual, Part III (Inspectional), B.4*  <https://www.fda.gov/media/75927/download>  *IU Health website for lab accreditations:*  <https://iuhealth.org/pathology-lab-services/accreditations> |
| Are normal value(s)/range(s) for medical, laboratory, technical procedures present? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.2.11, 8.3.6*  *Refer to the IU Health Pathology/Laboratory website for normal ranges:*  <https://iuhealth.org/pathology-lab-services/tests-specimen-handling> |
| Have all lab kits/supplies been utilized before the expiration date? |  |  |  |  | *N/A* |
| Are Specimen Logs present and current? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.25* |

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| **Clinical Aspects of the Trial** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are temperature logs for applicable clinic equipment complete and current (centrifuges, refrigerators, freezers, storage cabinets, etc.)? |  |  |  |  | *ICH GCP E6(R2) 4.2.3. 4.9.4, 8.2.12, 8.3.7*  *IU HRPP Policies: IRB Review Process 2.3; Research Personnel Responsibilities 2.1* |
| Are equipment maintenance and calibration records available and current (electronic scales, electronic blood pressure cuff, etc.) (if applicable)? |  |  |  |  |
| Have changes in facilities or equipment been documented appropriately? |  |  |  |  |

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| **Study Conduct** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Is the Subject Screening Log available? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.20* |
| Is the Subject Identification Code List available? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.21, 8.4.3* |
| Is the Subject Enrollment Log available? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.22* |
| Does subject enrollment exceed the number approved by the IRB? |  |  |  |  | *ICH GCP E6(R2) 3.3.7, 4.5.1*  *FDA 21 CFR 312.53(c)(1)(vi)(a), 312.30, 312.66, 812.35*  *IU HRPP Guidance: Reportable Events* <https://research.iu.edu/compliance/human-subjects/guidance/reportable.html> |
| If subjects have withdrawn, has the reason for withdrawal been documented? |  |  |  |  | *ICH GCP E6(R2) 4.3.4*  *FDA 312.33(b)(3 & 4)*  *IU HRPP Policies: Research Personnel Responsibilities 2.4* |
| Is there reason to believe that the Investigator has, and is continuing to provide appropriate oversight of the study and/or study team?  *TIP: In addition to PI initials/date on safety items including labs, ECGs, imaging reports, etc., often the PI & study team meet routinely to review enrollment, deviations, safety, etc. – agendas/sign-in sheets for these meetings can be maintained to help document the PI’s oversight of trial activities.* |  |  |  |  | *ICH GCP E6(R2) 4.2.4, 4.3*  *FDA 21 CFR 312.53 (c)(vi)(c), 312.60, 812.43(c)(4)(ii), 812.110 (c)*  *IU HRPP Policies: Research Personnel Responsibilities 2.0* |

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| **Communication and Correspondence** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Are all versions of the case report forms (CRFs) present? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.2.2, 8.2.7, 8.3.3*  *IU HRPP Policies: Research Data Management2.0; Research Personnel Responsibilities 2.5* |
| Has documentation of correspondence (letters, e-mails, meeting notes, telephone calls) with the research sponsor and/or contract research organization (CRO) been maintained and filed? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.2.6, 8.3.11, 8.3.17-18*  *FDA 21 CFR 312.55, 812.140(a)(1), 812.140(b)(1)*  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.5* |
| Is Monitoring Visit correspondence on file? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 5.18.6, 8.2.19-20, 8.3.10-11, 8.4.5*  *FDA 21 CFR 312.56(b), 812.140(a)(1), 812.140(b)(1)* |
| Has the monitoring log been signed and dated? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.10*  *Guidance for Industry: Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring, August 2013*  <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm269919.pdf> |
| Is there a DSMC/DSMB for this study?   * If Yes, are all DSMB reports and recommendations on file * Have all DSMB reports been submitted to the IRB? |  |  |  |  | *ICH GCP E6(R2) 4.9.4, 8.3.11, 8.3.18*  *IU HRPP Policies: Research Data Management 2.0*  *IU HRPP Guidance on Data Safety Monitoring:* <https://research.iu.edu/compliance/human-subjects/guidance/data-safety.html> |

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| **FDA Related Documentation** | **Yes** | **No** | **N/A** | **Not**  **Reviewed** | **REFERENCES** |
| Have investigator-initiated or internally sponsored protocols and amendments received necessary regulatory approvals from the FDA? |  |  |  |  | *ICH GCP E6(R2) 8.2.9, 8.3.4, 8.4.7*  *FDA 21 CFR 312.20(a), 312.23(e), 312.31, 312.40, 812.20, 812.35(a)*  *IU HRPP Policies: Research Personnel Responsibilities 2.7* |
| Is the Investigator Agreement (e.g. FDA Form 1572 for drug studies) completed and amended as needed?  Are all versions of the 1572 present? |  |  |  |  | *ICH GCP E6(R2) 5.1.4, 5.6.3*  *FDA 21 CFR 312.53(c)(1), 812.140(c)(4)*  *FDA Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs Frequently Asked Questions – Statement of Investigator (Form FDA 1572), May 2010*  <https://www.fda.gov/media/78830/download>  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.7* |
| Have all individuals listed on the 1572 (PI and Sub-I) completed and filed a Financial Disclosure? |  |  |  |  | *FDA 21 CFR 312.53(c)(4), 312.64(d), 812.110(d), 812.43(c)(5)*  *FDA Guidance for Clinical Investigators, Industry and FDA Staff: Financial Disclosure by Clinical Investigators, February 2013* <https://www.fda.gov/media/85293/download>  *IU HRPP Policies: Research Personnel Responsibilities 2.7* |
| Are all IND/IDE Application and supporting materials (if applicable) available?  Are annual reports, event reporting, and other communication with the FDA present? |  |  |  |  | *ICH GCP E6(R2) 5.10*  *FDA 21 CFR 312.22 – 312.38, 812.20 – 812.35*  *IU HRPP Policies: Research Data Management 2.0; Research Personnel Responsibilities 2.7* |
| Is a list of FDA-regulated studies for which the PI is/was responsible available and up to date? (should include title, start and stop dates, and enrollment information)  *TIP: Upon arrival for a Clinical Investigator (PI) inspection, the FDA Inspector will likely request such a list; QIO can assist you in retrieving this information from KC.* |  |  |  |  | *FDA BIMO Clinical Investigator Guidance Manual, Part III (Inspectional), C.2*  <https://www.fda.gov/media/75927/download> |

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| **Notes:** |
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Form Completed By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_