IUPUI

INDIANA UNIVERSITY–PURDUE UNIVERSITY INDIANAPOLIS

STANDARD OPERATING PROCEDURES

for Research Involving Human Participants

Indiana University Purdue University Indianapolis (IUPUI), Clarian Health Partners (Clarian), and their affiliates are dedicated to protecting the rights and welfare of human participants recruited to participate in research conducted under the auspices of these organizations. The IUPUI/Clarian SOPs provide a central resource for researchers to find important information on required federal and state regulations and institutional policies governing these research activities.

IUPUI
INDIANA UNIVERSITY–PURDUE UNIVERSITY INDIANAPOLIS

Standard Operating Procedures

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Title:	Auditing Human Subjects Research			
Current Version:	07/07		Previous Versions:	04/05, 02/05, 12/04, 02/03, 10/01

1. INTRODUCTION

One important element of a quality human research protection program (HRPP) is the audit function. The primary goal of an audit is to monitor the conduct of the research to assure the rights and welfare of human research participants are protected and to optimize compliance to federal regulations, state laws, and institutional policies.

Within the IUPUI/Clarian system, there exists a Human Subjects Research (HSR) and HIPAA Auditor (hereafter known as the "Auditor"), who conducts on-site reviews and directed (for-cause) investigations of research studies to ensure that human subjects research conducted at or on behalf of IUPUI/Clarian and their affiliates is of the highest quality and meets all applicable federal and state regulations and institutional policies. Researchers should view the Auditor as a partner in ensuring a high state of regulatory compliance and agency inspection readiness.

2. OBJECTIVES

2.1 Describe the audit planning process

2.2 Describe the audit process

3. SCOPE

This SOP applies to all research activities of faculty, staff, student, or others who are involved in human subjects research that falls under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVENT DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1 The Audit Plan and Audit Schedule

5.1.1 The Auditor will develop an audit plan and audit schedule for the IUPUI HRPP. Consideration will be given to risks associated with research studies. The plan and schedule will complement and augment any monitoring done internally within the research unit. The audit plan and schedule will be reviewed and approved by the IUPUI/Clarian IRB Executive Committee.

5.2 The Audit Process for Scheduled Audits

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5.2.1 Once the audit schedule has been approved by the IRB Executive Committee, each auditee listed on the audit schedule will ordinarily be notified at least a month in advance of the scheduled audit.

5.2.2 Prior to conducting the audit, the Auditor will meet with key personnel from the research team, who are expected to give full cooperation throughout the entire audit process. Following the audit, the Auditor will review the findings with the auditee and will provide education and counseling regarding the findings prior to writing the audit report. If the Auditor notes only minor issues during the audit he/she may opt to utilize an abbreviated report in the form of a worksheet. This worksheet will still contain the necessary information to convey the findings to the auditee while facilitating less time allocation to minor issues.

5.2.3 The audit report or abbreviated report, as appropriate, will then be sent to the auditee. If not done already, when the audit report is received, the auditee is expected to take steps to make necessary improvements to align the operation with institutional policies and regulatory agency standards. The auditee is expected to submit a response to the audit report or abbreviated report back to the Auditor within fourteen (14) days of receiving the report. The response should include a corrective action plan to correct any problems identified, as well as a preventive action plan to prevent recurrences. A point-by-point response should include the suspected "root cause" of the issues, the individual(s) responsible for corrective and preventive actions, and a timeline for their completion.

5.2.3.1 If findings are noted in the audit report that indicate unanticipated problems involving risks to subjects or others or noncompliance, they should be reported to the IRB in accordance with the Unanticipated Problems and Noncompliance SOP.

5.2.3.2 If the plan of action requires revisions to study documents, the auditee will need to follow the IRB amendment process. When applicable, copies of relevant documentation should be submitted with the response.

5.2.4 If the auditee has not provided a response to the audit report or renegotiated a revised response timeframe with the Auditor within fourteen (14) days of receipt of the audit report, the auditee will be contacted to bring about action. If no action is taken, the department chair will then be contacted for assistance. If the department chair does not provide adequate assistance, the issue will be taken to the IRB Chair or Chair's designee for action.

5.2.5 Upon receipt of the auditee's response, the Auditor will assess the response for completeness and appropriateness. The Auditor will work with the auditee if issues require further clarification until the response is complete and satisfactory. If at any time during this process it becomes apparent to the Auditor an appropriate IRB or other applicable authority needs to become involved for any reason, the Auditor will seek that involvement to the extent necessary.

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5.2.6 Once the above process has concluded, the audit report and response will be submitted to the appropriate IRB as a general information item for discussion and possible action. The completed audit report will also be immediately shared with the local VA Research Office.

5.2.7 Auditees will be solicited for feedback on the auditing process by means of direct contact with the Director of Research Compliance Administration or a survey or questionnaire.

5.2.8 Feedback on the performance of the Auditor or the audit itself will be directed to the Director of Research Compliance Administration and the IUSM Privacy Officer.

5.3 **For-Cause Audit Process**

5.3.1 For-cause audits will ordinarily receive about a week advance notice, unless otherwise directed by the authority requesting the audit. Auditees will give full cooperation to the Auditor throughout the audit process. The auditee is expected to take steps to make necessary improvements to align the operation with IUPUI/Clarian and regulatory agency standards as soon as possible following the audit and then make any necessary adjustments at the time of receipt of the audit report and/or feedback from the applicable authorities.

5.3.2 For-cause audits involving the VA, will be conducted in cooperation with the local VA research office.

5.3.3 The Auditor will follow the methods listed in section 5.2 above but will make adjustments as necessary depending on the circumstances surrounding the audit request and findings.

5.3.4 The required deadline to respond to the audit findings will also vary depending on the circumstances of the audit request and findings. This deadline will be communicated by the Auditor to the auditee. The auditee's response should include a corrective action plan to correct any problems identified, as well as a preventive action plan to prevent recurrences. A point-by-point response should include the suspected "root cause" of the issues, the individual(s) responsible for corrective and preventive actions, and a timeline for their completion.

5.3.4.1 If findings are noted in the audit report that indicate unanticipated problems involving risks to subjects or others or noncompliance, they should be reported to the IRB in accordance with the Unanticipated Problems and Noncompliance SOP.

5.3.4.2 If the plan of action requires revisions to study documents, the auditee will need to follow the IRB amendment process. When

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applicable, copies of relevant documentation should be submitted with the response.

5.3.5 If the auditee has not provided a response to an audit report or renegotiated a revised response timeframe with the Auditor by the determined deadline, the auditee will be contacted to bring about action. If no action is taken, the department chair will then be contacted for assistance. If the department chair does not provide adequate assistance, the issue will be taken to the IRB Chair or Chair's designee for action.

5.3.6 Auditees will be solicited for feedback on the auditing process by means of direct contact with the Director of Research Compliance Administration or a survey or questionnaire.

5.3.7 Feedback on the performance of HSR auditor(s) or the audit itself will be directed to the Director of Research Compliance Administration and the IUSM Privacy Officer.

5.4 **The Audit Findings**

5.4.1 The Auditor will track audit findings and corrective and preventive actions and prepare a semi-annual report, which will then be presented to the IRB Executive Committee. This report will describe general audit finding trends, any serious or continuing noncompliance, and unanticipated problems involving risks to subjects or others found during the previous two quarters. Also reviewed will be late responses to audits and the findings and outcomes from any regulatory agency inspections.

5.4.2 Based on audit finding trends, on new government agency regulations or guidelines, or on new institutional policies, RCA, in collaboration with other appropriate institutional entities (such as, the IUSM Office of Compliance Services or the Office of Clinical Research) will develop and deliver appropriate education to the IUPUI/Clarian research community.

5.4.3 The Auditor may be sent on special assignment to investigate allegations or reports of unanticipated problems involving risks to subjects or others or noncompliance.

5.4.4 The audit reports are meant to be "internal" to the University/Clarian system and will not be shared with outside agencies, unless the audit findings result in the termination or temporary suspension of a research project, in which case the IRB will notify the appropriate entities pursuant to the Reporting SOP.

5.5 **External Inspection Compliance Responsibilities**

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5.5.1 When an investigator (researcher) receives notification of an upcoming compliance inspection visit by a regulatory agency, funding agency, or study sponsor, he/she should immediately notify Research Compliance Administration at (317) 274-8289 (at IUPUI) or the Methodist IRB Office at (317) 962-8240 (at Methodist).

5.5.2 The investigator, or other authorized individual, who has authority to grant access shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where drugs or devices are held.

5.5.3 The investigator, or other authorized individual, shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect, copy and verify all records relating to a research study.

5.5.4 The investigator, or other authorized individual, shall permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

5.6 **Other Compliance Responsibilities**

5.6.1 The Auditor also develops and implements plans to measure and improve the Human Research Protection Program's (HRPP) effectiveness, quality and compliance with institutional policies and procedures, and applicable federal, state and local laws.

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The Audit Cycle (not for cause)

Audit plan and audit schedule developed by HS and HIPAA Auditor

⇩

Review and approval of audit plan and schedule by Vice Chancellor for Research, IUPUI and the IRB Executive Committee

⇩

Auditee contacted to schedule audit

⇩

Audit conducted, including introduction meeting, data review and interviews, key findings identified, closeout meeting

⇩

Audit report or abbreviated report written and sent to auditee

⇩

During these (2) steps there will likely be back-and-forth communication between the Auditor and auditee to ensure report and response are complete and accurate

⇩

Auditee provides response to audit report, which shall include corrective action plan to correct identified problems, a root cause analysis, and timeline for completion of corrective action, to Auditor

⇩

Final audit report and auditee response sent to appropriate IRB

⇩

Auditee notified of IRB's discussion and any further action required on the auditee's part. Audit closed when IRB satisfied that all provisions and corrective actions have been completed.

Please note that "for-cause" audits follow the same cycle described above, but adjustments may be made, as necessary, depending on the circumstances surrounding the audit request and findings; this includes the response time required by the auditee.

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Title:	Biological Specimens in Research			
Current Version:	07/07		Previous Versions:	08/04

1. INTRODUCTION

Legal obligations to protect human subjects apply not only to direct contact with a human subject, but also to items that are derived from a human subject, including medical records and biological specimens. For the purposes of this SOP, biological specimens can be broadly defined as a sample that originated from an organ system of a human. For example, this may include tissue samples (even when embedded in paraffin blocks), DNA, cells from the circulation or bone marrow, plasma, sera, feces, nail clippings and tissues removed for clinical purposes or due to a health condition (i.e. bowel from a surgical resection, tissue from an aborted fetus, embryos from a fertility clinic).

Such specimens may be collected for clinical purposes and stored per regulatory requirements for pathology accreditation, as part of a specific research study and then stored for future use, or as a purposeful collection of biological samples for the future distribution to investigators, such as a repository. In addition, the collection, storage and use of such specimens might also be for the purposes of genetics research. In all of these scenarios, identifiable health information may or may not be associated with the biological specimens.

Research studies which propose the collection and storage of human specimens are increasingly being reviewed by the IUPUI/Clarian Institutional Review Boards (IRBs) as are proposals for the use of such specimens. The process should be thought of as having three stages: 1) the collection and storage of the specimens for current and/or future research purposes; 2) the storage and management of specimen repositories; and 3) the use of previously collected/stored specimens for research purposes. Each stage requires IRB review and approval.

2. OBJECTIVES

Describe the appropriate ways to collect, store and use biological specimens for research purposes.

3. SCOPE

This SOP applies to all research activities of faculty, staff, student, or others who are involved in human subjects research that falls under the jurisdiction of the IUPUI/Clarian IRBs.

4. DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

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5.1 Existing Collections of Human Biologic Material

Existing collections of human biologic material may have been developed over a period of time without use of written consent from subjects, or a limited consent from subjects may have been obtained during clinical procedures. Recontact of donors may be difficult or impossible. In such situations, investigators should submit an application to the IRB for continued use (or a new use) of the collection or may adopt a procedure to de-identify their collection. Such procedures to de-identify a collection per HIPAA standards should be approved by the IRB.

5.2 IRB Review

5.2.1 IRB review is required under two scenarios for using biological specimens: **retrospective** use of previously stored specimens and **prospective** studies requesting the collection, storage or use of specimens for current and/or future research. Similarly, there are two categories of specimens: those obtained initially for clinical or diagnostic purposes only, and those obtained solely for research purposes.

5.2.2 In all cases, a description of the proposed research use of the specimens must be submitted to and reviewed by the IRB before the specimens may be utilized. The level of review and issues of informed consent will be decided by the IRB on a case-by-case basis but will be impacted by whether the samples are identifiable, coded or de-identified.

5.3 Creation of a Repository For Future Use

5.3.1 If housed at IUPUI/Clarian or one of their affiliates, the repository must establish an oversight mechanism (such as a committee) to evaluate each request for samples by investigators to see if the request is consistent with the IRB's conditions for sharing samples and with the original informed consent and authorization, if applicable. The committee membership and process should be outlined in the protocol submitted for IRB review. For details regarding the privacy and security of repositories, see the Data Management SOP.

5.3.2 Features of a Formalized Repository

5.3.2.1 Repository PI ("collector-investigator") obtains IRB approval for establishing and maintaining the repository

5.3.2.2 The protocol clearly outlines the conditions under which the investigators will share specimens or data from the repository with Recipient- Investigators (those who will receive specimens or data from the repository)

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5.3.2.3 A "**Submittal Agreement**" is developed as part of the protocol that describes conditions for placing specimens in the repository (see below)

- **Submittal Agreement:** A written submittal agreement between the collector-investigators and recipient-investigators must require written informed consent of the donor-subjects utilizing an informed consent document approved by the local IRB where the collection will take place. It must also contain an acknowledgment that collector-investigators are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained. (See sample)

5.3.2.4 A "**Usage Agreement**" is developed as part of the protocol that describes those conditions for sharing specimens or data with Recipient Investigators. Both the Repository PI (or designee) and Recipient Investigator must sign the agreement

- **Usage Agreement:** A written usage agreement between recipient-investigators and collector-investigators must include the following: "Recipient acknowledges that the conditions for use of this research material are governed by the repository Institutional Review Board (IRB) in accordance with Department of Health and Human Services regulations at 45 CFR 46. Recipient agrees to comply fully with all such conditions and to report promptly to the repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to the recipient's applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects. This research material may only be utilized in accordance with the conditions stipulated by the repository IRB. Any additional use of this material requires prior review and approval by the repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OHRP-approved Assurance." (See sample)

5.3.2.5 The protocol must contain plans for protecting identifiers related to the specimen, and links between the identifiers and samples. OHRP strongly recommends that one such condition stipulate that recipient-investigators not be provided access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained with the exception of data detailed in the informed consent. As such, IUPUI/Clarian and their affiliates have adopted this requirement. For more details on the measures and controls used to protect identified specimens, see Data Management SOP.

5.3.3 A Research Certificate of Confidentiality may need to be obtained from the federal government to protect confidentiality of repository specimens and data.

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The IRB will decide if this is necessary on a case-by-case basis. It the certificate of confidentiality is determined to be necessary, a copy must be submitted to the IRB that has oversight of the repository once received. For more details on the measures and controls used to protect identified specimens, see Data Management SOP.

5.4 Consent and Authorization Issues

5.4.1 The consent and authorization process and documentation (forms), if required, must be approved by an IUPUI/Clarian IRB. Elements of the consent and authorization process may be waived or modified by the IUPUI/Clarian IRB.

5.4.2 When informed consent to the research use of human specimens is required, it should be obtained separately from informed consent to clinical procedures (i.e., not combined with a general surgery or pathology consent). The person who obtains informed consent in the clinical setting should make clear to potential subjects that their refusal to consent to the research use of biological materials will in no way affect the quality of their clinical care.

5.4.3 The informed consent statement must include the usual required elements of an informed consent (see SOP on consent). For details regarding requirements for authorizations, see the SOP regarding Subject Confidentiality and Privacy. In addition, the use of biological samples requires special consideration of and explanation of the following issues. (See sample informed consent for suggested wording):

5.4.3.1 Collection and storage procedures

5.4.3.2 Procedures for oversight of security and maintenance of the sample

- Who has access to the samples?
- Will the specimens be discarded if the PI leaves, or given to someone in the same Department?
- Will third parties not part of the collection protocol have use in the future? Is so, under what conditions?

5.4.3.3 Procedures to protect privacy and confidentiality of the information linked to the specimen and results obtained from analysis of the specimen.

- Will the specimen be de-identified per HIPAA standards?
- Will the specimen be linked to other information- if so who controls that link?
- Will results of analyses be linked back to the subject?
- How will the subject be able to revoke use of the specimens? [Note: In some cases, HIPAA allows that it may be acceptable to use the data already collected up to the point of revocation if elimination of the data could cause harm to the study results.]

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5.4.3.4 Subjects rights and options for obtaining information of results obtained from use of the specimens

- Will the subject not be given any information or will the subject have the option of learning of the results? If the latter is a possibility, how will this occur?
- Are there specific risks related to the type of tests/analyses (i.e. risk of insurance problems, embarrassment, social risk, or knowledge of the presence of a genetic mutation)?

5.4.3.5 Possible future contact, if any

- Is it possible that the subject will be contacted for future information about themselves, or future use of the specimen? If so, the subject should be given the option of being contact or not.
- For genetic studies, if family contact is requested, the proband must specifically agree to this contact.

5.4.3.6 Explanation that participant samples will be stored for future research purposes.

5.4.3.7 Proposed use of stored samples, if known.

5.4.3.8 Procedures that will be used to protect the confidentiality and privacy of any personal identifiers that will be associated with the source of a specimen.

5.4.3.9 Information about the control and management of the specimens during storage. For more details regarding the control and management of specimens, see Data Management SOP.

5.4.3.10 The subject's rights to withdraw his/her consent or authorization at any time either by requesting that the specimens be destroyed or that all personal identifiers be removed.

5.4.3.11 Information about the length of storage.

5.4.3.12 Whether the subject can obtain future access to the stored samples for information that may be of clinical relevance to him/her. Similarly, subjects must be told if such information will not be available in the future (e.g. because personal identifiers are to be removed).

5.4.3.13 How the investigator will handle future third-party access.

5.4.3.14 Information about possible secondary uses of the stored specimens, or the possible creation of an immortalized cell line based on the specimen, if applicable.

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5.4.3.15 Procedures for collecting and identifying specimens submitted to the repository.

5.4.3.16 Who, in general, can use the repository?

5.4.3.17 Whether or not subjects will be told the results of any screening done on specimens.

5.4.3.18 Potential fiscal, psychological, and social risks of disclosure of test results if results will be shared.

5.4.3.19 Risks of participating in genetic studies including the effects of the knowledge that one is the carrier of a disease gene that might affect their life course, employability or insurability, if results will be shared. If subjects want to be told, precautions must be taken to minimize the potential harm of receiving bad news and to preserve the confidentiality of the results. The precautions needed in conveying genetic screening results depend upon the age of onset of the disorder, the burden of illness, and the availability of treatment or prevention. The communication of genetic information carries with it the responsibility to interpret the results and provide care for the individual; and thus, it is ideally done in the setting of a clinical rather than research relationship with the subject.

5.4.3.20 Risks to individual dignity, invasion of privacy, violation of confidentiality, stigmatization of a subject or group, discrimination in insurance or employment, psychological harm, generation of conflict within a family, harm to relatives, inappropriate commercialization of findings, or use of samples in projects objectionable to the subject.

5.4.3.21 Specify the general process for coding, identifying or anonymizing material. For details regarding de-identification, see the SOP on Subject Confidentiality and Privacy.

5.4.3.22 If identified material is to be de-identified for use, indicate what consideration has been given to the fact that de-identification may deny the donor or the donor's descendants of assured or implied access to results of research.

5.4.3.23 Indicate if access to existing medical records or contacting subjects is required for the project.

5.4.3.24 Indicate under what circumstances it is anticipated that subjects may be contacted.

5.4.3.25 For genetic studies, if the research investigator wishes to contact relatives of a proband, the proband must be asked whether this contact is

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acceptable. If the proband declines to allow contact of relatives, the project may not proceed. If permission is granted for contact, the investigator must design a consent form to address the issue of information that may be forthcoming from the research project. The relatives should be given the option to decide whether they are willing to contribute samples. If they are willing to donate, they must be given the option of accepting or declining information derived from the research study.

5.4.3.26 If a certificate of confidentiality has been obtained, participants should be told and an explanation of what such a certificate means should be offered.

5.4.4 **Other less common considerations for the consent**

5.4.4.1 There may be situations where a patient or research subject is known to possess biologic specimens with unique characteristics thought to have **commercial value**. In this case, if specimens are to be collected for research purposes and the investigator expects that they will be commercialized into a marketable product or sent to a commercial sponsor for development, the consent form must state this possibility. IRB policy requires that the consent form contain the following language:

> "As this is a research institution, specimens obtained in medical situations may later be used for research purposes. The investigator intends to include specimens taken from you along with other specimens that may also be used in an attempt to develop products to be sold, and it is not the intention of the investigator to enter into an agreement with you to become partners in sharing the profits or losses in the sale of those products."

5.5 INFORMATION REQUIRED IN THE REPOSITORY PROTOCOL

5.5.1 In addition to all of the elements listed in the above informed consent section, the following should be included in the protocol submitted to the IRB for review:

5.5.1.1 Indicate the general nature of tests that will be done on the samples, if known.

5.5.1.2 A full description of the mechanisms used to link specimens and identifiable information, and procedures used to maximize the protection against inadvertent release of confidential information.

5.5.1.3 If housed at IUPUI/Clarian, the repository must establish a mechanism such as a committee to evaluate each request for samples by investigators to see if the request is consistent with the IRB's conditions for sharing samples and with the original informed consent. The committee

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membership, and process, if applicable, should be outlined in the protocol submitted for IRB review.

5.5.1.4 If additional research is subsequently proposed that is not described in the current protocol, a new IRB application (or an amendment, if appropriate) must be submitted for review and approval.

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Title:	Confidentiality and Privacy			
Current Version:	07/07		Previous Versions:	09/03, 09/04, 08/05

1. INTRODUCTION:

A major tenet in the protection of human subjects is that persons can be wronged even if they are not physically harmed. This holds true for all forms of research including behavioral or social science research, physiologic studies, and therapeutic trials. Regardless of the type of research, it is important to remember that privacy is itself a form of personal protection, so a violation of an individual's privacy is harmful because it carries the loss of this protective barrier. The risk of loss of privacy includes public exposure of personal information, perceived loss of control or security, and erosion of trust on all levels. All individuals have a right to expect that privacy actions will remain private and that information that others have about them will be kept confidential and only used for their original purpose(s) as stated in the IRB-approved protocol.

Information on subject confidentiality is necessary in the Informed Consent document under the Common Rule, Title 45 CFR 46. In addition, the universal increase in electronic submission of insurance claims has led to increased concern for privacy. This has led to additional rules and regulations as part of the Health Insurance Portability and Accountability Act (HIPAA) Title 45 CFR Parts 160, 162 and 164. There are three components to HIPAA: 1) Electronic claims and transactions; 2) Privacy regulations effective April 14, 2003; and 3) Security regulations effective April 21, 2005. HIPAA regulations apply to any use of Protected Health Information (PHI) as defined under HIPAA and clarified in this Standard Operating Procedure. The IUPUI/Clarian Institutional Review Boards (IRBs) are committed to conducting research in compliance with all applicable laws, regulations and IUPUI/Clarian policies and procedures. As part of this commitment, the IUPUI and Clarian IRBs have adopted a standard operating procedure to clearly define the minimal requirements for the protection of subject confidentiality and privacy, and to detail the circumstances under which identifiable health information may and may not be used or disclosed in connection with research activities as regulated under HIPAA.

2. OBJECTIVES:

2.1. Define privacy and confidentiality;

2.2. Provide guidance on the appropriate methods for ensuring subject confidentiality and privacy in all research studies; and

2.3. For studies involving PHI and subject to HIPAA regulations:

2.3.1 **Define the requirements** related to the use and disclosure of PHI for research purposes;

2.3.2 P**rovide guidance** on how identifiable health information may be used to identify and recruit potential subjects;

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2.3.3 P**rovide guidance** on the types of safeguards that researchers should use to maintain the confidentiality, integrity and availability of electronic PHI; and

3. SCOPE

Sections 5.1-5.3 of this Standard Operating Procedure apply to all human subjects research including exempt, expedited, and full review protocols reviewed and approved by the IUPUI/Clarian Institutional Review Board (IRB).

Sections 5.4-5.23 in this Standard Operating Procedure (SOP) applies to all human subjects research that involves Protected Health Information (PHI), which is, or may be created, used or disclosed by, through or during research activities as defined and governed by HIPAA. This SOP applies to all personnel who conduct research, assist in the performance of research, or otherwise use or disclose identifiable health information in connection with research activities at or under the auspices of IUPUI/Clarian. Individuals who are in the School of Medicine, School of Dentistry, School of Optometry, or on staff at Clarian, Wishard, or the Veterans Affairs Medical Center will need to comply with HIPAA. Others may be exempt from HIPAA requirements. To determine if an individual study needs to comply with HIPAA, complete the "Checklist to Determine if you are a Covered Entity or are Involving a Covered Entity as Part of Your Research ".

4. DEFINITIONS

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5. POLICY AND RELATED PROCEDURES

5.1. It is the responsibility of Investigators and all research team members to ensure subject confidentiality and privacy in all forms of human subjects research.

5.2. An informed consent requires a statement describing the extent to which confidentiality of records identifying the subject will be maintained. The consent should delineate the possibility that the Institutional Review Board (IRB)or its designees, outside Federal agencies and representatives of other national organizations and Sponsors may inspect the records, as well as members of the research team.

5.3. The confidentiality and security of all records (e.g. medical, student, criminal history) should be maintained and the records should not be utilized for research purposes without the approval of the IRB or an authorization from the subject (if applicable). Research data collected for one study may not be utilized for a subsequent study without the approval of the IRB.

5.4. As determined by HIPAA, the use of protected health information (PHI) is only allowable for treatment, payment, and health care operations. Any other use (such as for research) is allowable only under certain circumstances:

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5.4.1 When the health information is de-identified (and therefore not PHI);

5.4.2 When the PHI is in a limited data set (and includes an associated Data Use Agreement);

5.4.3 With authorization from the subject (see Section 5.7);

5.4.4 With approval of a Waiver of Authorization from the IRB, which acts as the institution's Privacy Board;

5.4.5 When the PHI is only decedent information; or

5.4.6 For reviews preparatory to research.

Table 1: Summary of Mechanisms to Use PHI for Research Purposes

Six Mechanisms	Minimum Necessary Standard	Accounting for Disclosures (Section 5.16)	HIPAA Documentation Requirements	IRB Requirements
Use of De-Identified Data (Section 5.5)	Does Not Apply	No	Researcher documents that all 19 identifiers are removed under Safe Harbor Method (see section 5.5.2), or demonstrate how the data is statistically de-identified using the Statistical Method and that he/she has legitimate access to the PHI or is obtaining the de-identified data from someone who does have legitimate access to the PHI in order to create the de-identified data set..	IRB approval required for the process of de-identification. Typically this will require the submission of the Research Not Subjects to the FDA and Common Rule Definitions of Human Subjects Research Application form.
Research Using Limited Data Set (Section 5.6)	Applies	No	Researcher documents on application. Data Use Agreement between researcher and data source required.	IRB approval required. Typically this will require the submission of the Research Not Subjects to the FDA and Common Rule Definitions of Human Subjects Research Application form..
Authorization (Section 5.7)	Does Not Apply	No (Note: Accounting for disclosure is required only for psychotherapy notes – see HIPAA glossary for definition of psychotherapy notes.)	Patient-Subject Authorization	IRB approval required. Use of template authorization required.
Waiver of	Applies	Yes, but simplified if 50	Requirements as listed in	IRB approval required;

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Authorization (Section 5.8)		or more records will be utilized	5.8	may use this mode for recruitment purposes in addition to authorization and informed consent for the actual study procedures.
Research Involving Decedent Information (Section 5.9)	Applies	Yes, but simplified if 50 or more records will be utilized	Researcher documents in description of study.	IRB approval required. Typically this will require the submission of the Research Not Subjects to the FDA and Common Rule Definitions of Human Subjects Research Application form.
Review Preparatory to Research (Section 5.10)	Applies	Yes, but simplified if 50 or more records will be utilized	Researcher documents to covered entity supplying information.	No IRB approval necessary.

5.5. Use or Disclosure of "De-Identified" Health Information

De-identified health information is not considered PHI and may be used or disclosed for research purposes without an authorization from the research subject, or a waiver of authorization from the IRB. However, researchers must provide documentation to the IRB that the health information has been de-identified by one of the following two methods/processes:

5.5.1 Statistical Method. The IRB may determine that health information is de-identified for purposes of this policy, if an independent, qualified statistician that is not the researcher or involved in the conduct or analysis of the study in any manner:

5.5.1.1 Determines that the risk of re-identification of the data, alone or in combination with other data, is very small; and

5.5.1.2 Documents in writing the methods and results by which the health information is de-identified, and the expert makes his/her determination of risk.

5.5.2 Safe Harbor Method (Removal of All Identifiers).
Identifiers concerning the individual and the individual's employer, relatives and household members that must be removed include:

5.5.2.1 Names

5.5.2.2 Geographic subdivisions smaller than a state

5.5.2.3 Zip codes

5.5.2.4 Dates directly related to an individual

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5.5.2.5 Telephone numbers

5.5.2.6 Fax numbers

5.5.2.7 Electronic mail addresses

5.5.2.8 Social security numbers

5.5.2.9 Medical record numbers

5.5.2.10 Health plan beneficiary identifiers

5.5.2.11 Account numbers

5.5.2.12 Certificate/license numbers

5.5.2.13 Vehicle identifiers and serial numbers, including license plate numbers

5.5.2.14 Device identifiers and serial numbers

5.5.2.15 Web universal resource locators (URL)

5.5.2.16 Internet protocol (IP) address numbers

5.5.2.17 Biometric identifiers, including finger and voice prints

5.5.2.18 Full face photographic images; and

5.5.2.19 Any other number, characteristic or code that could be used to identify the individual.

The following demographic information may be used and still be considered "de-identified":

5.5.2.20 Age with dates limited to the year (age 90 and over must be aggregated to 90+ to prevent the identification of very old individuals)

5.5.2.21 Aggregated zip codes in the form of the initial three digit zip codes to include at least 20,000 people

5.5.2.22 Race

5.5.2.23 Ethnicity

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5.5.2.24 Marital status

5.5.2.25 Codes

5.5.3 If a researcher will be ***creating*** his/her own de-identified data set, he/she must provide justification that he/she has legitimate access to the PHI used to create the de-identified data set. If a researcher will be ***obtaining*** de-identified data from another individual, he/she must provide documentation that that individual has legitimate access to the PHI in order to create the de-identified data set. In the review of research involving the use or disclosure of de-identified data sets, the IRB or designee will consider whether the researcher (or appropriate other individual) has legitimate access to the PHI in order to de-identify the PHI.

5.5.4 Re-identification Code. The de-identified information may be assigned a code that can be affixed to the research record that will permit the information to be re-identified if necessary, provided that, the key to such a code is not accessible to the researcher requesting to use or disclose the de-identified health information. Codes may not be a derivative of the individual's social security number or other identifiable numerical codes, e.g. birth date, medical record number, fax number, etc.). If such a code is utilized, the data will not be considered "de-identified" and research must be submitted to the IRB as an expedited review.

5.6. Limited Data Set

A researcher may use or disclose PHI as a limited data set for a research purpose without an authorization or waiver of authorization.

5.6.1 A limited data set is identifiable health information that excludes direct identifiers. This means that the same identifiers described in 5.5.2 above must be removed, with the exception of the following direct identifiers:

5.6.1.1 Town, city, state and zip code;

5.6.1.2 All elements of dates directly related to an individual, including birth date, admission date, discharge date, and date of death.

5.6.2 A covered entity may disclose a limited data set to someone who is not a member of the same covered entity. In this situation, the covered entity disclosing the Limited Data Set must enter into a Data Use Agreement with the recipient of this information.

5.6.3 Uses or disclosures of PHI as limited data sets for research purposes are subject to the minimum necessary rules.

5.6.4 Uses and disclosures of PHI as limited data sets are **NOT** subject to accounting

of disclosures (see 5.16).

5.7. **Authorization from the Research Subject**

An authorization must be utilized with any informed consent for a research study using PHI that is signed (or re-signed) after April 14, 2003. Exceptions to this will be rare and will require IRB approval. The IRB will date-stamp approved authorizations and these forms should be used.

5.7.1 An authorization to use and disclose identifiable health information for research purposes must be written in plain language, and must contain all of the following core elements and approved by the IRB for each research approved protocol.

5.7.1.1 A specific and meaningful description of the information to be used or disclosed that is written in a language understandable to the subject. Any translation of the authorization must be IRB approved.

5.7.1.2 The name or identification of the persons or class of persons authorized to make disclosures of health information (i.e. who is releasing information).

5.7.1.3 The name or identification of the persons or class of persons authorized to receive the identifiable health information and to use the information for research-related purposes (i.e. the researchers and other individuals that are part of the research team, this should be written as broadly as possible to cover all possible circumstances).

5.7.1.4 A description of the purpose of each use or disclosure of identifiable health information.

5.7.1.5 An expiration date or event, or a statement like, "end of research study" or "none" when appropriate (e.g. for a research database).

5.7.1.6 The individual's signature (or that of his/her authorized representative, including a description of that representative's authority to act on behalf of the individual, if applicable) and date.

5.7.1.7 A statement that the individual may revoke the authorization if done in writing to a member of the research team, except to the extent that the principal investigator had already acted in good faith on the signed authorization. (see 5.7.4).

5.7.1.8 A statement that an individual's clinical treatment may not be conditioned upon whether or not the individual signs the research authorization. However, participation in research may be conditioned on a signed authorization.

5.7.1.9 A statement that information disclosed under the authorization could potentially be re-disclosed by the recipient and would no longer be protected under federal privacy regulations.

To ensure compliance with these elements, a template authorization has been provided and should be utilized and must be approved by the IRB prior to use (http://www.iupui.edu/%7Eresgrad/hipaa/sample_authorization.rtf). Any modifications to this template are discouraged (even if suggested by a Sponsor), will require additional review, may delay processing, and have no guarantee of being approved.

The principal investigator is responsible for assuring that the authorization form provided to subjects is revised whenever there is a change in any of the core elements of the authorization including when the persons or classes of persons who will receive disclosures of individually identifiable health information change. Any such change will require prospective IRB approval.

5.7.2 The individual must be provided with a copy of the signed authorization.

5.7.3 When authorization is required, the principal investigator or designee will file the original signed authorization form with the subject's research records. A copy of the signed authorization form should also be kept in the subject's medical records when appropriate. HIPAA regulations require the authorization to be kept for a minimum of six (6) years from the date it was obtained. However, Indiana state law requires the retention of medical records for seven (7) years, so it is recommended that signed authorizations be maintained for seven (7) years.

5.7.4 As a general rule, an individual may revoke his/her authorization, in writing, to a person on the research team, at any time. The revocation will be applicable to the protocol or protocols specified by the individual. However, the researcher may continue to use and disclose, for research integrity and reporting purposes, any identifiable health information that is collected about the individual at the time there was an active authorization up until it was revoked. Continued use of data after revocation will be allowed only on a case-by-case basis. The principal investigator shall maintain copies of all revocations of authorizations for a specific protocol, and report them to the IRB at the time of continuing review.

5.7.5 The IRB may require children to give written authorization prior to enrollment into a study under certain circumstances, e.g. a written authorization may be obtained directly from a child when a child's assent to participate is also being obtained.

5.8. **Waiver of Authorization from the IUPUI/Clarian IRB (Privacy Board)**

5.8.1 The IUPUI/Clarian IRB may approve a waiver of an authorization, provided the following criteria are satisfied and documented:

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5.8.1.1 The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, based on the presence of the following three elements:

5.8.1.1.1 An adequate plan presented to the IRB to protect the identifiers from improper use and disclosure;

5.8.1.1.2 An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and

5.8.1.1.3 Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted by the Privacy Rule.

5.8.1.2 The research could not practicably be conducted without the waiver; and

5.8.1.3 The research could not practicably be conducted without access to and use of the PHI.

5.8.2 A written request for waiver of authorization must be submitted to the IRB as part of the Summary Safeguard Statement for review and approval, and include a brief description of the PHI covered by the waiver.

5.8.3 Approved waivers of authorization must document that the waiver was reviewed and approved under full or expedited IRB procedures, and include the IRB or Privacy Board Chair's signature, or that of a designee.

5.8.4 The IRB (Privacy Board) shall maintain the required documentation about the waiver.

5.8.5 Uses or disclosures of PHI made pursuant to a waiver of authorization are subject to the minimum necessary rules.

5.8.6 Disclosures of PHI made pursuant to a waiver of authorization are subject to accounting of disclosures (see Section 5.16).

5.8.7 Investigators will likely be asked to provide a copy of the IRB-approved waiver when requesting records or other PHI from a covered entity.

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5.9. **Research Involving Decedent PHI**

5.9.1 Researchers may use and disclose decedent only health information for research purposes without an authorization from the legally authorized representative of the individual or waiver of authorization approved by the IRB (Privacy Board), provided that the researcher documents that all the following criteria are satisfied:

5.9.1.1 The use will be solely for research on the identifiable health information of decedents;

5.9.1.2 The PHI sought is necessary for the purposes of the research; and

5.9.1.3 Upon request, the covered entity disclosing the data may require the researcher to provide documentation of the death of the individual about whom information is being sought.

5.9.2 Researchers will be required to provide the covered entity a written statement regarding the intended use of the decedent information and must keep the information confidential and secure.

5.9.3 In most cases these studies will be subject to review under the Application for Research Not Subject to FDA or Common Rule Definitions of Human Subjects Research.

5.9.4 Uses or disclosures of a decedent's identifiable health information for research purposes are subject to the minimum necessary rules.

5.10. **Reviews Preparatory to Research (Pre-Research/Feasibility Studies)**

5.10.1 Researchers may use or disclose identifiable health information without an authorization from a subject or a waiver of authorization approved by the IRB (Privacy Board) for reviews preparatory to research. For a covered entity to release this information, the researcher must document to the covered entity (the holder of the PHI) that all the following criteria are satisfied:

5.10.1.1 The use or disclosure of identifiable health information is solely to prepare a research protocol or for similar purposes that are preparatory to research; and

5.10.1.2 The researcher shall not record or remove the information from the provider's facility or office. Researchers may access PHI electronically in order to review the information, but may not record, store, or otherwise retain the information after the review.

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5.10.1.3 The information sought is necessary for the purposes of the research. Examples include feasibility analysis to determine number of potential subjects with a certain disease for submission in a grant.

5.10.1.4 This does not include identifying specific individuals for recruitment purposes, but rather identifying the number of individuals with a specific disease to determine or demonstrate a researcher's ability to successfully recruit.

5.10.2 Uses or disclosures of PHI for reviews that are preparatory to research are subject to the minimum necessary rules.

5.10.3 Uses or disclosures of PHI for reviews that are preparatory to research are subject to accounting of disclosures unless the information is in a de-identified or limited data set format as defined above in Section 5.5.2. and 5.6.1

5.10.4 Reviews preparatory to research that fulfill these criteria do not require IRB review and approval.

5.11. Notice of Privacy Practices

If being recruited or enrolled into a research study is the patient's first contact with the hospital/clinic/office of the health care provider at IUPUI/Clarian, a Notice of Privacy Practices must be given to the subject upon contact (e.g. this may also apply for subjects who are recruited through advertisement rather than recruited through clinics). The notice given should be the relevant notice of the facility or covered entity where the research is taking place (i.e., if the research is taking place in Wishard Hospital, Wishard's Notice of Privacy Practice should be given to the subject). The patient/subject must sign and acknowledge that they received the notice for any studies involving direct treatment.

5.12. Recruitment

Identifying, contacting and/or recruiting potential subjects for research purposes must also abide by HIPAA. Studies involving informed consent/authorization will need to provide specific details to the IRB in the Summary Safeguard Statement and a Recruitment Checklist as to how potential research subjects will be identified prior to obtaining informed consent/authorization. The following provides scenarios for recruitment allowable under HIPAA and are from the Recruitment Checklist that must be submitted with the Summary Safeguard Statement.

5.12.1 **Care Provider**: Recruitment will be done by the researcher who is a physician, dentist, nurse or other licensed independent practitioner who has provided care for the patient.

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Neither an Authorization from the Subject nor approval from the IRB to waive authorization is required in order for that physician or practitioner to contact the subject.

5.12.2 **Authorized Delegate-Same Organization**: Recruitment will be done by a researcher who did not provide care for the patient, but who will act as an authorized delegate of the treatment provider and who is part of the same Department or practice plan. (In the case of the Departments of Pediatrics, Surgery and Medicine, this will be limited to providers within the same Division.) This may include the researcher's Coordinator as long as the Research Coordinator is part of the same Division, Department or Practice Plan as the PI or co-investigator. The researcher must obtain approval from the treatment provider to act as a representative contacting the potential subject. For example: "I am a colleague of Dr. "X,"" or "I work for Dr. X who gave me permission to contact you regarding…." However, the IRB will judge the appropriateness of this approach on a case-by-case basis.

Neither an Authorization from the Subject nor approval from the IRB to Waive Authorization is required.

5.12.3 **Authorized Delegate-Separate Organization**: If the researcher is not the treatment provider and is not part of the same Division, Department or practice plan of the treatment provider, then contact must be made as follows: (NOTE: This includes Research Coordinators who are not part of the treatment provider's Division, Department or practice plan.)

5.12.3.1 The treatment provider will direct the prospective subject to contact the researcher.

Neither an Authorization from the Subject nor approval from the IRB to Waive Authorization is required.

5.12.3.2 The treatment provider will obtain an authorization from the potential subject to release the subject's demographic and/or health information to the researcher.

An Authorization from the Subject is required.

5.12.3.3 Neither of the previous options applies to your study. A waiver of authorization will be required, but will only be allowed in limited circumstances where the appropriate justification is provided to the IRB.

Approval from the IRB to Waive Authorization is required.

5.12.4 **Self Referral**: In those situations where a subject responds to an ad for a specific study, or contacts IUPUI/Clarian directly regarding participation in research

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studies in general:

5.12.4.1 If you need to do a basic initial screening, you may gather minimal information necessary to determine whether the individual is eligible for further screening and/or enrollment. For instance, obtaining the individual's contact information and explaining two or three major inclusion/exclusion criteria would be acceptable. Covering the entire Informed Consent or an exhaustive list of inclusion/exclusion criteria does not constitute a "basic" initial screening.

Neither an Authorization from the Subject nor approval from the IRB to Waive Authorization is required.

5.12.4.2 If you need to gather additional detail about an individual's health to determine the individual's eligibility, an authorization or waiver of authorization is required. Please note that a telephone script must be submitted unless an authorization will be obtained.

An Authorization from the Subject or approval from the IRB to Waive Authorization is required.

5.12.4.3 If you wish to add an individual's information to an IRB-approved recruitment database for future research, an authorization or waiver of authorization is required. (See database questions below.)

An Authorization from the Subject or approval from the IRB to Waive Authorization is required.

5.12.4.4 If you wish to refer the individual to another research area/department, you must give the potential subject the researcher's contact information*:
** This does not prohibit or interfere with the ability to refer patients for treatment purposes to other providers.*

Neither an Authorization from the Subject nor approval from the IRB to Waive Authorization is required.

5.13. **Use and Disclosure of Psychotherapy Notes Used in Research**

Federal regulations require special restrictions concerning psychotherapy notes. An authorization is required for use and disclosure of psychotherapy notes for research in all instances including for recruitment by the direct treatment provider.

5.14. **HIV/Sexually Transmitted Disease Notes Used in Research**

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In the State of Indiana, PHI about sexually transmitted diseases or HIV status requires specific authorization prior to use and disclosure. This law is taken into account in the IUPUI/Clarian authorization template.

5.15. **Individual's Access to Research Information**

5.15.1 Individuals who participate in research have a right to access their own identifiable health information that is maintained in a designated record set. However, individuals participating in research protocols that include treatment may be denied access to their research records obtained in connection with that research protocol, provided that:

5.15.1.1 The identifiable health information was obtained in the course of the research;

5.15.1.2 The individual agreed to the denial of access in the research authorization;

5.15.1.3 The research is ongoing; and

5.15.1.4 The individual's rights to access such health information are re-instated once the research study has ended and the research authorization has expired.

5.16. **Accounting of Disclosures**

5.16.1 A research subject may request that the principal investigator provide a history or list of the disclosures made regarding the subject's identifiable health information for research purposes. **NOTE**: **If you have an authorization from a research subject, you do not need to account for disclosures, providing the individuals to whom phi is disclosed are listed on the authorization. Thus, all parties to whom phi will be shared should be listed on the authorization**.

5.16.2 If a subject did not provide authorization for the disclosure of his/her PHI, the principal investigator must keep accounting records of all disclosures of PHI in the following circumstances:

5.16.2.1 Disclosures made in research conducted with a waiver of authorization approved by the IRB (Privacy Board) for the study or for recruitment purposes.

5.16.2.2 Disclosure of PHI to a person or entity not on the authorization.

5.16.2.3 Disclosure of PHI to or from a federal or state mandated registry.

5.16.2.4 Disclosure of PHI that is used for reviews preparatory to research

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unless the information is de-identified or in a limited data set.

5.16.2.5 Disclosure of a decedent's PHI used for research.

5.16.3 Upon request, the principal investigator must provide the patient/subject with a written accounting of disclosures of PHI for the preceding six years, starting April 14, 2003. The following information must be given to the subject:

5.16.3.1 For studies where <50 subjects are involved (including screening and recruitment).

- Date of disclosure;
- Name and address, if known, of the entity or person who received the health information;
- Brief description of the health information disclosed; and
- Brief statement that reasonably informs the individual of the purpose for disclosure.

If multiple disclosures are made to the same entity or person for the same reason, the principal investigator may summarize the disclosure by describing the first disclosure in detail and by noting the frequency or number of disclosures made during the accounting period and the date of the last disclosure in the accounting period (i.e. information to sponsor three times from X to Y date).

5.16.3.2 For studies where PHI from ≥50 individuals were utilized (including screening and recruitment), a simplified accounting procedure can be used. The individual must be provided a list of research protocols in which the individual's information may have been used. The list must provide the following:

- The name of the protocol or other research activity;
- A description of the purpose of the study and the type of information disclosed; and
- The timeframe during which such disclosures occurred.
- Upon request, the principal investigator, or his/her designee, will assist the individual in contacting those researchers to whom it is likely that the individual's health information was actually disclosed.

5.17. **Use and Disclosure of a Health Care Provider's Patient Information for Research Purposes**

5.17.1 A physician or other licensed independent practitioner may contact their own patients to ask if they are interested in a research study or may review their patients' PHI to determine eligibility for a research study without an authorization or waiver of authorization.

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5.17.2 In some cases, a physician or other licensed independent practitioner may delegate the items in 5.17.1 to a research assistant who is directly under their supervision without an authorization or waiver of authorization. (Note: Delegation of authority and/or responsibilities should be outlined in the Summary Safeguard Statement and Recruitment Checklist; in some circumstances the IRB may not allow this delegation.)

5.17.3 A physician or other licensed independent practitioner who reviews their own patients' records to determine eligibility and/or to contact to ask about interest in a research study does not need to keep track of disclosures for this recruitment purpose.

5.17.4 A physician or other licensed independent practitioner accessing PHI for research purposes other than recruitment must obtain an authorization from the patient/subject or waiver of authorization from the IRB.

5.17.5 If a waiver of authorization is granted (i.e. for studies with waiver of informed consent such as chart reviews or outcomes studies) then any disclosure of this data in an identifiable format (i.e. not de-identified and not a limited data set) to an individual outside the covered entity needs to be tracked. Examples include sending identifiable data to statistician, cancer registries, multi-center data repository sites, or monitors/auditors.

5.17.6 If physicians or other licensed independent practitioners plan to share any of their patients' data initially collected for patient care purposes with individuals outside of their covered entity and/or outside of their research team for recruitment or research purposes, it is recommended that a separate study be submitted for approval by the IRB for this purpose, including authorization from the subject for inclusion in this database. If such an authorization is obtained from the patients (research subjects) under this IRB approved database protocol, then there is no need to track disclosures for recruitment or studies done under waiver of authorization.

5.17.7 If the physician or other licensed independent practitioner performs quality control (i.e. CQI) programs, no IRB approval or authorization is required as this is considered health care operations. However, if there is any forethought or afterthought of presentation/publication outside of the covered entity then IRB approval is required.

5.17.8 If the physician or other licensed independent practitioner reports data to public health authorities or government agencies that is not for billing purposes, authorization is not required; however, this disclosure must be tracked (i.e. tumor registries, etc.).

5.18. **Use of human biological samples labeled with or linked to PHI (i.e. name, medical record number etc.) for research purposes**

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5.18.1 Biological samples (tissue blocks, cells, DNA, serum etc.) collected for clinical purposes and sent to a research (or clinical) laboratory for analyses to be used solely for clinical/patient care are considered treatment and do not require IRB approval, authorization or waiver of authorization.

5.18.2 Biological samples collected solely for research purposes under an IRB approved study prior to April 14, 2003 do not require additional IRB approvals, or changes in the labels on the specimens.

5.18.3 Biological samples collected solely for research purposes under an IRB approved study after April 14, 2003 require either an authorization from the research subject or a waiver of authorization from the IRB (see Sections 5.7 and 5.8)

5.18.4 Biological samples originally collected for patient care that are to be used for research after April 14, 2003 require IRB approval AND must be either:

5.18.4.1 De-identified as per section 5.5 by someone who has clinical authority to be in possession of the specimens (i.e. the physician caring for the patients or the pathologist analyzing the samples for patient care purposes). This entails removal of all identifiable information contained on the labels, containers or any other method that links the information to the sample, if such information is affixed; or

5.18.4.2 Labeled with and/or connected to PHI that is in a limited data set format (See Section 5.6.1). In this scenario, the clinician who obtains the specimens must complete a data use agreement with the researcher, in addition to the IRB approval, if the clinician and researcher are not within the same covered entity, practice plan, or Division.

5.18.5 If the samples are not de-identified or linked to a limited data set, the Researcher must obtain: 1) an Authorization from each individual to use the sample for a specific study; or 2) a Waiver of authorization from the IRB to use the samples for a specific study, and keep an accounting of disclosures (See section 5.16).

5.18.6 Core laboratories/Pathology departments or other Departments/Divisions within the School of Medicine, School of Dentistry, or another covered entity, that keep/store samples cannot release these samples to anyone else for research purposes without IRB approval and according to appropriate HIPAA guidelines. If at all possible, the samples should be released in a de-identified format (See Section 5.3), which would minimize or eliminate HIPAA documentation requirements. It is suggested that guidance be sought regarding the responsibilities of the sample holder when they are not de-identified.

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5.19. **Use of PHI for quality improvement projects or case presentations**

5.19.1 Use of a patient's PHI or biological sample for quality improvement projects is deemed health care operations and does not require IRB approval or authorization or waiver of authorization. A quality improvement project, by definition, is a project to look at outcomes or other assessments of patient care for **INTERNAL** use only. Thus, the PHI will not be shared outside of the covered entity, nor published or presented. Should an analysis of a quality improvement project generate information that may contribute to generalizable knowledge and the clinician caring for the patient wishes to publish or present the information, then IRB approval is needed and, a HIPAA approval is required from the IRB (i.e. waiver of authorization if the information is identifiable).

5.19.2 Use of a patient's PHI or biological sample for a case report for **education/teaching purposes** is deemed health care operations and does not require IRB approval or authorization or waiver of authorization. Care should be taken to ensure that no patient identifiers are used.

5.19.3 Use of a patient's PHI or biological sample for a single case report for publication does not require IRB approval or authorization/waiver of authorization, providing the patient was treated by the person reporting the case(s) and the information is de-identified. **HOWEVER, should there be two or more cases, any systematic study such as a query of any database for additional cases**, **or analyzing serum by additional assays, etc., then this becomes RESEARCH** and requires IRB approval, and must be conducted using one of the mechanisms as detailed in this SOP (Sections 5.5 through 5.9).

5.20. **Data Use Agreements or Business Associate Agreements.**

There are several instances when an investigator will need to enter into a legal agreement to protect a research subject's identifiable health information. Faculty should not generate or sign a Data Use or Business Associate Agreement without first consulting with an attorney. In the School of Medicine, contact the School of Medicine Privacy Officer at (317) 278-4891. For other Schools, contact your Privacy Officer for advice. In some circumstances, master agreements that cover research may already be in place.

5.20.1 In general, a Data Use Agreement is utilized when you are sharing Limited Data Sets with someone outside of your practice plan or covered entity, or at another Institution (i.e. multi-center trials) in a mutually beneficial arrangement. This is required to adhere to the minimum necessary rule, and ensure that the recipient of the information will not disclose the PHI beyond what is described in the Data Use Agreement.

5.20.2 If a subject authorizes you to release their PHI for this purpose, no Data Use Agreement is necessary. In certain circumstances where an agreement is needed, confidentiality agreements may suffice.

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5.20.3 A Business Associate (BA) Agreement is utilized when an individual, group, company, or contractor that is outside of the covered entity performs a service involving PHI on behalf of the covered entity. Examples of this include data storage services, outsourced personnel that may perform certain components of the protocol such as a survey company, transcription, private auditors, and statistical services. Whenever possible, these outside entities should always be listed on the authorization form as parties that may review or receive PHI and then a Business Associate Agreement would not be necessary. However, there may be rare situations when a Business Associate agreement is needed, such as when the service is not or can not be part of the authorization, or the services occur as part of a waiver of authorization.

5.21. Training

The principal investigator is responsible for assuring that all members of the research team are knowledgeable about the appropriate uses and disclosures of identifiable health information for the study, the authorization process, and safeguards that must be employed to secure the information. The latter includes, but is not limited to, the security regulations as it pertains to electronic data and databases. These persons should be listed on the Summary Safeguard Statement.

5.22. Electronic data and databases

Special provisions exist regarding the use, disclosure, retention, and transmission of PHI in electronic form. See the IUPUI/Clarian SOP for Data Management.

5.23. Safeguarding Protected Health Information

A principal investigator is responsible for ensuring that researchers involved with the study use appropriate safeguards to maintain the confidentiality, integrity and availability of PHI that is collected, used, shared and/or stored for research purposes.

Safeguards should be explained in the Summary Safeguard Statement and should consider the data source (i.e. the types of records that are used to gather the data) and the data collection or recording method.

A principal investigator should work with the research team to ensure that PHI is safely stored and disposed of when it is no longer needed and exchanged. This includes safeguarding the data source, the recording / collection method and data disposal.

5.23.1 Data Source

Following are general guidelines for safeguarding the data source when PHI is accessed or gathered for research purposes.

5.23.1.1 When treatment or test results, medical records and other clinical records are accessed to gather data for a study, proper safeguards

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should be used.

5.23.1.2 Any treatment or test results, medical records and other clinical records should be kept in a secure location.

5.23.1.3 Data collected from surveys or questionnaires should be gathered in a secure manner and should be safeguarded when recorded, stored and transmitted.

5.23.1.4 Video and audio data should be recorded in a secure manner, considering both the logistics of the subject and researcher, as well as how the data is stored. For instance, the video or audio recording should take place in a private location where possible to ensure that an individual's PHI is not inadvertently disclosed to anyone except members of the research team.

5.23.2 **Data Recording / Collection Method**

Following are general guidelines for safeguarding PHI once it is recorded or collected:

5.23.2.1 Data collected using a computer (e.g. a laptop, hard drive, local shared drive, web-based system, CDs, floppy disks, flash drive etc.) or a PDA should be safeguarded using various methods.

5.23.2.2 Paper (e.g. Notes, Case Report Form, etc.)

- Data recorded in a researcher's notes, on a case report form or in other documents must be kept in a secure location, such as a locked office, locked cabinet or other area with limited public access.
- Printed PHI should be shredded when it is disposed.

5.23.2.3 Video and Audio

- Once the video or audio recording is completed, ensure that the tapes, CDs or other media are stored in a secure location (such as a locked cabinet or office).
- Recordings should be destroyed when they are disposed.

5.23.3 **Data Recording / Collection Method**

In addition to safeguarding the data as it is collected and stored, consider who needs access to PHI and determine the level of access that is appropriate for their particular role, for the following:

5.23.3.1 Principal Investigator

5.23.3.2 Research Coordinator

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5.23.3.3 Co-Investigators

5.23.3.4 Governmental Agencies

5.23.3.5 Research Sponsor, Monitor, Other Research Organizations

5.23.3.6 Institutional Review Board or its designees

5.23.3.7 Other groups assisting with a study, such as BioStats or other colleagues not listed on the Summary Safeguard Statement.

5.23.4 **Secure Disposal**

PHI (or other confidential data) must be safeguarded until the data is securely disposed. Following are guidelines for appropriately disposing of PHI (or other confidential data).

5.23.4.1 Determine the length of time you are required to retain the data:

5.23.4.1.1 Minimum of three (3) years for non-health data;

5.23.4.1.2 Minimum of seven (7) years for health data per State and HIPAA laws;

5.23.4.1.3 Indefinitely or per sponsor requirements;

5.23.4.1.4 Other timeframes.

5.23.4.2 Consider how data should be discarded:

5.23.4.2.1 Shred paper;

5.23.4.2.2 Permanently delete data from computers, PDAs;

5.23.4.2.3 Delete files from or destroy diskettes and CDs.

5.23.5 **Sharing Health Data**

5.23.5.1 It is not only important to safeguard health data as it is collected, stored and destroyed, but also when sharing the information. For the purpose of this SOP, sharing may include releasing, transmitting or providing access to research and health data within the research team, outside the university, to research sponsors, etc. You must use reasonable safeguards when sharing any form of research data, health or non-health.

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5.23.5.2 When sharing health data, consider the type of data being shared, who has a legitimate need and right to know, as well as how the data will be shared.

5.23.5.3 Also, consider the following when data will be shared in any of the following formats:

5.23.5.3.1 Non-health data is not subject to HIPAA protections;

5.23.5.3.2 De-identified Data is not subject to HIPAA protections and does not have to be safeguarded; however, re-identification codes must be carefully safeguarded since these codes contain the link that re-identifies the data;

5.23.5.3.3 A Limited Data Set contains certain identifiers and is still protected by HIPAA. A Limited Data Set must be safeguarded as PHI;

5.23.5.3.4 Identifiable Data (i.e. includes patient identifiers, names, initials, Subject ID numbers, etc.) is protected by HIPAA and must be safeguarded appropriately;

5.23.5.3.5 Identifiable health data should not be shared with anyone who is not listed on the Summary Safeguard Statement or the Authorization. If a study requires sharing data with others (e.g. multi-center studies, cooperative studies, individual colleagues within or outside of IUPUI, etc.), principal investigators will be expected to explain how the information will be safeguarded. This may involve asking the recipient of the data to explain their safeguards and to provide a written assurance that they will safeguard the data.

5.23.5.3.6 Examples of safeguarding methods for sharing data include: secure websites, encrypted emails, and faxing in secure areas.

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Title:	Conflict of Interest Reporting to the IRB			
Current Version:	07/07		Previous Versions:	04/05, 02/05

1. INTRODUCTION

The regulations protecting human research subjects are based on the ethical principles described in the Belmont Report: respect for persons, beneficence, and justice. These principles should not be compromised by financial relationships. Openness and honesty are indicators of respect for persons, characteristics that promote ethical research and can only strengthen the research process.

Investigators at IUPUI/Clarian have a major responsibility to discover and transmit new knowledge through scholarly activities. Financial support for such activities comes from both public and private entities usually external to the University or Clarian. Increasingly, relationships between faculty or staff and external entities have become a significant feature of academic research and educational activities. As these relationships become more common and complex, possibilities for conflicts of interest, or at least the appearance of such conflicts, increase.

In order to ensure that protection of human research subjects takes precedence over such collaborations or benefits (financial and others), it is the obligation of all individuals conducting human subjects research to report financial relationships and, where appropriate, cooperate in the management of such conflicts of interest

2. OBJECTIVE(S)

This SOP is designed:

2.1. To help investigators understand how and what to report;

2.2. To describe how reported information gets disseminated to the IRB;

2.3. To describe the IRB review process for evaluating potential conflicts;

2.4. To describe possible methods that the IRB might use to address identified potential conflicts in human subjects protocols such that subjects are protected.

3. SCOPE

This SOP applies to all research activities of faculty, staff, student, or others who are involved in human subjects research that falls under the jurisdiction of the IUPUI/Clarian IRBs.

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4. RELEVANT DEFINITIONS

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5. POLICY AND RELATED PROCEDURES

5.1. Policy and Procedure for IUPUI

5.1.1 It is the responsibility of the Faculty/Staff at IUPUI to disclose all potential or real conflicts of interest based on the University Policy for Conflict of Interest in Research.

5.1.2 Individuals must report potential conflicts using IUPUI's disclosure forms. The disclosure forms describe what financial interests must be disclosed. All disclosure statements must be annually submitted to the Office of Compliance Services. After submission of the disclosure statement, the Compliance Officer will determine whether the decisions can be administered by the Office of Compliance Services or if the activities need to be referred to the Conflict of Interest Committee. The Office of Compliance Services will work with the individual to develop a management plan to minimize the potential conflict of interest issues. The disclosure statement and proposed management plan will be reviewed by the Conflict of Interest Committee. The Committee recommendations will be transmitted back to the investigator for implementation.

5.2. Policy and Procedure for Clarian

It is the responsibility of Clarian employees and employees in private practice offices who submit human subjects research protocols to the Methodist IRB for review and approval to disclose all potential or real conflicts of interest according to the Clarian conflict of interest policy. The Clarian legal office will review the disclosures. Notification to the IRB will be made as described below.

5.3. When to Disclose

Investigators must complete information disclosure forms annually and update this information if change occurs during the conduct of any study. Additional information should be reported if a change occurs that the investigator believes may either a) give rise to a conflict of interest or the appearance of such a conflict or b) eliminate a conflict previously disclosed.

5.4. IRB Review of Conflict of Interest

5.4.1 The IRB staff will review each protocol to ensure all investigators and co-investigators involved in the design, conduct or reporting of the research have submitted an annual disclosure form.

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5.4.2 If IRB staff determines that any investigator has declared a financial interest they will contact the Office of Compliance Services to obtain a written evaluation of the conflict and the recommended management plan. The IRB will not approve any protocols until a written determination has been received. The written determination will be submitted to the IRB for review.

5.4.3 At the time of new study submission and at the time of continuing review the IRB will evaluate whether the financial interest with the management plan suggested by the conflict of interest committee affects the conduct of the research or research subjects. In that review, the IRB will consider the effect of the financial interest on the criteria for approval and on the credibility of the human research protection program.

5.4.4 The IRB can approve, require modifications in, or disapprove the conflict of interest committee's determination and management plan (if any). In the case of disapproval, the IRB will refer the protocol back to the conflict of interest committee with a written summary of its concerns. Modifications the IRB may consider include:

5.4.4.1 Require disclosure of the conflict in the informed consent.

5.4.4.2 Require disclosure of the conflict and its management in the informed consent. NOTE: A conflicting interest that may interfere with the protection of subjects should not be managed solely by disclosure.

5.4.4.3 Require partial or complete financial divestiture in order for the investigator to be involved in the design, conduct, or reporting of the research.

5.4.4.4 Limit the enrollment of participants to a maximum percentage (not more than 20%) of the national projected enrollment for multi-centered clinical trails.

5.4.4.5 Require an independent investigator to obtain consent.

5.4.4.6 Require an independent investigator to conduct the study.

5.4.4.7 Require independent safety monitoring.

5.4.4.8 Require frequent continuing review.

5.5. Food and Drug Administration (FDA) Required Reporting

The FDA requires that sponsors submit financial disclosure forms for each of the Investigators involved in any study mentioned in their New Drug Application (NDA)

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report. Since these forms will be sent to the Investigators from the Sponsor, this will not be discussed further in this SOP (also see PI Responsibilities SOP).

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Title:	Data Management			
Current Version:	07/07		Previous Versions:	05/05, 02/05, 12/04

1. INTRODUCTION

Standardized methods of data collection and recording are essential to enable others to reconstruct the events of a study, to confirm protocol compliance and to verify that the data are complete, accurate, and appropriate. Document retention, storage and disposal requirements allow data to be reviewed by sponsors and auditors to enable studies to be recreated, to demonstrate that the IRB approved protocol was followed, and to ensure that confidentiality of research documents are secured until such a time that it is appropriate to destroy such documents. Guidelines for document retention, storage and disposition will assist the principal investigator and the research team in determining the appropriate steps for keeping and destroying documents after the research has been completed. Ultimately, it is the principal investigator's responsibility to ensure that all study related activities are completely and accurately documented and that documents are retained in accordance with University policies, federal and state regulations and sponsor requirements.

In order to protect the integrity of the data, as well as the confidentiality of the information being collected, stored, and transmitted, it is essential to have standards for data management. Researchers, including their colleagues and support staff, are ethically bound to minimize all risks to human subjects, including the loss of confidentiality. In addition, they are legally bound to manage this information/data according to existing regulations and policies.

2. OBJECTIVES:

2.1. Define policies related to data ownership and transfer of responsibility;

2.2. Define the different types of documentation;

2.3. Define minimum requirements related to data source documentation;

2.4. Define minimum requirements for the retention of research-related documents;

2.5. Define minimum safeguard requirements when sharing research data;

2.6. Suggest methods of storing research study documents;

2.7. Suggest methods of disposing of research documents at the end of the prescribed retention period; and

2.8. Describe the minimum requirements for administrative, physical, and technical compliance in the management of electronic data and databases.

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3. SCOPE

This SOP applies to all research activities of faculty, staff, student, or others who are involved in human subjects research that falls under the jurisdiction of the IUPUI/Clarian IRBs; specifically, data, databases, and data management systems that are being used in the conduct of research involving human subjects and/or other data being used to support a study that is governed by the regulations of a federal regulatory body, e.g. NIH or FDA.

4. RELEVENT DEFINITIONS

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5. POLICY AND RELATED PROCEDURES

5.1. Ownership of Data

5.1.1 Research data generated with external funding (such as NIH, foundations, grants), that does not involve a contract or agreement that explicitly details ownership, is the property of Indiana University. Sponsored research agreements are entered into with Indiana University, and not with the individual investigator. Thus, it is the University that is legally responsible for meeting all obligations of such agreements with respect to the creation, distribution and preservation of the data. The VA claims ownership of its patients' data generated with funding by the VA or contract with the Indiana Institute for Medical Research, the VA claims ownership

5.1.2 In the case of externally sponsored or funded research involving a contract (e.g. a pharmaceutical or device company), the contract will define data ownership. In such cases, the data ownership typically lies with the sponsoring company; however, the details of the contract should define all policies, procedures, and issues related to ownership and will be the determining document for resolution of disputes.

5.1.3 Non-externally funded research data is the property of the principal investigator(s) except in the following circumstances: (i) Indiana University and the relevant researchers otherwise have agreed in writing; (ii) the data arises out of an Institutional Work, or (iii) the data arises out of University owned web-based instructional materials. In such cases, the research data is the property of Indiana University.

5.1.4 If research is done by individuals who are employees of, or conduct work at, the Veterans Affairs Department or other Government Agency, and Indiana University, ownership is generally shared among the University and the government agency. Investigators should seek guidance from administrative officials at both Institutions.

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5.1.5 Regardless of ownership, the PI has custodial responsibility for the management, custody, retention and destruction of the research data as detailed in this SOP.

5.1.6 If an investigator leaves the Institution they may only take copies of the original data. The original data must remain with the owner as outlined in 5.1.1 through 5.1.4 above unless a specific request is granted by the Department or School.

5.2. **Data Management Responsibility**

5.2.1 The PI has primary responsibility for the collection, management, custody and retention of research data.

5.2.2 The PI should adopt an orderly system of data recording, organization, and safeguards and should ensure all members of the research team (including appropriate administrative personnel) understand and follow the system.

5.2.3 The PI should ensure that appropriate safeguards and security are employed by all members of the research team. See Confidentiality and Privacy and Security of Research Data SOPs for additional guidance.

5.3. **Data Collection**

5.3.1 Study records and data collection methodology must enable the reconstruction of the entire study process and verification of the accuracy of all data with sufficient clarity, completeness, and organization that an external reviewer could readily determine that the IRB approved protocol was followed, the data are true and accurate, and that all regulatory responsibilities have been met.

5.3.2 The ICH Guidelines (Section 8) contain a complete listing of "essential" documents. These documents are generally collected in three phases: before the data collection phase commences, during the conduct of the study, and after termination of the study.

5.3.3 During each of these phases, different types of information will be collected:

5.3.3.1 Regulatory: Regulatory documents record the official conduct of the study as prescribed by the sponsor, IRB-approved protocol, and regulatory agencies. This information is generally not subject specific, but rather relates to the project and/or all study subjects. Examples of regulatory information include, but are not limited to: regulatory binder, IRB forms, FDA Form 1572, IND/IDE submissions, lab normals and certifications, MedWatch forms, enrollment and drug accountability logs, etc. For a more complete list of items considered appropriate for the regulatory binder/files, see Appendix AA.

5.3.3.2 Source: Source documents are the original documents (or certified copies of originals) onto which information, findings or observations are first recorded. In most cases this is not the same as the data collection or case report forms, but rather the first place that the information is recorded, e.g. handwritten hospital or clinic notes, subject's diary, photographic negative, lab notebooks, or x-rays. When original observations or data are entered directly into computerized systems, including laptops and Personal Digital Assistant's (PDA), the electronic record is the source document. With PDA's, not only the PDA but also the associated synchronized files become the source documents.

5.3.3.3 Case Report Form (CRF) or Data Collection Forms: Case report/data collection forms typically represent the summary or collation of data from the original source documents. They may be in electronic, optical, or paper formats, e.g. forms or spreadsheets. While not the original source documents, they may be used as such only when they are the first place in which the original observation is recorded and must be signed and dated by the original observer/recorder. While CRF's are typically designed as a method to report subject-specific information to the study sponsor, they are also necessary in investigator-initiated studies. CRF's allow one to quickly review subject specific information as well as analyze data trends, e.g. number and types of specific serious adverse events.

5.4. Transcription of Data

5.4.1 The transcription of source documents to case report or data collection forms, including remote data entry, requires care and accuracy. Therefore, the following procedures should be followed:

5.4.1.1 For paper documents, record all observations/data in black or blue ballpoint pen.

5.4.1.2 Correct errors by striking through the error, dating and initialing it, and making the correction. Ensure the original entry is not obliterated. If necessary, note an explanation in the right margin. Note that in FDA regulated studies involving electronic data, a similar yet electronic audit trail must be created to track data corrections. (See 21 CFR 11: Electronic Records; Electronic Signatures)

5.4.1.3 Complete all fields on the forms according to sponsor or other pre-determined specifications.

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5.4.1.4 If the sponsor/protocol requires remote data entry, ensure that staff is appropriately trained and that data are entered by computer according to sponsor/protocol specifications promptly from the source documentation.

5.5. Retention of Documents

The retention and maintenance of study-related documents are governed by several regulatory bodies. Their specific requirements are discussed below. Ultimately, it is the principal investigator's responsibility to ensure that documents are retained in accordance with University policies, federal regulations, and sponsor requirements.

5.5.1 IUPUI/Clarian Policy

5.5.1.1 These Minimum Standards apply to all research with human subjects, unless there are more stringent retention requirements from a sponsor, funding agency, employer, or other regulatory body.

5.5.1.2 All records produced or collected in connection with a research project, including primary (e.g., laboratory, medical, interview), financial, statistical, supporting, administrative and regulatory documentation, shall be retained for a period of **three** (**3) years** from the date of the submission of the final expenditure report to the funding agency or for 3 years from the date of study closure with the IRB, whichever is longer. For studies involving individually identifiable health information (e.g. medical records), HIPAA requires that supporting documentation be kept for at least **six (6) years** whereas Indiana's state law requires that supporting documentation be kept for at least **seven (7) years**.

Important Note: In the state of Indiana, standard medical records may be destroyed after **seven (7) years**. Therefore, if retention of source documents is required for longer than 7 years (i.e. for most Sponsored trials), the PI should make copies of relevant source data. The investigator may need to make arrangements to obtain original documents before they are destroyed to prevent destruction of source documents or make certified copies of relevant medical records to be kept with study documents.

5.5.1.3 Data must be kept for as long as may be necessary to protect any intellectual property claims resulting from the work;

5.5.1.4 If any charges regarding the research arise, such as allegations of misconduct in research or financial conflict of interest, data must be retained until such charges are fully resolved;

5.5.1.5 If a student investigator is involved in a research project, data must

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be retained at least until the degree is awarded or it is clear that the student has abandoned the work or for (3) three years from the date of study closure from the IRB, whichever is longer.

5.5.1.6 The retention requirements of sponsors may exceed the minimal standards of IUPUI/Clarian; therefore, contractual obligations with sponsors will determine requirements in those instances.

5.5.2 **Policy for Studies Regulated by the Food and Drug Administration (FDA)**

5.5.2.1 For FDA regulated studies involving electronic documentation, particularly electronic source documents, it may be necessary to retain not only the electronic media, but the device on which it is recorded so that the data is retrievable in years to come. For example, data recorded on VHS tapes may require the storage of a VCR as DVD players may replace VCRs in the years to come.

5.5.2.2 **Investigational New Drug (IND) Clinical Trials.** Pursuant to 21 CFR 312.62(c), the Investigator shall retain required clinical trial-related material for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated. If no application is to be filed or if the application is not approved for such indication, the records should be retained for a period of 2 years after the investigation is discontinued and the FDA is notified. Note: For sponsors conducting global clinical trials, international retention policies may apply. In many cases this may be 15 years or longer. In those instances, the contractual obligations to the sponsor will supersede institutional minimum standards.

5.5.2.3 **Investigational Device Exemption (IDE) Clinical Trials.** Pursuant to 21 CFR 812.140(c), the Investigator shall maintain the documents required during the investigation and for a period of two (2) years after the latter of the following two dates: the date on which the investigation is terminated or completed or the date that the records are no longer required for purposes of supporting a pre-market approval application or a notice of completion of a product development protocol. Note: For sponsors conducting global clinical trials, international retention policies may apply. In many cases this may be 15 years or longer. In those instances, the contractual obligations to the sponsor will supersede institutional minimum standards.

5.5.2.4 **Policy for Studies Subject to ICH Guidelines.** The International Conference on Harmonization (ICH) guidelines are very similar to FDA regulations and state that the investigator /institution should ensure that the essential documents relating to the clinical trial be

retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents can be discarded and no longer need to be retained.

5.5.2.5 **Financial Disclosure and Conflict of Interest Documents.** Investigators who are involved in the submission of a marketing application for an IND or IDE are required to retain documentation relating to "financial disclosure" for 2 years after the date of approval of the application. Similarly, any documents related to conflict of interest should be kept for the same time period as is applicable for the research project as detailed above.

5.5.3 **Veterans Affairs**

Pursuant to the VHA Handbook 1200.5 (j), for studies funded by the Veterans Affairs Administration or generated by employees of Veterans Affairs, the investigator must maintain research records for at least five (5) years after completion of the research study and in accordance with the VHA's Records Control Schedule (RCS 10-1), applicable FDA and DHHS regulations, or as required by outside sponsors.

5.6. **Transfer of Responsibility**

5.6.1 If an investigator is leaving the university and a study is to remain open with the IRB, notification of a transfer of responsibility must be made to the IUPUI/Clarian IRB in the form of a study amendment that identifies the researcher who has agreed to become the new Principal Investigator. Upon approval by the IRB, the new PI will become responsible for all future data management issues pertaining to the study. This includes, but is not limited to, submissions to the IRB and other regulatory agencies, storage, retention, and final disposition and arranging access for authorized monitors and/or auditors.

5.6.2 If an investigator is leaving the university and a study is closed with the IRB, the investigator may withdraw from the responsibility of maintaining the research documents for the period required above and transfer the responsibility and custody of the documents to any other appropriate person who will accept responsibility for them as described above. The Investigator who is leaving is responsible for notifying his/her department and division regarding who has agreed to accept this responsibility. The department/division then becomes responsible for keeping record of the person who has agreed to accept this

responsibility in case of future inquiries, e.g. requests for inspection by authorized University and/or federal auditors. In the absence of someone willing to accept responsibility for the documents, the department chairman will become responsible for assuring that documents are stored per regulatory and University requirements.

5.6.3 For studies conducted under the jurisdiction of the FDA where an investigator is leaving the university, the investigator may withdraw from the responsibility of maintaining the research documents for the period required above and transfer the responsibility and custody of the documents to an appropriate person who will accept responsibility for them as described in 5.6.1 and 5.6.2 above, Notice of such a transfer of responsibility shall be given to the Sponsor and FDA within 10 working days after the transfer occurs. (21 CFR 812.140).

5.7. **Data Integrity**

5.7.1 Data integrity must be maintained through appropriate security measures. All data must be retrievable, identifiable, and relate to an actual subject.

5.7.2 Records and source documents must be retained to enable reconstruction of the study (See Appendix D for suggestions on data documentation).

5.7.3 Audit trails must identify who made the changes, when, and why they were made.

5.7.4 Studies conducted under the regulation of the FDA (IND, IDE studies) must maintain full audit trails. All original entries made in source documents, case report forms, spreadsheets or databases and all subsequent modifications must be maintained. New entries and/or corrections must not obscure or obliterate the previously entered data. The original data must remain visible within the system. For paper records, this includes drawing one line through the original entry, entering the correction in a way that does not obliterate the original entry, initialing and dating the change.

5.7.5 Studies conducted under FDA regulations must also comply with 21 CFR 11: Electronic Records; Electronic Signatures. This regulation applies to all records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth by the FDA. It also applies to electronic records submitted to the Agency under the Federal Food, Drug, and Cosmetic Act and Public Health Service Act, even if such records are not specifically identified in agency regulations. However, this regulation does not apply to paper records that are, or have been, transmitted by electronic means. The regulation deals with electronic systems, electronic signatures, including security, validation, audit trails, data integrity, legacy systems, equipment, documentation, copies of records, and record retention. Similar to the requirements for paper records, this regulation requires that original data remain in the system, and that all changes must indicate the date of the change, the

person who changed the data, and the reason for the change. It is important to note that standard database software such as Excel, Access, and FileMaker are not capable of an electronic audit trail. Thus, Investigators are encouraged to utilize paper records for FDA regulated studies unless they have specific software programs to allow for these requirements. For specific details, consult FDA 21 CFR 11, Electronic Records; Electronic Signatures at: http://www.fda.gov/ora/compliance_ref/part11/.

5.7.6 NOTE: It is a requirement that researchers review the "Guidelines for Researchers Using Electronic Data in the Conduct of FDA Regulated Research Studies," (Appendix G) which includes a Research Unit Self-Assessment Tool (Appendix A) and Eight Simple Rules for Managing Research Data. (Appendix K).

5.8. **Data Security**

5.8.1 For data containing PHI, additional measures may be required under the Health Information Privacy and Accountability Act (HIPAA). See the Confidentiality and Privacy SOP for additional guidance.

5.8.2 For all research data, there are three levels of data safeguards that must be undertaken to ensure security of data: They are:

5.8.3 **Administrative Safeguards**, which include documented practices to manage the selection and execution of measures used to protect data and the conduct of personnel. Examples include: trust agreements, backup plans, recovery plans, access authorization plans, security management plans, security incident plans, training, accounting for disclosures, and disposal plans.

5.8.4 **Physical Safeguards**, which include protection of the actual locations of computer systems, related buildings, and equipment from natural or environmental hazards, e.g. fire, as well as from intrusion. Examples include: locks, keys, controlled access, and access tracking.

5.8.5 **Technical Safeguards**, which include processes to monitor, protect, and control information access. This includes the prevention of unauthorized access to data transmitted via communications networks. Examples include: access plans, audits, authorization, authentication, encryption, and firewalls.

5.9. **Sharing Data**

5.9.1 When sharing data within the research team or collaborators at IUPUI/Clarian, appropriate security measures should be undertaken as described above.

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5.9.2 If data containing PHI is shared, additional requirements may apply. See the SOP on Confidentiality and Privacy for detailed information.

5.9.3 Pursuant to Indiana law 4-1-10, the disclosure of Social Security Numbers outside the University is prohibited, except in the following circumstances:

5.9.3.1 The individual has expressly consented in writing to the disclosure;

5.9.3.2 The disclosure is made to a state, local, or federal agency;

5.9.3.3 The disclosure is made by a state law enforcement agency (which would include IUPD) for purposes of furthering an investigation;

5.9.3.4 The disclosure is expressly required by federal or state law or a court order;

5.9.3.5 The disclosure is for the purpose of administering the health benefits of a state agency employee or his/her dependent;

5.9.3.6 Only the last four digits of the SSN are disclosed;

5.9.3.7 The disclosure is made in order to comply with certain anti-terrorism provisions of the USA PATRIOT Act or a corresponding Presidential Executive Order addressing anti-terrorism efforts; or

5.9.3.8 The disclosure is made to a commercial entity for certain uses that are allowed under one of three federal laws – the Driver's Privacy Protection Act, the Fair Credit Reporting Act, or the Financial Services Modernization Act (popularly known as "Gramm Leach Bliley").

5.9.3.9 For additional information related to this Indiana law, please refer to http://www.ai.org/legislative/ic/code/title4/ar1/ch10.html.

5.9.4 Effective October 1, 2003, **NIH** requires a written plan to share data with the public and general research community for all NIH grants totaling $500,000 in direct cost or more in any single year. These projects must have a data sharing plan that includes a description of how investigators will share the data OR explain why that is not possible. See NIH Data Sharing Policy at: http://grants.nih.gov/grants/policy/data_sharing/ and the NIH Data Sharing Policy and Implementation Guidance at: http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm.

5.9.5 Both federal and state laws may impact public access to university records relating to research. For example, Indiana's Access to Public Records Act excepts from disclosure, "… Information concerning research, including actual

research documents, conducted under the auspices of an institution of higher education, including information: (A) concerning any negotiations made with respect to the research; and (B) received from another party involved in the research…." Under applicable federal law, research data relating to published research findings produced under an award that were used in developing an agency action that has the force and effected of law may be available to the public through a federal Freedom of Information Act request. Thus, public access requests seeking documents containing information concerning research should be carefully evaluated and forwarded to the IU Office of University Counsel located at IUPUI for further review and analysis, including a determination as to whether the records requested are or are not publicly available.

5.10. **Storing of Research Documents**

5.10.1 All documentation from a research study should be stored in such a manner that a request from the sponsor, regulatory agency, or internal audit can be met promptly and efficiently. Data that are archived or placed in long-term storage should be securely stored. Storage of documents containing PHI in a commercial facility may require the establishment of a business associate agreement between the covered entity to which the Principal Investigator belongs and the storage company. The PI should maintain an inventory of the records/files placed in internal or external long-term storage. The following points are provided as a guide for suggested steps to take for appropriate storing. Each department and/or investigator should have a specified method for accomplishing each of the following tasks:

5.10.1.1 Generate a master inventory list

5.10.1.2 Collect all study documentation

5.10.1.3 Define location of all study documentation

5.10.1.4 Determine retention policy (i.e., whether institutional, federal, and/or sponsor requirements apply)

5.10.1.5 Prepare documents ensuring they are secured and protected against breaches of confidentiality

5.10.1.6 Finalize Inventory and Accounting

5.10.1.7 Obtain and ensure appropriate storage container

5.10.1.8 Notify Sponsor, if applicable

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5.10.2 A sample checklist is attached as Appendix Q to assist with preparation, organization, and labeling of documents for long-term storage.

5.10.3 For additional information see the IUPUI/Clarian SOP on Security of Research Data.

5.11. **Disposition of Research Documentation**

5.11.1 After the specified period of time has elapsed, the Investigator may dispose of the documentation relating to a research study.

5.11.2 The following are suggested ways to securely dispose of documents containing PHI:

5.11.2.1 Shred paper documents.

5.11.2.2 Destroy diskettes, CDs, and/or hard drives

5.11.2.3 Permanently delete files and data from computers and PDAs using special programs. (Note: hitting the "delete" key on a computer does NOT permanently remove it from the hard drive.)

5.11.2.4 Destroy video or audiotapes, files or other media.

5.11.2.5 Depending on the funding agency, an investigator should not discard documentation until notification has been given to the sponsor and sponsor has confirmed in writing that the documentation will no longer be required. The sponsor may specify the method for disposal or request documents be transferred to them. If not, arrangements for destruction should be made in a manner that adequately protects the confidentiality of the information (e.g. shredding).

5.11.3 Pursuant to Indiana Code IC 24-4-14, certain measures to protect against access by a third party are required to be taken when disposing of "personal information." Acceptable methods of disposal include: encrypting, shredding, incinerating, mutilating, erasing, and otherwise rendering the information illegible or unusable. For additional information, please refer to IC 24-4-14 (http://www.ai.org/legislative/ic/code/title24/ar4/ch14.html).

5.11.4 For additional information see the IUPUI/Clarian SOP on Security of Research Data.

5.12. **Laws for Artifacts**

For research involving historical artifacts, additional special handling procedures may apply. Indiana state laws regarding curation can be found at: Archaeological Review and

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Recovery. This includes curation standards, which are governed at the federal level by 36 CFR 79. The National Park Service, which is federally charged with maintaining federal archaeological policy is summarized at: Curation of Federally Owned and Administered Archaeological Collections.

5.13. **IRB Records – Retention and Access**

5.13.1 IRB membership rosters, agendas, minutes, or other general correspondence with investigators, faculty, students, or staff will be retained indefinitely or until the Director, Research Compliance Administration, gives the authority to dispose of such records.

5.13.2 After a research protocol is closed, terminated, or has expired, the IRB study file will be kept for a period of three years.

5.13.3 Until disposal of IRB records has occurred, they will be made accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.

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Title:	Emergency Use of Investigational Agents			
Current Version:	12/07		Previous Versions:	02/05, 04/05

1. INTRODUCTION

FDA regulations exempt research from prospective IRB review for the use of a test article in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB approval, provided that such emergency use is reported to the IRB within 5 working days. However, this exemption does not apply to the regulatory requirements for obtaining and documenting informed consent. Additionally, there are a number of criteria that must be met before proceeding with the emergency use of a test article. HHS regulations for the protection of human subjects (i.e. 45 CFR 46) do not permit research activities to be started, even in an emergency, without prior IRB review and approval. However, pursuant to 45 CFR 46.116(f), the regulations are not intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

2. OBJECTIVES

2.1. Define what qualifies as a one-time emergency use, how to report the use, and the timeframe for reporting

2.2. Define other options if one-time emergency use is not available.

2.3. Explain the exception to informed consent requirements for planned emergency research.

3. SCOPE

These requirements apply to all research using investigational agents/devices that are normally subject to approval by the IUPUI and Clarian IRBs.

NOTE: This SOP does not apply to compassionate use, which is a term used for a method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for compassionate use of a drug or therapy. Participation in compassionate use programs requires the submission of a protocol and IRB approval. This SOP also does not apply to treatment or open-label studies, meaning IRB approval may still be required for these types of studies. Additionally, off-label use of approved drugs in emergent situations can be done without IRB approval if used in the course of clinical care.

4. RELEVANT DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1. Procedures for the Emergency Use of a Test Article

5.1.1 **Unapproved Investigational Drug or Biologic**. The emergency use of an unapproved investigational drug or biologic requires an Investigational New Drug (IND) application. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. The investigator and/or sponsor are required to contact the FDA for this determination.

5.1.2 **Unapproved Medical Device**. In general, an unapproved medical device may be used only on human subjects when the device is under clinical investigation and when used by investigators participating in a clinical trial. However, the FDA recognizes that there may be circumstances under which a health care provider may wish to use an unapproved device to save the life of a patient or to prevent irreversible morbidity when there exits no other alternative therapy.

5.2. Procedures to Request an Emergency Use of a Test Article

5.2.1 If an investigator has determined that all of the conditions described in 21 CFR 56.102(d) exist (i.e. a human subject is in a life-threatening situation, as defined in this SOP, in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval), the investigator shall:

5.2.1.1 Enroll the subject into an existing IRB-approved research study using the particular test article if the subject qualifies; or

5.2.1.2 During regular business hours, notify the Research Compliance Administration (RCA) office ((317) 274-8289 for IUPUI and (317) 962-8240 for Clarian/Methodist) of the need to obtain an emergency waiver if no IRB-approved research study using the particular test article exists.

5.2.1.2.1 RCA will assist the investigator in determining whether the test article has been previously used at the institution and will also consult with an IRB Chair to determine if the conditions described in 21 CFR 56.102(d) are met.

5.2.1.2.2 If the IRB Chair determines that the conditions described in 21 CFR 56.102(d) are met, the investigator will be notified. However, such notification should not be construed as an IRB approval, but rather a tracking mechanism for the IRB to ensure that the investigator files a report within the five day timeframe required by 21 CFR 56.104(c). If assistance is required in dispensing the test article, Investigational Drug Services (IDS) should be contacted at (317) 274-1900.

5.2.1.2.3 If, however, the conditions described in 21 CFR 56.102(f) are not met, the investigator cannot be granted an emergency waiver.

5.2.1.2.4 If the test article has already been used at the institution, subsequent use of the test article must be prospectively reviewed and approved by the IRB. The FDA and IRB acknowledge, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

5.2.1.3 After regular business hours, contact Investigational Drug Services (IDS) at (317) 274-1900 for assistance in determining if the test article has been previously used at the institution and for assistance in dispensing the test article, if required.

5.2.2 If RCA or the pharmacy cannot be reached or the emergency use does not involve an investigational drug, the investigator may proceed with the emergency use provided the conditions described in 21 CFR 56.102(f) are met. The RCA office must be notified of the use the following business day.

5.3. Reporting Requirements for an Emergency Use of a Test Article

5.3.1 Pursuant to 21 CFR 56.104(c), emergency use of a test article is exempt from prospective IRB review provided that such emergency use is reported to the IRB within 5 business days. Thus, the investigator must notify the IRB of an emergency use within 5 business days and shall include the following information in the report:

5.3.1.1 A full description of the situation, including justification for the emergency use;

5.3.1.2 A full description of the test article, including the trade name, generic name, chemical name, and/or device name, the IND or IDE number, and name of sponsor/manufacturer;

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5.3.1.3 A full description of the procedure(s) employed;

5.3.1.4 A description of the consent process used, including an unsigned copy of the informed consent and authorization documents.

5.3.2 Pursuant to HHS regulations, whenever emergency care is initiated without prior IRB review and approval, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. However, if the emergency care involves drugs, biologics, or devices that are considered to be investigational by the FDA, then the emergency use of a test article in a life threatening situation initiated without prior IRB review and approval is considered research and the person given the test article(s) on an emergency basis is a research subject. In order to maintain this distinction, data from persons given test articles on an emergency basis may not be included in any prospectively conceived research study. The IRB may consider granting an exemption determination to a retrospective review of existing data from one or more emergency uses, provided the emergency use provisions were not used as a mechanism to circumvent IRB review for a prospectively conceived research study.

5.3.3 The investigator should evaluate the likelihood of a similar need for emergency use of the test article. If the need is likely, prospective FDA (if not already in existence) and IRB approval should be initiated. FDA regulations and University policy require that any subsequent use of the test article at the institution have prospective IRB review and approval.

5.3.4 Likewise, in its review of the emergency use, the IRB shall request the investigator submit a new study, including a protocol and associated new study material for prospective IRB review and approval when it anticipates that the test article may likely be used again. Although subsequent use of the test article at the institution is subject IRB review, the FDA and IRB acknowledge that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

5.3.5 If the need for a subsequent emergency use of a test article should occur, please see section 5.2 of this document for guidance.

5.3.6 When the IRB is notified of an emergency use that has taken place, RCA staff will review the report to determine if the use complied with FDA and institutional requirements. If requirements were met, an acknowledgement letter will be sent to the investigator. If it is determined that requirements were not met, the matter will be handled according to the noncompliance procedures delineated in the Unanticipated Problems and Noncompliance SOP.

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5.4. **Procedures for a New Study Submission When a One-Time Emergency Use Does Not Qualify**

5.4.1 If the use of the test article does not qualify for a one-time emergency use, prospective IRB approval is required. Once it is determined that an emergency IRB review is required, the following process will be followed:

5.4.1.1 If there is sufficient time, a new study application should be completed and submitted for review at the next regularly scheduled IRB meeting.

5.4.1.2 If there is not sufficient time to wait for a regularly scheduled IRB meeting, RCA or the Methodist IRB office may convene a meeting of the Emergency Review Committee. Because of the IRB's concern that protocols receive thorough IRB review, the Committee may approve a protocol for use in one patient only with a request that the investigator submit the protocol (with requested revisions) for full Board review for future patients.

5.4.1.3 If there is not sufficient time to convene an emergency meeting, RCA or the Methodist IRB office will consult with an IRB Chair (or his/her designee) to determine the appropriateness of the test article's use. In this case, the investigator is required to report the use in the manner explained in 5.3 above.

5.5. **Informed Consent and Authorization Requirements**

5.5.1 Unless any of the exceptions listed in 5.6 below apply, the investigator is required to obtain prospective informed consent from the subject or the subject's legally authorized representative. The consent should clearly document the rationale for using the test article in emergency use situations and describe potential risks. See Appendix T for additional emergency consent guidance.

5.5.2 In addition, if an informed consent is required, the investigator is also required to obtain an authorization to use the subject's health information for research purposes.

5.6. **Exception from Informed Consent Requirements for Clinical Investigations.** Pursuant to 21 CFR 50.23(a), the obtaining of informed consent shall be deemed feasible unless, before use of the test article both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

5.6.1 The subject is confronted by a life-threatening situation necessitating the use of the test article.

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5.6.2 Informed consent or authorization cannot be obtained because of an inability to communicate with or obtain legally effective consent or authorization from the subject.

5.6.3 Time is not sufficient to obtain consent or authorization from the subject's legally authorized representative.

5.6.4 No alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the life of the subject.

5.7. If, in the investigator's opinion, immediate use of the test article is required to preserve the life of the subject and time is not sufficient to obtain the independent determination required in advance of using the test article:

5.7.1 The determination shall be made by the investigator and, within five (5) business days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

5.7.2 The investigator shall notify the IRB within five (5) business days after the use of the test article according to the reporting requirements outlined in 5.3 above. In its review of a one-time emergency use which employed an exception to the informed consent requirement, the IRB will ensure that all regulations were appropriately followed.

5.8. **Waiver of Informed Consent Requirements for Planned Emergency Research**

5.8.1 Pursuant to 21 CFR 50.24, the IRB may approve research (clinical investigation) without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

5.8.1.1 The human subjects are in a life-threatening situation, available treatments are either unproven or unsatisfactory; **and** the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

5.8.1.2 Obtaining informed consent is not feasible because:

5.7.1.2.1 The subjects will not be able to give their informed consent as a result of their medical condition;

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5.7.1.2.2 The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; **and**

5.7.1.2.3 There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

5.8.1.3 Participation in the research holds out the prospect of direct benefit to the subjects because:

5.7.1.3.1 Subjects are facing a life-threatening situation that necessitates intervention;

5.7.1.3.2 Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; **and**

5.7.1.3.3 Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

5.8.1.4 The clinical investigation could not practicably be carried out without the waiver.

5.8.1.5 The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

5.8.1.6 The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with § 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used

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when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with §50.24(a)(7)(v).

5.8.1.7 Additional protections of the rights and welfare of the subjects will be provided, including, at least:

5.7.1.7.1 Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

5.7.1.7.2 Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

5.7.1.7.3 Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

5.7.1.7.4 Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; **and**

5.7.1.7.5 If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

5.8.1.8 The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject

remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

5.8.1.9 The IRB determinations required by 21 CFR 50.24(a) and the documentation required by 21 CFR 50.24(e) are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 21 CFR 56.115(b).

5.8.1.10 Protocols involving an exception to the informed consent requirement under 21 CFR 50.24 must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under 21 CFR 50.24 may not be submitted as amendments under 21 CFR 312.30 or 21 CFR 812.35.

5.8.1.11 If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under §50.24(a) or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

5.8.2 **Planned emergency research that is subject to HHS regulation.** Pursuant to 45 CFR 46.101(i), HHS has waived the general requirements for informed consent at §46.116(a) and (b) and §46.408 (to be referred to as the "Emergency

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Research Consent Waiver") for a class of research consisting of activities, each of which have met the following strictly limited conditions:

5.8.2.1 **Research subject to FDA regulations**

5.8.2.1.1 The IRB has approved both the activity and a waiver of informed consent and found and documented that the research activity is subject to 21 CFR 50 and will be carried out under an FDA investigational new drug (IND) application or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent; **AND**

5.8.2.1.2 The requirements for exception from informed consent for planned emergency research in 21 CFR 50.24 have been met relative to those protocols.

5.8.2.2 **Research <u>not</u> subject to FDA regulations**. The IRB has approved both the research and a waiver of informed consent and has (i) found and documented that the research is not subject to 21 CFR 50 and (ii) found and documented and reported to OHRP that the conditions outlined in 5.8.1.1-5.8.1.8 above have been met relative to the research.

5.8.3 This exception from informed consent requirements for planned emergency research is **not** applicable to VA research and research involving vulnerable populations, except children.

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Title:	Exempt and Expedited New Study Process			
Current Version:	12/07		Previous Versions:	05/05, 04/05, 02/05

1. INTRODUCTION

Research involving human subjects is reviewed at a convened IRB meeting unless it is classified as minimal risk and only involves research activities defined in the federal regulations at 45 CFR 46.101(b) and 45 CFR 46.110(a) and (b). The type of review depends on the risks posed to potential subjects. These risks not only include physical risks, but also psychological, emotional, legal, social and financial risks. Although the regulations allow for the use of expedited review procedures for a variety of research submissions (e.g. certain amendments and continuing reviews), this SOP only addresses the review procedures for new exempt and expedited research submissions.

2. OBJECTIVE

2.1 Define the research categories for exempt and expedited reviews; and

2.2 Explain the process for review and approval of exempt and expedited research.

3. SCOPE

These policy and procedures apply to all research activities of faculty, staff, student, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVANT DEFINITIONS

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5. POLICIES AND ASSOCIATED PROCEDURES

5.1. **Exempt Human Subjects Research.** Pursuant to 45 CFR 46.101(b), research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from 45 CFR 46, Subpart A. It is the policy of the IUPUI/Clarian IRB that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the exemption categories described in the federal regulations and complies with IUPUI and Clarian ethical standards. Because investigators do not have the authority to make an independent determination that research involving human subjects is exempt and only the IRB can make this determination, investigators must submit an application to the IRB for final determination. Pursuant to 45 CFR 46.101(b)(1) - §46.101(b)(6), the following research activities are considered "exempt:"

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5.1.1 Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as 1) research on regular and special education instructional strategies; or 2) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

5.1.2 Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless all of the following are true:

5.1.2.1 Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **and**

5.1.2.2 Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, or reputation.

5.1.2.3 If the research involves children as participants, the research must be limited to educational tests (cognitive, diagnostic, aptitude, achievement) and observation of public behavior when the investigator(s) do not participate in the activities being observed. Research involving children that uses survey procedures, interview procedures, or observation of public behavior when the investigator(s) participate in the activities being observed cannot be granted an exemption.

5.1.3 Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under 5.1.2 above, if:

5.1.3.1 The human subjects are elected or appointed public officials or candidates for public office; **or**

5.1.3.2 Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

For the above three categories (45 CFR 46.101(b)(1)-(3): If information will be obtained using audio or video taping, these exempt categories can only be used if the investigator can provide adequate assurance that the identity of the subjects and/or link to the information obtained or the information recorded does not place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, or reputation.

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5.1.4 Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.]

5.1.4.1 To qualify for this exemption, data, documents, records, or specimens must exist at the time the research is proposed and not prospectively collected.

5.1.4.2 Under this exemption, an investigator (with proper institutional authorization) may ***inspect*** private, identifiable records, but may only ***record*** information in a non-identifiable manner. The data must be permanently and completely de-linked at the time of extraction. A code may be used to organize data as it is collected; however, the code may not be a means of re-linking the data set to the original source and/or other sources.

5.1.5 Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

5.1.5.1 Public benefit or service programs;

5.1.5.2 Procedures for obtaining benefits or services under those programs;

5.1.5.3 Possible changes in or alternatives to those programs or procedures; **or**

5.1.5.4 Possible changes in methods or levels of payment for benefits or services under those programs.

5.1.5.5 The program under study must deliver a public benefit (for example, financial or medical benefits as provided under the Social Security Act) or service (for example, social, supportive, or nutrition services as provided under the Older Americans Act).

5.1.5.6 The research or demonstration project must be conducted pursuant to specific federal statutory authority, must have no statutory requirement that an IRB review the project, and must not involve significant physical invasions or intrusions upon the privacy of the subjects.

5.1.5.7 This exemption is for projects conducted by or subject to approval of Federal agencies and requires authorization or concurrence by the funding agency.

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5.1.6 Taste and food quality evaluation and consumer acceptance studies:

5.1.6.1 If wholesome foods without additives are consumed; **or**

5.1.6.2 If food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (also 21 CFR 56.104(d))

5.2. **Exempt Human Subjects Research Considerations**

5.2.1 The preliminary determination that a research project is eligible for exempt review may be made by the investigator; however, the IRB (or authorized Research Compliance Administration [RCA] staff member) may deny the study as exempt. If this happens, the project must be resubmitted at the appropriate level of review, as appropriate.

5.2.2 The exemptions outlined above do not apply to research involving prisoners.

5.2.3 The exemptions outlined above do not apply to research involving pregnant women that is conducted at or funded by the VA.

5.2.4 The IRB will not consider any research exempt that involves a test article regulated by the FDA, unless the research meets the criteria for exemption described in 45 CFR 46.101(b)(6) and 21 CFR 56.l04(d).

5.2.5 The exempt categories outlined above are based solely on methods of research, and do not take the level of risk into consideration. Although most exempt research requires no further oversight to be conducted ethically, some exempt research raises ethical concerns or requires measures to protect participants. As such, the IRB will not consider any research exempt that does not fulfill ethical principles reflected in the Belmont Report. These basic ethical principles are:

5.2.5.1 Respect for Persons (Autonomy) – individuals should be treated as autonomous agents and persons with diminished autonomy are entitled to protection.

5.2.5.2 Beneficence – individuals should not be harmed and the research should maximize possible benefits and minimize possible harms.

5.2.5.3 Justice – the benefits and risks of research must be distributed fairly.

5.3. **Exempt Human Subjects Research Submission Requirements**

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5.3.1 **Submission Requirements**. The following documents must be submitted to the IRB for review:

5.3.1.1 Exempt Research Checklist;

5.3.1.2 Grant Proposal, if the study is funded by the National Institutes of Health (NIH).

5.3.2 **Deadline Requirements**. There are no deadline requirements for exempt study submissions. However, 5-10 working days should be allowed for processing.

5.3.3 **Granting Exemptions**. At IUPUI, the IRB has granted authority to RCA staff to grant exemptions. However, if RCA staff has questions as to whether or not the research appropriately meets an exempt category, they may request a member of the IRB designated by the Chair to review and grant such an exemption, as appropriate. **EXCEPTION**: Exemptions for studies conducted at or funded by the VA must be granted by an IRB Chair or IRB member designated by the Chair. This IRB member need not be a VA representative. At Methodist, exempt applications are sent to the IRB Chair or designee for review and acceptance.

5.3.4 **Consultants**. Consultants with specific expertise may be utilized to assist in the review of exempt research, when appropriate. Their comments will be documented and forwarded to an IRB member (or designated RCA staff) for review and final approval.

5.3.5 **Continuing Review Requirements**. Exempt research studies are not required to undergo continuing review. However, the RCA office should be notified via a memo when the research is complete.

5.3.6 **Changes to Exempt Studies.** Any proposed changes to an approved exempt study should be requested via a memo sent to the RCA office. If the changes do not affect the exempt status, the investigator will be notified. If the changes are determined to be significant enough such that the original goal of the study has changed, the risk has increased, or the research no longer meets the criteria for exempt research, the investigator will be notified that a new research application reviewed under expedited or full review is necessary.

5.4. **Expedited Human Subjects Research.** Research activities that (1) present no more than minimal risks to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research

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involve no more than minimal risk to human subjects. The expedited research categories include:

5.4.1 Clinical studies of drugs and medical devices only when either condition below is met:

5.4.1.1 Research on drugs for which an investigational new drug application (21 CFR 312) is not required. Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review;

5.4.1.2 Research on medical devices for which (1) an investigational device exemption application (21 CFR 812) is not required; or (2) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

5.4.2 Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

5.4.2.1 From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

5.4.2.2 From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

5.4.3 Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:

5.4.3.1 Hair and nail clippings in a nondisfiguring manner;

5.4.3.2 Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

5.4.3.3 Permanent teeth if routine patient care indicates a need for extraction;

5.4.3.4 Excreta and external secretions (including sweat);

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5.4.3.5 Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;

5.4.3.6 Placenta removed at delivery;

5.4.3.7 Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

5.4.3.8 Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

5.4.3.9 Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; or

5.4.3.10 Sputum collected after saline mist nebulization.

5.4.4 Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared / approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications). **Examples**:

5.4.4.1 Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

5.4.4.2 Weighing or testing sensory acuity;

5.4.4.3 Magnetic resonance imaging;

5.4.4.4 Electrocardiography; electroencephalography, thermo-graphy detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;

5.4.4.5 Moderate exercise, muscular strength testing, body composition assessment and flexibility testing where appropriate given the age, weight and health of the individual.

5.4.5 Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as

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medical treatment or diagnosis). Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects [45 CFR 46.101(b)(4)]. This listing refers only to research that is not exempt.

5.4.6 Collection of data from voice, video, digital, or image recordings made for research purposes. If the data collected is considered individually identifiable health information, the data must be protected from inappropriate use and disclosure.

5.4.7 Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101(b)(2) and (b)(3)] This listing refers only to research that is not exempt.

5.5. **Expedited Human Subjects Research Considerations**

5.5.1 Expedited categories 1-7 (5.4.6.1-5.4.6.7) in the list apply regardless of the age of subjects, except as noted.

5.5.2 Expedited categories 1-7 (5.4.6.1-5.4.6.7) in the list below pertain to both initial and continuing IRB review.

5.5.3 The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

5.5.4 The expedited review procedure may not be used for research involving prisoners or classified research involving human subjects.

5.5.5 The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e. expedited or full) utilized by the IRB.

5.5.6 **Expedited Determination**. Although investigators make a preliminary determination about whether a research study meets the criteria for expedited review procedures, the IRB makes the final determination. If the IRB does not concur with the investigator's determination, it may request modification to the research study or require that the research be submitted for full IRB review in accordance with the requirements and deadlines for full review studies.

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5.5.7 **Expedited Review Procedures**. Under expedited review procedures, the IRB Chair, or one or more experienced reviewers designated by the Chair from among the members of the IRB, shall review the research protocol. At IUPUI, two reviewers are assigned to review research protocols where a request for a waiver of informed consent is included. If the reviewers do not agree on the justification for the informed consent waiver, the study shall be reviewed at a convened IRB meeting for final determination.

5.5.8 **Expedited Review Authorities**. In conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB, except that they may not disapprove the research. A research activity may be disapproved only after review by the convened IRB.

5.5.9 **Consultants**. Consultants with specific expertise may be used to assist in the review of expedited research, when appropriate. Their comments will be documented and forwarded to IRB reviewer(s) for review and approval.

5.5.10 **Reporting of Expedited Research**. Research proposals that have been approved under the expedited review procedure will be reported to the IRB in order to ensure all IRB members are kept advised of such research approvals.

5.6. **Expedited Research Submission Requirements.** Investigators must submit appropriate documentation to ensure a complete review by the IRB. Please see Section 5 of the IRB Instruction Packet for a complete list of documents that must be submitted to the IRB for review.

5.6.1 **Deadline Requirements**. There are no deadline requirements for submitting an expedited study; however it is recommended that the study be submitted a few weeks prior to meeting deadlines in the event that full review is required. Ten-fifteen working days should be allowed for processing.

5.6.2 **Waiver of Informed Consent**. To request a waiver of informed consent, complete section XII in the summary safeguard statement. Generally, if the investigator will be face-to-face with subjects, informed consent must be obtained. For additional information, see the IUPUI/Clarian SOP for Informed Consent.

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Title:	Facilitated Review			
Current Version:	07/07		Previous Versions:	New policy

1. INTRODUCTION

Pursuant to the federal regulations on human subjects research (45 CFR 46, the Common Rule), the Institutional Review Board (IRB) was created. Indiana University (IU), Clarian Health Partners (CHP) and their affiliates each maintain a Federalwide Assurance (FWA) with the Department of Health and Human Services (DHHS), which requires that all human subjects research, whether funded or not, conducted at or on behalf of these institutions be reviewed and approved by an IRB prior to initiating a research study. There are eight (8) IRBs for Indiana University-Purdue University Indianapolis (IUPUI), and Clarian Health Partners (CHP), including the 7 IRBs managed by the institution and the National Cancer Institute Central IRB (NCI CIRB). Pre- or proceeding references to the IUPUI/Clarian Institutional Review Board(s) (IRB) may include the NCI CIRB as appropriate.

IUPUI/Clarian participates in the NCI CIRB Initiative and has negotiated an agreement and amended its FWAs to include the NCI CIRB as a designated review board for certain adult and pediatric national multi-center cancer treatment trials. In order for the NCI CIRB to serve as a designated review board for a particular protocol, the protocol must be reviewed and approved through a "facilitated review" process at IUPUI/Clarian. Local investigators who wish to enroll patients onto NCI CIRB approved protocols may utilize this process in order to allow the IUPUI/Clarian IRBs to review the protocol on an expedited basis to determine if NCI CIRB oversight is appropriate. Once NCI CIRB oversight is granted for that protocol, amendments, continuing reviews, and reports of external unanticipated problems (adverse events) are managed by the NCI CIRB; however, the IUPUI/Clarian IRB is still kept informed of the progress of the protocol and is responsible for the local management of that protocol, as well.

2. OBJECTIVES

2.1 Describe the documentation requirements and submission procedures to the IUPUI/Clarian IRB for investigators requesting "facilitated review" for NCI CIRB adult and pediatric national multi-center cancer treatment trials.

2.2 Outline the process of NCI CIRB and IUPUI/Clarian IRB approval before, and where applicable, during research.

3. SCOPE

These policies and procedures apply to certain adult and pediatric national multi-center cancer treatment trials conducted by faculty, staff, students, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

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4. RELEVANT DEFINITIONS

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5. POLICIES AND ASSOCIATED PROCEDURES

5.1. Division of Responsibilities Between the NCI Central IRB and IUPUI/Clarian

5.1.1. The following division of responsibilities is based on the premise that the CIRB's primary function is initial and continuing review of Adult and Pediatric research protocols and that the local institution's primary function is consideration of local context and oversight of local performance for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the CIRB or to conduct its own review of the protocol. For the purposes of this SOP, the "local IRB" referred to below is the IUPUI/Clarian IRB system.

5.1.2. The responsibilities of the CIRB are to:

5.1.2.1. Perform initial reviews of new research protocols, discuss any issues with the lead organization and Study Chair, and make a final decision of approval or disapproval of the protocol.

5.1.2.2. Maintain and make accessible to a designated local IRB at the local institution the CIRB application, protocol reviews, letters to Study Chairs, approvals and disapprovals, and minutes of the CIRB meetings.

5.1.2.3. Carry out Continuing Reviews, reviews of Serious Adverse Events, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the lead organization or Study Chair.

5.1.2.4. Notify each local institution that has accepted the CIRB review of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status.

5.1.2.5. Maintain a Board membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56 and provide special expertise as needed from Board members or consultants to adequately assess all aspects of each protocol.

5.1.2.6. Make available to the local institution the roster of CIRB membership and the CIRB Standard Operating Procedures and policies.

5.1.2.7. Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subjects protections.

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5.1.2.8. Notify the local institution immediately if there is ever a suspension or restriction of the CIRB's authorization to review protocols.

5.1.2.9. Notify the local institution of any CIRB policy decisions or regulatory matters that might affect the institution's reliance on CIRB reviews or performance of the research at the local institution.

5.1.3. The responsibilities of the local institution are to:

5.1.3.1. Ensure the safe and appropriate performance of the research at its institution. This includes, but is not limited to, monitoring protocol compliance, any major protocol violations, and any serious adverse events occurring at the institution, and providing a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified in these areas shall be shared with the CIRB and reported as required by the procedures established by the protocol's lead organization.

5.1.3.2. Ensure that the investigators and other staff at the local institution who are conducting the research are appropriately qualified and meet the institution's standards for eligibility to conduct research.

5.1.3.3. Notify the CIRB immediately if there is a suspension or restriction of a local investigator.

5.1.3.4. Provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the local IRB, such as the local IRB administrator.

5.1.3.5. Establish a written procedure by which the local IRB will receive and review the CIRB materials for protocols to be performed at the local institution. Refer to section 5.2 and Appendix A for detailed procedures regarding this process; however, in general, for each CIRB reviewed protocol (approval or disapproval) that is submitted to the local IRB by a local investigator, IUPUI/Clarian IRB will:

5.1.3.5.1. Review the CIRB's materials.

5.1.3.5.2. Determine if there are any local context issues that must be addressed by the local IRB.

5.1.3.5.3. Determine if the CIRB review is acceptable to the local IRB.

5.1.3.5.4. Decide whether to accept the CIRB review or conduct a separate local full board IRB review.

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5.1.3.6. Report to the CIRB the decision about local acceptance/rejection of the CIRB review. Notify the CIRB if there is ever a change in the acceptance/rejection of the CIRB review.

5.1.3.7. As appropriate, add local restrictions, stipulations, or substitutions to CIRB approved informed consents. Deletion of CIRB approved requirements in the protocol and Informed Consent Statement is not allowed, and substantive changes that affect the meaning of CIRB approved requirements are not allowed.

5.1.3.8. If the local IRB accepts the CIRB approval of a protocol, maintain in the local IRB records documentation of the decision and evidence that it has received and considered all CIRB material relevant to the protocol.

5.1.3.9. Maintain an OHRP-approved Assurance for human subjects research.

5.1.3.10. Maintain a local IRB whose membership satisfies the requirements of 45 CFR 46 and 21 CFR 56.

5.1.3.11. Maintain a human subjects protection program, as required by the DHHS OHRP.

5.1.3.12. Ensure that local IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections.

5.1.3.13. Notify the CIRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review protocols.

5.1.3.14. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects.

5.2. **Facilitated Review Process**

5.2.1. The PI must conduct all procedures in accordance with NCI CIRB policy (www.ncicirb.org). The principal investigator (PI) or designee will download and print all CIRB documentation from the Participants Area of the CIRB website (www.ncicirb.org). The PI or designee will then submit all CIRB documentation related to the protocol for review to the RCA office.

5.2.1.1. Documentation should include, but is not limited to:

5.2.1.1.1. Verification that the protocol has been approved by the Scientific Review Committee (SRC), General Clinical

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Research Center (GCRC), and Radiation Safety Committee (RSC), as applicable.

5.2.1.1.2. All documentation from the Participants Area which has been downloaded from the CIRB website, including but not limited to, the CIRB application, protocol, informed consent statement, any site reports, and amendments.

5.2.1.1.3. The IUPUI/Clarian NCI Facilitated Review Form and any relevant attachments.

5.2.1.1.3.1. Local requirements (e.g., the passing of the Human Subjects Protection Test, co-investigator acknowledgements, PI eligibility, and recruitment issues) are identified on this form and must still be met even though there is a request to allow the CIRB to serve as the IRB of record.

5.2.1.1.4. One copy of any other documents which the PI feels would be useful for the IRB's deliberation regarding the protocol.

5.2.1.2. The PI and research staff should note that the CIRB-approved informed consent form(s) which are submitted with the protocol must be modified to conform to IUPUI/Clarian IRB approved language and standard statements.

5.2.1.2.1. Local boilerplate additions to the CIRB-approved informed consent dealing with contact information, confidentiality, injury statements, state and local law, or IRB policies must be added.

5.2.1.2.2. The PI or local IRB reviewer may also request substitutions or additions in the CIRB-approved informed consent document, particularly to facilitate comprehension by the local population, as long as the proposed changes do not alter the meaning of CIRB approved content.

5.2.1.2.3. Revisions/changes to the local consent form other than those designated in Sections 5.2.1.2.1 and 5.2.1.2.2 will require full board review at the local level, and facilitated review may not be used.

5.2.2. Upon receipt of required documentation, RCA office staff will contact either an IRB Chair or an IRB member so designated for the NCI CIRB Facilitated Review Process to notify him/her of such a submission. Protocol submission materials will be sent to that IRB member for local review. Using the criteria outlined in Section 5.2.1, the

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IUPUI/Clarian IRB reviewer will determine on a case-by-case basis whether to accept the review of the CIRB, or to conduct a local review of the protocol.

5.2.3. The purpose of the local IRB review is to concentrate on whether any local context issues exist which would suggest that local IRB review and oversight should be required. It is anticipated that local IRB review will be completed in 2-4 working days.

5.2.4. The IRB member conducting the facilitated review for IUPUI/Clarian may review the item him/herself or may seek additional review or advice from other IRB members, the PI, or other institutional officials as necessary. Acceptance from the local IRB member may be documented via email or via signature on the NCI CIRB Facilitated Review Form.

5.2.5. Local IRB review may result in two outcomes. Note that communication between the IRB reviewer and PI, facilitated by the RCA office, may be required to achieve intended outcomes.

5.2.5.1. **Accept CIRB Review -** The CIRB will be designated as the IRB of record, and is responsible for continuing (ongoing) review, review of subsequent amendments, and adverse events. However, the PI will still be responsible for submitting to the IUPUI/Clarian IRB notification regarding local personnel or site changes, adhering to local requirements such as the SOP for Unanticipated Problems and Noncompliance, and any other locally-initiated alterations or updates.

5.2.5.2. **Not to Accept the CIRB review –** Full IUPUI/Clarian IRB oversight is required. In this circumstance, the RCA office will submit the study to the next regularly-scheduled IRB meeting for full-board review. With this outcome, the CIRB will not be involved in protocol oversight.

5.2.6. Notification of IUPUI/Clarian IRB review results will be communicated to the PI in accordance with the IRB Operations SOP.

5.2.6.1 Note: the approval stamp on the informed consent statement will reflect the local IRB approval date and the CIRB expiration date.

5.2.7. For any CIRB protocol, regardless of its disposition, the RCA office and PI/designee will maintain a copy of the protocol file, including documentation regarding any subsequent reviews and other CIRB documentation. These documents shall be retained in accordance with University Policy and federal requirements. Refer to the SOP on Data Management.

5.2.8. Once accepted by the IUPUI/Clarian IRB reviewer, the RCA Office will accept the review of the protocol by visiting the NCI CIRB website, clicking on the "Facilitated Review Acceptance" button, and completing the Facilitated Review

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Acceptance Form for the applicable protocol. This acceptance designates the NCI CIRB as the IRB of record.

5.2.9. Once the CIRB is designated as the IRB of record, the CIRB will conduct continuing reviews and reviews of serious adverse events, data safety monitoring board reports, protocol amendments, and recruiting reports, and will post these actions on the CIRB website for prompt access. The PI and designated research staff will receive email updates of these events. Upon notification of approval from the CIRB, the PI will update the newly approved consent form(s) to incorporate the current IUPUI/Clarian IRB approved language and standard statements, if necessary. The CIRB documents are accepted pending local IRB approval.

5.2.9.1. Local unanticipated problems shall be reported in accordance with the IUPUI/Clarian SOP on Unanticipated Problems and Noncompliance.

5.2.9.2. Local personnel changes shall be communicated to Research Compliance Administration as per current practice.

5.2.10. For studies which the IUPUI/Clarian IRB has accepted the CIRB as the IRB of record, it should be noted that at any time during the conduct of the protocol, the local IRB can issue suspensions or restrictions on the conduct of the protocol and/or require that the study be reviewed by the local IRB and that the designation of CIRB oversight can be discontinued.

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Title:	Humanitarian Use Devices			
Current Version:	07/07		Previous Versions:	09/04

1. INTRODUCTION

Because there exist several sets of regulations governing the use of medical devices, there is much confusion related to how these devices can be used. Of particular confusion is the use of Humanitarian Use Devices (HUDs). These devices fall somewhere between research and ordinary clinical practice. They do not undergo the same stringent requirements that investigational devices do in order to commercially market them, yet they may be recognized as the "approved" standard, and in some cases, preferred medical device.

A HUD, because of its small expected market, is not expected to ever be able to get the type of efficacy data required by ordinary premarket approval (PMA), so the FDA grants a special exemption, humanitarian device exemption (HDE), from some of the requirements for marketing approval. Although an HDE does not require results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose, it must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use; taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. An HDE must, however, demonstrate that no comparable device is available to treat or diagnose the disease or condition, and that the device could not otherwise be brought to market unless it is granted HUD status.

An approved HDE authorizes marketing of the HUD for clinical use; however, clinical use of the device is limited to the indication specified in the product labeling. Also, a HUD may only be used in facilities that have established a local institutional review board (IRB) to oversee the clinical introduction and use of the device within that institution.

2. OBJECTIVES

2.1. Explain humanitarian use devices (HUDs) and humanitarian device exemptions (HDEs);

2.2. Explain the procedures for obtaining IRB approval for the use of a HUD and associated continuing review requirements; and

2.3. Explain the role of the IRB in review and approval of the use of a HUD.

3. SCOPE

These policies and procedures apply to all research activities of faculty, staff, student, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

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4. RELEVANT DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1. The IRB's Role in the Use of a Humanitarian Use Device (HUD)

Pursuant to 21 CFR 814.124(a), the FDA requires IRB review and approval before a HUD is used, as well as continuing review of the use of the HUD. The IRB must ensure that the proposed use is within the FDA-approved indication and that the use of the device does not exceed the scope of the FDA's approval.

5.2. Initial IRB Approval of the Use of a HUD

5.2.1. Once a device has received a HUD designation from the FDA, whether for treatment, diagnosis, or research, the use of a HUD must be initially reviewed at a convened IRB meeting and approved before the device can be used. To request this review, the physician (investigator) must submit the following documentation:

5.2.1.1. The HUD manufacturer's product labeling, clinical brochure, and/or other pertinent manufacturer informational materials.

5.2.1.2. The FDA HDE approval letter.

5.2.1.3. A cover letter addressing the following items, unless these are already addressed in the above-listed documentation:

5.2.1.3.1. A description of the device and how it will be used.

5.2.1.3.2. The clinical indication(s) for which the HUD will used;

5.2.1.3.3. Where (location) and by whom the HUD will be used;

5.2.1.3.4. The criteria (inclusion/exclusion) that will be used to determine eligibility for use of the HUD;

5.2.1.3.5. A discussion of possible benefits, risks, side effects, and/or adverse events associated with the clinical use of the HUD;

5.2.1.3.6. A discussion of any alternative treatments or procedures (if any); and

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5.2.1.3.7. A statement that specifies the use of the HUD will be limited to the clinical indication(s) listed in the FDA-approved product labeling.

5.2.1.4. The clinical consent form. Since the HUD is approved for clinical use by the FDA, words such as "research" or "study" should be avoided. The consent form should be generally modeled after other clinical consent forms for invasive procedures and should include the following:

5.2.1.4.1. A description of the HDE/HUD approval process; e.g.

5.2.1.4.2. A description of the HUD and how this device will be used in the clinical setting. Based on this description, it should be clear to the patient why s/he is a candidate for the use of this device.

5.2.1.4.3. A discussion of possible risks, side effects, and/or adverse events associated with the HUD and its proposed clinical use.

5.2.1.4.4. A discussion of the possible benefits associated with the clinical use of the HUD.

5.2.1.4.5. A discussion of any alternative treatments or procedures (if any) that the patient may wish to consider in lieu of clinical use of the HUD.

5.2.1.4.6. Voluntary Consent statement(s) with patient signature and date lines.

5.2.1.4.7. Physician Certification statement with physician signature and date lines.

Note: See Appendix U for HUD consent template

5.2.2. Materials must be submitted to the IRB (via RCA or the Methodist IRB office, as appropriate) according to the published deadlines for the IRB meetings.

5.3. **Continuing Responsibilities for the Use of a HUD**

5.3.1. In accordance with 21 CFR 56.109(f), the IRB must conduct continuing review of research (in this case, the use of the HUD) at intervals appropriate to the degree of risk, but no less than once per year.

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5.3.2. The RCA or Methodist IRB office will provide the physician-investigator with a continuing review form at the appropriate time for completion. Continuing review of the use of a HUD must occur within the appropriate timeframe as specified by the IRB or the use of the HUD must cease until such time that it can be reviewed.

5.3.2.1. The physician-investigator should track and/or be prepared to report the following at the time of continuing review:

5.3.2.1.1. The number of patients who received the HUD for all physicians/investigators listed on the project since the last review.

5.3.2.1.2. All unanticipated problems, including serious adverse events and deviations since the last review. **Note: HUD physicians/investigators must comply with the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.**

5.3.2.1.3. Summary of actual benefits experienced by enrolled HDE patients.

5.3.2.1.4. Any recent published/presented literature having a significant impact on the HUD's use and well-being of patients.

5.3.2.1.5. Any audits conducted since the last review from a federal agency that identified significant deviations or problems.

5.3.2.1.6. Any new conflicts of interest that have arisen since the last review.

5.4. **Modifications to the HUD or Device Labeling**

5.4.1. After the FDA has granted approval for use of the HUD for additional clinical indications, IRB approval is required before the HUD can be used for these additional indications.

5.4.2. The physician-investigator should submit the following documentation to the IRB for review of a HUD modification:

5.4.2.1. An amendment form describing the modifications to the device, the proposed clinical use of the device, and the rationale for such modification(s).

5.4.2.2. A copy of the FDA's approval of the modification.

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5.4.2.3. A copy of the HUD manufacturer's amendments to the HUD product labeling, clinical brochure, and/or other pertinent manufacturer information materials corresponding to the requested modification(s).

5.4.2.4. A copy of the revised clinical use statement and clinical consent form with the modifications highlighted.

5.5. **Off-Label Use of a HUD in Emergency or Compassionate Situations**

5.5.1. It is recognized that there may be circumstances in which "off-label" use of a HUD may be necessary to save the life or protect the well-being of a patient. When this situation arises, the physician-investigator should:

5.5.1.1. Determine if the situation meets the requirements for a one-time emergency use. To make this determination and for additional information on how to proceed, the procedures outlined in the IUPUI/Clarian SOP for Emergency Use of an Investigational Agent should be followed.

5.5.1.2. If the emergency use does not qualify for the one-time emergency procedure, a new study application needs to be completed and submitted according to the process outlined in the IUPUI/Clarian SOP for Emergency Use of an Investigational Agent. In emergency situations, the RCA or Methodist IRB office may convene an emergency IRB meeting to consider the emergency use.

5.5.2. Prior to requesting emergency or compassionate use from the IRB, the following should occur:

5.5.2.1. The device manufacturer (i.e. IDE holder) must obtain approval from the FDA for the "off-label" use of the HUD.

5.5.2.2. The physician-investigator must obtain authorization for the proposed "off-label" use of the HUD from the device manufacturer (i.e. IDE holder).

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Title:	Informed Consent			
Current Version:	03/08		Previous Versions:	09/04, 02/05, 04/05, 06/05

1. INTRODUCTION

The ethical conduct of research on human subjects is based upon the voluntary consent of the subject who has been appropriately informed of the study's risks and benefits. Informed consent is an ongoing process that provides 1) the prospective subject or the subject's legally authorized representative with adequate information pertaining to the research study; 2) sufficient opportunity to consider aspects of the research, including the risks and benefits, and whether or not to participate; and 3) the opportunity for the subject to ask questions and receive answers to those questions; thus, minimizing the possibility of coercion or undue influence. Unless waived by the Institutional Review Board (IRB), the informed consent process must be appropriately performed and documented. In clinical research, documentation must be done in the source documents for each subject. It is the responsibility of the principal investigator to obtain IRB approval or waiver for the informed consent process to be used and to ensure that all federal and state regulations and IUPUI/Clarian policies have been satisfied in the language of the informed consent documents, as well as by the process, and that any informed consent documents have been approved by IRB prior to being presented to potential subjects.

2. OBJECTIVE

The objective of this SOP is to describe activities and procedures for obtaining and documenting informed consent in research involving human subjects.

3. SCOPE

This SOP applies to all personnel involved in the implementation and coordination of research involving human subjects by all departments of IUPUI/Clarian. Personnel responsible include principal investigator/co-investigator(s), *others delegated by the investigator*, research coordinators or field staff (e.g. students, hourly staff), and others appropriately experienced and trained. (See SOP for Research Personnel Requirements).

4. DEFINITIONS

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5. POLICY AND PROCEDURE

5.1. Pursuant to 45 CFR 46.116 and 21 CFR 50.20, unless waived or altered, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue

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influence. The information that is given to the subject or the representative (whether oral or in writing) shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include or have the appearance of including any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

5.2. **The Informed Consent Document.** Pursuant to 45 CFR 46.116 and 21 CFR 50.25, certain basic elements must be included in any informed consent document that is presented to potential research subjects. Additional elements should be included, when appropriate. An informed consent checklist and template are available at: http://www.iupui.edu/%7Eresgrad/spon/download2.htm. Basic elements required in the informed consent include:

5.2.1 A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, including identification of any procedures that are experimental;

5.2.2 A description of any reasonably foreseeable risks or discomforts to the subjects. If relevant animal data are available, the significance should be explained to potential participants;

5.2.3 A description of any benefits to the subject or to others which may reasonably be expected from the research;

5.2.4 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

5.2.5 A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, including a statement that notes the possibility that specific regulatory authorities (e.g. DHHS, FDA) may inspect the records;

5.2.6 For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

5.2.7 An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights , and whom to contact in the event of a research-related injury to the subject; and

5.2.8 A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the

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subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. Language limiting the subject's right to withdraw from the study is not permitted.

NOTE: If a subject wishes to discontinue participation in the research and the investigator would like to continue to follow the subject's health and collect clinical data from his/her medical records, a separate IRB-approved informed consent containing all required elements must be developed and presented to the subject at the time of his/her withdrawal from the study requesting this follow-up to be done. The subject must give permission (i.e. sign this separate informed consent document) in order for clinical data to be collected.

5.3. When appropriate and pursuant to 45 CFR 46.116(b) and 21 CFR 50.25(b), one or more of the following additional elements are required in the informed consent:

5.3.1 A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable. If measures to prevent pregnancy should be taken while in the study, that should also be explained;

5.3.2 Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent. An unexplained statement that the investigator or sponsor may withdraw subjects at any time, does not adequately inform the subjects of anticipated circumstances for such withdrawal. A statement that the investigator may withdraw subjects if they do not "follow study procedures" is not appropriate. Subjects are not in a position to know all the study procedures. Subjects may be informed; however, that they may be withdrawn if they do not follow the instructions given to them by the investigator;

5.3.3 Any additional costs to the subject that may result from participation in the research;

5.3.4 The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject. An unexplained statement that the subject will be asked to submit to tests prior to withdrawal, does not adequately inform the subjects why the tests are necessary for the subject's welfare.;

5.3.5 A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

5.3.6 The approximate number of subjects involved in the study.

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5.4. The IRB follows applicable Federal, state, or local laws, which may require additional information to be disclosed in order for informed consent to be legally effective.

5.5. Additionally, the IRB may require that information, in addition to that specifically required by applicable regulation, be given to subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

5.6. For studies conducted or supported by PHS involving HIV testing, PHS requires that subjects whose test results are associated with personal identifiers must be informed of their own test results and provided the opportunity to receive appropriate counseling unless the situation calls for an exception under special circumstances.

5.7. **The Informed Consent Process.** Informed consent is more than just a signature on a form, it is a process of information exchange that may include, in addition to reading and signing the informed consent document, subject recruitment materials, verbal instructions, question/answer sessions, and measures of subject understanding. The responsibility for ensuring that the informed consent process is adequate is shared by research sponsors, investigators, and the IRB. The following should be considered when consenting a subject to a research study:

5.7.1 The consent process begins when a potential research subject is initially contacted. This means that the use of direct advertising is the start of the informed consent and subject selection process.

5.7.2 Giving the subject adequate information concerning the research in language that is as non-technical as possible (eighth grade language or lower if more appropriate for subject population);

5.7.3 Providing ample time and opportunity for the subject or the subject's legally authorized representative to inquire about the details of the research project and to decide whether or not to participate in the research, as well as to consider other available options, if any;

5.7.4 Responding to subject's or the subject's legally authorized representative's questions to his/her/their satisfaction;

5.7.5 Ensuring to the degree possible that the subject has comprehended the information provided about the research;

5.7.6 Obtaining the subject's or the subject's legally authorized representative's voluntary consent;

5.7.7 Documenting that the process has occurred;

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5.7.8 Continuing the informed consent process throughout the subject's participation in the study.

5.8. **PI Responsibilities Regarding the Informed Consent Document**

5.8.1 Unless informed consent is waived, the PI must ensure that informed consent is obtained from each research subject or subject's legally authorized representative (LAR) before participation in the research study may begin.

5.8.2 Although the PI is ultimately responsible for assuring that an appropriate informed consent process is approved and carried out; he/she is not required to personally conduct the consent interview. If permitted by the IRB, the PI may delegate the responsibility of conducting the consent interview, including obtaining informed consent, to appropriate members of the research team. The PI is responsible for assuring that any such designee is knowledgeable about the specific research study and the process of informed consent. Because the IRB needs to be aware of who will be conducting the consent interview, the PI's designee, as well as any member of the research team interacting with subjects as part of the informed consent process, must be listed on the summary safeguard statement and pass the IUPUI human subjects protection test.

5.8.3 A copy of the consent document must be provided to the subject (or LAR) and the original signed consent document must be retained in the study records. A copy of the consent document should also be placed in the subject's medical record, if appropriate. The copy provided to subjects does not need to be signed, although a photocopy with signature(s) is preferred.

5.8.4 **Subjects Enrolled at the VA**. The original signed consent document must be retained in the study records, with a copy of the consent document placed in the subject's medical record, along with a progress note documenting the informed consent process. For subjects enrolled at the VA, however, an original signed consent document must be provided to the subject (or LAR).

5.8.5 Although the PI is ultimately responsible for assuring that the content of the written consent document, if required, is in compliance with IRB requirements and GCP regulations, if applicable; he/she PI may delegate the development of the consent document to appropriate members of the research team.

5.8.6 Upon identification of a potential study subject, the PI or appropriate member of the research team will be responsible for identifying who is legally authorized to give consent for the subject, if consent is required. The PI also needs to explain when informed consent will be obtained, including any waiting period (between informing the subject and obtaining the consent) that will be observed. If the subject is physically or mentally unable to provide consent, then the legally authorized representative may be approached to give consent for the subject.

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Careful attention should be given to any potential impairment to informed consent.

5.8.7 At the time of continuing review, the PI must submit a clean copy of the currently approved consent document(s). After the IRB reviews and approves the consent document(s), it(they) will be "stamped" with a new approval and continuing review due date. This newly stamped consent document becomes the "current" consent document for the study and must be the version signed by all subjects from that date until such time that a revision to it is approved by the IRB. Previously consented subjects are not required to sign the newly approved consent document.

5.8.8 **Research involving patients.** Informed consent must be obtained from each patient prior to altering his/her care for the purpose of research. Informed consent must be obtained prior to performing any non-routine procedures, for example, testing for eligibility, if being done exclusively for the purpose of screening for, or participating in, the research study. This could be done using an abbreviated screening informed consent document and/or the regular main study consent document.

5.9. **Required Informed Consent Document Signatures**

5.9.1 The subject (or subject's LAR) must sign a copy of the stamped, IRB-approved informed consent document before any study-related procedures are initiated. In addition to signing the consent document, the subject (or LAR) must enter the date of signature on the consent document to permit verification that consent was actually obtained before the subject began participation in the study. The subject's medical records/case report form should document that the consent process occurred prior to participation in the research.

5.9.2 The person conducting the consent interview must also sign and date the informed consent document as the "person obtaining consent." The signature of the PI is not required on the consent document, unless he/she is the person conducting the consent interview.

5.9.3 There may be situations when the subject wishes to take the consent document home in order to review it and/or consider participation in the research study further before signing the consent document. In fact, all subjects should be encouraged to do so. In these situations, the person conducting the consent interview (i.e. explaining the details of the study) may sign the consent document at that time, signifying that the consent interview took place. Once the subject has decided to participate, he/she (or LAR) will sign the consent document at that time. Thus, it is possible for the signature date of the person obtaining consent to precede that of the subject.

5.9.4 **Specific VA Requirements.** Pursuant to the VHA Handbook 1200.5, Appendix C, a witness whose role is to witness the subject's or the subject's LAR's

signature must also be obtained. This individual cannot be the person obtaining consent. If a sponsor or the IRB requires a witness to the consenting process in addition to the witness to the subject's (or LAR's) signature and if the same person needs to serve both capacities, a note to that effect must be placed under the witness's signature line. See VA Form 10-1086 template.

5.9.5 When required, an impartial witness must sign and date the informed consent document signifying that the consent interview took place.

5.9.6 Other signatures must be provided as required by the sponsor and/or IRB if specified on the IRB-approved consent document.

5.10. **Revisions to the Informed Consent Document**

5.10.1 Although the PI is ultimately responsible for assuring that the written consent document and any other written information to be provided to subjects is revised whenever important new information becomes available that may be relevant to the subject's willingness to participate, he/she may delegate this responsibility to appropriate members of the research team. Any such revisions must receive IRB approval prior to use.

5.10.2 When revised informed consent documents have been approved by the IRB, they will be appropriately stamped with the new approval date; however, the continuing review due date will remain the same (unless the informed consent is approved at the time of continuing review). Newly enrolled subjects must sign this now approved version of the consent document.

5.10.3 While some changes to the informed consent document do not require currently enrolled subjects to reconsent, for example minor changes that do no affect the risk/benefit ratio, there are some situations that do require currently enrolled subjects to reconsent, for example, the discovery of a previously unknown serious side effect. When an already enrolled subject reconsents using a new informed consent document, a note should be made in the subject's record. Additionally, the original signed new consent document must be retained in the study records and a copy provided to the subject (or LAR). Any previously signed consent documents should be retained and not discarded.

5.10.4 In cases where subjects have completed active study or follow-up procedures and new safety information is discovered that may affect a subject's participation or long-term risks from the treatment, the subject must be informed of this new information. This may be accomplished through reconsenting subjects with a revised consent document which explains this new information or by other methods of notification approved by the IRB. The timeliness of informing subjects and/or reconsenting them will depend on the seriousness of the new information.

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5.11. Informed Consent Procedures for Non-English Speaking Subjects

5.11.1 Pursuant to 45 CFR 46.116 and 21 CFR 50.20, information that is given to a subject or a subject's representative shall be in language understandable to the subject or the representative. Thus, when speaking to a potential subject who speaks English, the consent interview shall be conducted in English and the consent document shall be written in English. Likewise, when speaking to a potential subject who does not speak English, the consent interview shall be conducted in a language understandable to the individual and the consent document shall be written in a language understandable to the individual. If the investigator anticipates that non-English speaking individuals will likely be enrolled in the study, plans for language-appropriate consent procedures should be considered and described in the IRB submission.

5.11.2 If a non-English speaking subject is unexpectedly encountered and plans do not exist for conducting the consent interview, including providing the potential subject with a language-appropriate consent document, investigators should carefully consider the ethical and legal implications of enrolling a subject when a language barrier exists. If, after careful consideration, the investigator believes it would be in the best interest of the potential subject to enroll in the study and there is not time to develop and submit a language-appropriate consent document to the IRB for review, the subject may still be enrolled as long as the consent interview is conducted in a language understandable to the subject, for example, with the use of a translator or other appropriate individual. This process shall be documented in the subject's records. The translator or other appropriate individual should be part of the ongoing communication throughout the research study. However, ongoing verbal translation of the consent document for either one or multiple subjects cannot substitute a translated consent document. If such a situation occurs, it shall be reported to the IRB within five (5) business days using the Prompt Reporting Form. The IRB will consider the circumstances of the subject's enrollment and determine the appropriateness of requiring the investigator to develop a language-appropriate consent document for future enrollment purposes.

5.12. Informed Consent Procedures for Illiterate English-Speaking Subjects

5.12.1 A person who can understand and comprehend spoken English, but does not read or write, can be enrolled in a study. However, special care must be taken to ensure the individual is able to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained verbally.

5.12.2 The informed consent document should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study, such as signing the consent document, or "making their mark," if appropriate.

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5.12.3 An impartial witness should witness the entire consent process and sign the consent document. Although not required, a video tape recording of the consent interview is recommended.

5.13. Informed Consent Procedures Via Telephone

5.13.1 There may be situations when obtaining informed consent from subjects over the **telephone** is appropriate. In these situations, the person obtaining consent must document that the informed consent process took place by making appropriate notation regarding the process in the proper files.

5.13.2 Informed consent may only be obtained via telephone when written documentation of informed consent has been waived by the IRB. Alternatively, if subjects will be signing the informed consent document after having discussed the research study with a member of the research team over the telephone, a waiver of written documentation of the informed consent is not required. In this case, the person discussing the research study with the potential subject should sign and date the consent document prior to mailing or faxing it to the potential subject. Appropriate notation should be made in the subject's records indicating that the process took place. Once the subject receives, signs, and returns the informed consent document to the study site, the document should again be signed and dated by the appropriate member of the research team who receives the document. **Before implementing either of these processes, the PI must first obtain appropriate IRB approval to do so.**

5.14. Informed Consent Procedures Via Fax

5.14.1 There may also be situations when obtaining informed consent from subjects via **fax** is appropriate. This is acceptable in situations where the informed consent process has already been appropriately conducted in person. For example, it is acceptable for the informed consent process to take place in person, to allow the potential subject time to take the consent document home in order to consider participation, and then have the subject sign and fax the informed consent document back to the research site. In this case, the consenter should sign the informed consent document and make appropriate notes to the subject's records upon completion of the informed consent discussion. The subject may then fax a signed copy of the informed consent document to the research site (preferably to the consenter and/or investigator). Upon receipt, the PI or appropriate designee should again sign and date the document as acknowledgement of receipt and make appropriate notations to the subject's record. The subject should still return the signed original informed consent document (either at the next visit or via mail) to the research site at his/her earliest opportunity. The appropriate recipient of the signed original informed consent document should sign and date it, file it with the faxed copy, and make appropriate notes to the subject's record. The notes to file coinciding with the dates and signatures on the informed consent documents provide the source documentation that confirm and explain how the process occurred.

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5.15. **Informed Consent Procedures With Special Populations.** Because of the special vulnerability of certain populations of subjects, including children, prisoners, pregnant women, and cognitively impaired individuals, federal regulations, state and local laws, and institutional policies require additional protections regarding their consent to participate in a research study. Please see the Vulnerable Populations SOP for guidance on the additional consent requirements when involving these vulnerable populations in research.

5.16. **Alteration or Waiver of Informed Consent**

5.16.1 Pursuant to 45 CFR 46.116(c), the IRB may approve a consent procedure which does not include, or which alters some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

5.16.1.1 The research or demonstration project is to be conducted by or subject to the approval of state or local government officials, and is designed to study, evaluate, or otherwise examine: (i) public benefit of service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternative to those programs or procedures, or (iv) Possible changes in methods or levels of payment for benefits or services under those programs;

5.16.1.2 The research could not practicably be carried out without the waiver or alteration;

5.16.1.3 The research is not subject to FDA regulations.

5.16.2 Pursuant to 45 CFR 46.116(d), the IRB may approve a consent procedure which does not include, or which alters some or all of the elements of informed consent set forth above, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

5.16.2.1 The research procedure involves no more than minimal risk to the subjects;

5.16.2.2 The waiver or alteration will not adversely affect the rights and welfare of the subjects;

5.16.2.3 The research could not practicably be carried out without the waiver or alteration (Note: The IRB typically considers face-to-face interaction between the PI, or other member of the research team, and the subject to practicably enable the informed consent process to take place, and thus would likely not grant a waiver of the informed consent process);

5.16.2.4 Whenever appropriate, the subjects will be provided with additional pertinent information after participation; and

5.16.2.5 The research is not subject to FDA regulations.

5.16.3 The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for information consent to be legally effective.

5.16.4 Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

5.17. **Documentation of Informed Consent**.

5.17.1 Pursuant to 45 CFR 46.117(a), except as provided at 45 CFR 46.117(c), informed consent shall be documented by the use of a written consent document approved by the IRB and signed and dated by the subject or the subject's representative at the time of consent. A copy shall be given to the person signing the form.

5.17.2 Pursuant to 45 CFR 46.117(b)(1), the written consent document must embody the elements of informed consent required by §46.116, unless the IRB has approved a waiver or modification of informed consent. The investigator shall give the subject and/or the subject's representative adequate opportunity to read it before it is signed. This institution does not allow the use of short form written consent documents as described in 45 CFR 46.117(b)(2).

5.17.3 Pursuant to 45 CFR 46.117(c) and 21 CFR 56.109(c)(1), the IRB may waive the requirement for the investigator to obtain a signed consent document for some or all subjects if it finds and documents either:

5.17.3.1 That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. The research is not subject to FDA regulations; or

5.17.3.2 The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; and

5.17.4 In cases in which the documentation requirement for informed consent is waived, the investigator shall still provide subjects with a written document that includes

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all elements of an informed consent document (unless otherwise waived by the IRB), which the IRB must review and approve.

5.17.5 The investigator may request these alterations or waivers to the informed consent process by completing the appropriate section of the summary safeguard statement. The IRB will use the responses provided within that section in considering this request.

5.18. **Exception from Informed Consent Requirements for Planned Emergency Research.** Pursuant to 21 CFR 50.24, the IRB may approve a clinical investigation without requiring that informed consent of all research subjects be obtained. Please see the SOP on Emergency Use of Investigational Agents for additional information.

5.19. **Exception from Informed Consent Requirements for Clinical Investigations.** Pursuant to 21 CFR 50.23(a), there are certain allowable circumstances when an exception to the informed consent requirements may be appropriate. Please see the SOP on Emergency Use of Investigational Agents for additional information.

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Title:	Investigational Device Accountability			
Current Version:	07/07		Previous Versions:	06/05, 02/05, 12/04, 02/03

1. INTRODUCTION

Pursuant to 21 CFR 812.100, the investigator is responsible for control of devices under investigation. This standard operating procedure (SOP) describes the policy at IUPUI/Clarian for the responsible accountability of medical devices and radiologics (hereafter jointly referred to as study devices) being tested in IUPUI/Clarian IRB approved research studies involving human subjects. This accountability includes: receipt, labeling, storage, dispensing, reconciliation and return or authorized destruction of the study devices, and suggested procedural operations to fulfill this policy. The Food and Drug Administration oversees medical devices and radiologics through their Center for Device and Radiological Health (CDRH). This SOP is not meant to replace, but to supplement federal regulations, the study protocol and to assist the investigator with compliance.

2. OBJECTIVE(S)

2.1. To create uniform study device dispensing and accountability standards;

2.2. To provide the minimal standards necessary to conform to regulations created by the United States Food and Drug Administration, and the Center for Device and Radiologic Health (CDRH); and

2.3. To ensure appropriate implementation of specific device accountability procedures from Sponsors as applicable.

3. SCOPE

This SOP applies to all device studies that involve human subjects, which are approved by an IUPUI/Clarian IRB and (when applicable) the appropriate Radiation Safety Committee. This includes but is not limited to Sponsored and Investigator Initiated Studies, with or without an Investigational Device Exemption (IDE). This SOP may be used as a reference to assist those investigators conducting human subjects research involving devices or radiation-emitting products, for a non-medical (i.e. non-therapeutic or non-diagnostic, etc.) research, that is subject to FDA regulations.

4. DEFINITIONS

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5. POLICY

The guidelines to dispense investigational device products at facilities associated with Clarian Health, Wishard Memorial Hospital, Roudebush VAMC and all other affiliates of Indiana University as defined by the Federal Wide Assurance are delineated below.

5.1. Investigators conducting studies in which investigational devices will be used must demonstrate understanding of the handling and control of investigational test articles by reviewing the Investigational Device Accountability SOP.

5.2. **Receipt and inventory of study device**. This section applies to those study devices the investigator dispenses/administers to the study subject. The investigator (or designated research associate) is responsible for ensuring that:

5.2.1 Upon receipt (preferable within 2 working days, but definitely prior to dispensing) of the study device, inventory the shipment, ensuring that the information on the packing slip matches exactly with what has been sent to the site, including the receipt date, lot numbers, device type, batch number, code mark, and quantity. Additionally, the identification of the person who received the shipment of devices should be noted. Documentation of this shipment inventory should be maintained.

5.2.2 Promptly (usually within 2-3 working days) bring any discrepancies to the attention of the Sponsor/supplier of the device(s).

5.2.3 Retain a copy of the shipping inventory, packing slips and document inventory in the study files.

5.2.4 Maintain an accountability log (most Sponsors will issue/supply a device accountability log). See also Sample Device Accountability Log.

5.3. **Study device labeling**

5.3.1 Study devices from Sponsor companies are pre-labeled and these should not be defaced, relabeled or changed in any way without written permission of the Sponsor. It is recommended that an additional label may be placed to include the study staff contact name/number, but ONLY if the Sponsor agrees.

5.3.2 If the Principal Investigator is responsible for labeling, he/she should be aware of applicable FDA regulations. Examples of what may appear on a label are: name of device, model number, serial number, and manufacturer.

5.3.3 When a study device is designated as "Investigational" per FDA regulations, there should be a label with the following information:

- Name and place of business of the manufacturer, packer, or distributor.

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- Quantity of contents if appropriate, and the following statement: "CAUTION-Investigational device. Limited by Federal (or United States) law to investigational use."
- The label or other labeling shall describe all relevant contraindications, hazards, side effects, interfering substances or devices, warnings, and precautions.

5.4. **Storage of the study device (including devices that record data from automated instruments)**

5.4.1 Establish and maintain access controls for essential and appropriate research personnel.

5.4.2 Develop procedures for verifying physical access.

5.4.3 Store the study device in a secure environment to include locks on doors and controlled access.

5.4.4 Establish equipment control both into and out of the research site.

5.4.5 Develop Security Incident Procedures to report any privacy breaches.

5.4.6 Assess any privacy risks anticipated and develop methods to avoid those risks.

5.4.7 Develop data backup, storage, and emergency mode procedures, if applicable.

5.4.8 Ensure the study device is stored at the appropriate temperature, and maintain a storage area temperature log, if appropriate.

5.5. **Dispensing of study device**

5.5.1 The investigator shall permit an investigational device to be used only with participants under his/her personal supervision or under the supervision of a co-investigator responsible to the investigator.

5.5.2 The investigator shall not use or supply an investigational device to any person not authorized to receive it.

5.5.3 Create an access log to document each time the study device is dispensed/used, where it is dispensed/used, to whom it is dispensed/used, and the date and signature or initials of the person dispensing/using the study device, (plus any other information dictated by the study protocol).

5.6. **Return/destruction of study device (as applicable to the specific device)**

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5.6.1 At the conclusion of the study, ensure that all documentation regarding receipt, storage, dispensing, return of used containers, and accountability is complete and accurate.

5.6.2 An explanation of why and how many device units have been returned to the sponsor, repaired, or otherwise disposed of should be noted. When a device is disposed of, the identification of the person who doing so should also be noted.

5.6.3 Devices obtained from a Sponsor for the specific purpose of a research study must be returned to Sponsor. Only with the written authorization (i.e. in the protocol or other written correspondence) of the Sponsor (and in compliance with Federal regulations and Institutional policies) may the investigator discard the device on site, or retain the device.

5.6.4 Pursuant to 21 CFR 812.110, upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

5.6.4.1 Unused study devices that include individually identifiable health information must **not** be transferred to other investigators without IRB approval or an authorization from the study subject.

5.6.4.2 Unused study devices without individually identifiable health information must not be transferred to other investigators, used for animal research, or dispensed to non-study patients unless written consent is obtained from the Sponsor/Provider of the device.

5.6.5 Device study records must be kept for a duration of seven years (according to federal regulations and the IUPUI/Clarian SOP for Data Management).

5.7. **Research on FDA approved devices for FDA approved indications**

5.7.1 Requires documentation of receipt, storage, dispensing and return of the device as above.

5.7.2 The FDA approved label is adequate, although including information specific to the study is recommended.

5.8. **Radiologics**

Radiation emitting devices have similar requirements as above. However, there may be specific requirements based on the device and the study design and thus each study should be discussed with the Radiation Safety Officer at the Institution where the study is conducted.

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Title:	Investigational Drug Accountability			
Current Version:	07/07		Previous Versions:	02/05, 06/05

1. INTRODUCTION

Pursuant to 21 CFR 312.60, the investigator is responsible for the control of drugs under investigation. This standard operating procedure (SOP) describes the policy at IUPUI/Clarian for the responsible accountability of investigational drugs and biologics. This accountability includes: receipt, storage, labeling, prescribing, dispensing, reconciliation and return or authorized destruction of the investigational drug (biologic), and suggested procedural operations to fulfill this policy. The Code of Federal Regulations for drugs and biologics does not differ and, thus, the term "drug" used in this SOP can be interchanged with biologics.

2. OBJECTIVE(S)

2.1. To create uniform study drug dispensing and accountability standards.

2.2. To provide the minimal standards necessary to conform to regulations created by the Indiana Board of Pharmacy and United States Food and Drug Administration.

2.3. To ensure appropriate implementation of specific drug accountability procedures from the study protocol, Sponsors , and supplier of the investigational drug, as applicable.

3. SCOPE

These policies and procedures apply to all clinical investigations that fall under the jurisdiction of the IUPUI/Clarian IRBs involving investigational drugs or biologics. This SOP is meant to compliment applicable federal and state regulations, Institutional policies and the IRB approved study protocol. While drug studies not subject to 21 CFR 312 are not covered by this SOP, it is strongly suggested that those studies use this SOP for guidance. For studies not subject to 21 CFR 312, the Investigator must comply with all applicable federal and state regulations, Institutional policies and the IRB approved study protocol.

4. DEFINITIONS

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5. POLICIES AND ASSOCIATED PROCEDURES

The guidelines to dispense investigational drug products at facilities associated with Clarian Health, Wishard Memorial Hospital, Roudebush VAMC and all other affiliates of Indiana University as defined by the Federalwide Assurance are delineated below. In most cases, the type of drug under investigation as well as the facility where the protocol will be conducted dictates the dispensing procedures that need to be utilized. For instance, a protocol requiring the admixture of an intravenous product will have dispensing

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guidelines that differ from a protocol requiring dispensing of a tablet formulation that utilizes unit-dose packaging. In addition, inpatient studies have different dispensing guidelines than outpatient studies.

5.1. Use of Investigational Drug Services

5.1.1 Inpatient studies

5.1.1.1 All inpatient studies being conducted at a Clarian, Wishard or Roudebush VA hospital **should** utilize the Investigational Drug Service (IDS) provided by the hospital's pharmacy department.

5.1.1.2 The only exceptions to not using IDS are:

- Studies conducted at Centers that have their own Investigational drug dispensing policies, e.g. The General Clinical Research Center (GCRC) at University Hospital, or the Eli Lilly Research Center.
- If the PI (after consulting with IDS) determines that they have the manpower, facilities, knowledge and time to assume all the duties the IDS would have provided.

5.1.2 Outpatient studies

5.1.2.1 Those conducting outpatient studies may utilize an IDS if they choose.

5.1.2.2 There are a number of situations in which use of IDS for an outpatient study is strongly recommended. Some examples include investigational drug(s):

- that require preparation in a sterile hood (ALL IV drugs),
- that require admixing of any kind, and
- studies that require third party blinding[4.2].

For a description of Investigational Drug Pharmacies, the services they provide and contact information, see attached Resources sheet.

5.1.2.3 Hospitalization: If a subject in an outpatient study is hospitalized, and the study drug needs to be administered to the subject while in the hospital, a physician caring for the subject should write an order that allows the subjects to continue to take the investigational drug from their own supply. The order must clearly document that the subject is enrolled in a study with an investigational drug. If the study investigator used an Investigational Drug Service (IDS) to dispense the study drug(s), he/she, upon becoming aware of the subject's hospitalization, should make the (dispensing) IDS aware of the hospitalization.

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5.1.3 If the investigator will not be using the IDS, he/she must demonstrate understanding of the handling and control of investigational test articles by reviewing the Investigational Drug Accountability SOP.

5.2. **Study Drug Prescription/Order**

5.2.1 Study drugs will be dispensed only by those who are authorized by the IRB approved protocol, Principal Investigator (PI), state and federal regulations, and hospital/clinic policies. This may include the nurses (LPN or RN) within this department and the MDs, DOs, DDSs, Podiatrists or PharmDs and others listed as sub/co-investigators on the IRB Summary Safeguard Statement.

5.2.2 Study drug will be dispensed according to the dose, route and frequency written in the specific protocol.

5.2.3 Standing additional orders (compliant with the study protocol) may be written and placed in the individual subject's chart.

5.2.4 Used containers and unused study drug will be collected back from the subject(s). Exception: If the study protocol (in compliance with federal and state regulations and Institution facility policies) states other means of disposition.

5.2.5 Subjects will be properly instructed in the storage, use and precautions and potential known risks of the study drug.

5.2.6 Study drug will be properly accounted for and tracked with adequate documentation.

5.2.7 Deviations from the (IRB approved) protocol described treatment are only allowed if it is to protect the subject from newly discovered risks.

5.3. **Receipt and inventory of study drug**

5.3.1 The PI or designated individual will:

5.3.1.1 Upon receipt of the investigational drug, inventory the shipment, ensuring that the information on the packing slip matches exactly with what has been sent to the site, including the amount, lot numbers and quantity and document the results of this inventory.

5.3.1.2 Promptly bring any discrepancies, breakage or evidence of tampering to the attention of the Sponsor.

5.3.1.3 Retain a copy of the shipping inventory, packing slips and document inventory in the study's records.

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5.3.1.4 For all FDA-regulated studies, all progress reports related to the drug shall be furnished to the drug sponsor who is responsible for collecting and evaluating the results. The sponsor shall then submit annual reports to the FDA on the progress of the study.

5.4. **Study drug labeling**

The goal is to provide enough information that appropriate care of the subject can be given in an emergency situation.

5.4.1 Study drugs from Sponsoring companies are pre-labeled and these should not be defaced, relabeled or changed in any way without written permission of the Sponsor. It is recommended that an additional label be placed to include the study staff contact name/number, but ONLY if the Sponsor agrees.

5.4.2 If the Investigator is responsible for labeling, he/she should utilize an IDS whenever possible.

5.4.3 There are certain state labeling requirements. If study drug is to be dispensed by study personnel (i.e., performed locally by the investigator or local pharmacy) under the IND of a University faculty member, the minimal labeling requirements include:

5.4.3.1 Name of institution.

5.4.3.2 Full name of subject and/or subject number/initials*.
For a prescription drug(s), the subject's full name is required.

5.4.3.3 Name of study drug/placebo.

5.4.3.4 Directions for use by the subject and amount to be taken by the subject. Prescription drugs also require a cautionary statement.

5.4.3.5 Name of authorized prescriber and telephone or pager number.

5.4.3.6 Required precautionary information, (e.g. Controlled Substance information, if applicable, food, water, alcohol, etc. restrictions or requirements. Federal and State laws also require the placement of a No Transfer label if it is a controlled substance (i.e. "Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed").

5.5. **Storage of the study drug**

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The study drug(s) shall be stored in a secure environment, with access limited to essential and appropriate research personnel, according to the storage requirements detailed in the protocol or supplied by the Sponsor in a supplementary document. The drug(s) shall be kept locked (i.e. cabinet) in a locked/secure area. The study drug(s) shall be stored at the appropriate temperature, with an area temperature log maintained, if appropriate. Follow any special requirements for Controlled Substances required at the investigative site in addition to those specified by the regulations.

5.6. **Dispensing an Investigational Drug**

5.6.1 The investigator shall dispense or administer the investigational drug only to subjects under his/her personal supervision or under the supervision of a co-investigator responsible to the investigator.

5.6.2 The investigator shall not dispense or supply the investigational drug to any person not authorized to receive it.

5.6.3 If an investigator conducting an outpatient study wishes to dispense study drug(s) from his/her office/clinic, the following steps documented in the protocol or in the study record file should be done **prior** to initiation of the study:

5.6.3.1 Define and document who is authorized to prescribe/write orders for the study drug (investigator and sub-investigators, who are listed on the IRB Summary Safeguard Statement and, for IND studies, the Form 1572).

5.6.3.2 Documentation of the order or prescription (an order form, or script) signed by those who are authorized (by law and according to section 5.6.1.1 of this SOP).

5.6.3.3 Document any changes, titrations, or deviations to dosing orders or to protocol dosing with a signature by those authorized to write orders. The investigator must appropriately report any dosing changes to the IRB if they represent events that require prompt reporting to the IRB as described in the Unanticipated Problems and Noncompliance SOP

5.6.3.4 Report any deviations from the protocol dosing schedule to the IRB.

5.6.3.5 Define and document who may dispense study drugs (PI, sub-PI, coordinator, other research personnel; see attached sample).

5.6.3.6 Assemble a signature and initial list for all involved in study (see attached sample).

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5.6.4 Each time study drug is dispensed, document the amount dispensed, to whom it is dispensed, the date and the signature or initials of the person dispensing drug. The dispenser may be the Clarian, Wishard or VA IDS pharmacy, or the authorized study staff.

5.6.5 Advise subjects to return all used and unused containers/units to the site of original dispensing. Study personnel should record the amount (number of bottles and pills) and date of return. Document attempts to retrieve the containers/units from the subject who has not returned it. A certified letter may serve as a final attempt.

5.6.6 Note any discrepancies between amounts used (actual or suspected) by subjects and amounts returned. Document the reasons for discrepancies. If major discrepancies are encountered, immediately follow up with subjects and/or the pharmacy to obtain an explanation.

5.6.7 Special circumstances for distributing drug to subjects require the authorization of the Sponsor.

5.6.8 Alternative sites of administration of the drug (e.g., outlying clinics) not listed on the FDA 1572 and/or the Summary Safeguard Statement must be approved by the Sponsor and require an amendment to the Summary Safeguard Statement.

5.7. **Return/destruction of study drug.**

5.7.1 If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR 312.59.

5.7.2 Drug obtained from a Sponsor for the specific purpose of a research study must be returned to Sponsor or be discarded on site upon written authorization from the Sponsor to do so. Contact the facility pharmacy for instructions for appropriate procedures if on-site destruction of investigational drug is performed,

5.7.3 Unused study drug must **NOT** be passed on to other Investigators, used for animal research, or dispensed to non-study subjects.

5.7.4 Drug study records must be kept for a duration of years according to the IUPUI/Clarian SOP for Data Management, federal regulations and the study protocol.

5.8. **Investigator Recordkeeping and Record Retention**

5.8.1 The investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by participants.

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5.9. **Studies Sponsored/Supported by a Federal Agency.**

The guidelines for investigational drug handling in studies sponsored or supported by NIH, DOD, CDC, etc. may differ from the FDA and, therefore, it is the PI's responsibility for insuring that all appropriate regulatory policies are followed. Contact the specific funding institute for appropriate procedures.

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Title:	IRB Operations			
Current Version:	07/07		Previous Versions:	08/05, 05/05, 04/05, 02/05

1. INTRODUCTION

The Indiana University Purdue University Indianapolis (IUPUI)/Clarian Health Partners (Clarian) IRB was established to protect the rights and welfare of human research subjects. The IRB is charged with ensuring that those individuals participating in research are not subject to undue or inappropriate risks, that participation remains a voluntary right, and that the conduct of research is upheld as a privilege. The Belmont Report established three basic ethical principles – autonomy/respect for persons, beneficence, and justice – which is the cornerstone for regulations involving human subjects. It is these three basic ethical principles that IUPUI and Clarian follow to govern the conduct of human subjects research.

Pursuant to the federal regulations on human subjects research (45 CFR 46, Protection of Human Subjects, also known as "the Common Rule"), institutions engaged in human subjects research (not otherwise exempt) that is conducted or supported by any agency of the U.S. Department of Health and Human Services (DHHS) must have an Office for Human Research Protections (OHRP)-approved assurance of compliance for the protection of human subjects. This is known as a Federalwide Assurance (FWA). IUPUI, Clarian, and their affiliates each have an OHRP-approved FWA. These FWAs apply to all human subjects research conducted at or on behalf of these institutions, regardless of the source of support for a particular research activity.

Because IUPUI, Clarian, and their affiliates conduct research with human subjects supported by and/or subject to regulations and requirements in addition to 45 CFR 46, these institutions will also comply with regulations and requirements, when appropriate. This includes, but is not limited to, clinical investigations regulated by the Food and Drug Administration (FDA), research involving human subjects supported by the Department of Education, Department of Defense, Department of Veterans Affairs, or the Bureau of Prisons .

IUPUI/Clarian have seven (7) IRBs that are charged with understanding and applying their obligation to protect the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable University and Clarian policies and federal and state regulations. To that end, the IUPUI and Clarian IRBs will maintain and implement consistent policies and procedures.

2. OBJECTIVE

The objectives of this SOP are to:

2.1 Describe documentation required by local laws and federal and state regulations regarding the composition and procedures of the various IUPUI/Clarian IRBs; and

2.2 Outline the process of IRB approval before, and where applicable, during research.

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3. SCOPE

These policies and procedures apply to all research activities of faculty, staff, student, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVANT DEFINITIONS

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6. POLICIES AND ASSOCIATED PROCEDURES

5.1 Authority of IUPUI/Clarian Institutional Review Boards (hereafter referred to as "IRB")

5.1.1 Authority to develop, implement, and monitor all human subjects protection programs has been designated by the President of Indiana University and the Chancellor of Indiana University Purdue University Indianapolis (IUPUI) to the Vice Chancellor for Research, IUPUI (IO). The IRB is authorized by the IO to review human subjects research projects and clinical investigations conducted by faculty, staff, students, or others who fall under the jurisdiction of the IRB. All such projects and clinical investigations must be submitted for IRB review, regardless of funding source (or lack thereof). IRB approval or acknowledgement is required before a project may begin. Additionally, the IRB will review student projects to ensure appropriate ethical principles have been considered and research not subject to FDA or Common Rule definitions of human subjects research to ensure HIPAA requirements have been considered. Refer to the Checklist for Determining Whether an Activity Requires Review by the IRB for additional information.

5.1.2 Except for research that is exempted or waived under 45 CFR 46.101(b) or 45 CFR 46.101(i), all human subjects research conducted at or on behalf of IUPUI, Clarian, or their affiliates will be reviewed, prospectively approved, and subject to continuing oversight and review at least annually by the IRB. The review will address all the criteria listed in 45 CFR 46.111 and 21 CFR 111. The IRB will evaluate whether resources are adequate to protect subject's rights and welfare.

5.1.3 The IRB may approve, require modification to secure approval ("provisionally approve" or "table"), or disapprove research proposals. IRB review and approval of projects and exemption determinations are required BEFORE research can begin. IRB disapproval may not be overruled by any other Institutional authority. However, if research is approved by the IRB, but not permitted by the institution, Research Compliance Administration (RCA) will promptly notify the investigator and the IRB that the research cannot be conducted, including the reasons for that determination.

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5.1.4 The IRB may suspend, place restrictions upon, or terminate approval of research activities falling within its jurisdiction that are not being conducted in accordance with IRB requirements or that have been associated with unexpected serious harm to subjects.

5.1.5 The IRB may have the consent process, or the research procedures, of any research study under its jurisdiction observed by a third party if the IRB determines that such observation is indicated. This is typically done by the Human Subjects and HIPAA Auditor.

5.2 IRB Membership

5.2.1 Pursuant to 45 CFR 46.107(a), each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by IUPUI, Clarian, and their affiliates. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

5.2.2 Pursuant to 45 CFR 46.107(b) every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

5.2.3 Pursuant to 45 CFR 46.107(c) each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. The non-scientist's primary concerns are unambiguously in nonscientific areas, meaning little or no scientific or medical training or experience. Nurses, pharmacists and other biomedical health professionals are not considered to have "primary concerns in the non-scientific area."

5.2.4 Pursuant to 45 CFR 46.107(d) each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. This unaffiliated

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individual can have a primary concern in a nonscientific area, in which case, the individual would satisfy two of the membership requirements.

5.2.5 Pursuant to 45 CFR 46.107(e) no IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

5.2.6 Pursuant to 45 CFR 46.107(f) an IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

5.2.7 **Appointment of IRB Chairs**

5.2.7.1 **IUPUI Policy**. The IUPUI Chancellor or Chancellor's designee shall appoint Chairs of the IRBs biannually. The Chair may be reappointed for an unlimited number of terms.

5.2.7.2 **Methodist Policy.** The Executive Vice President of Academic Affairs at Clarian, with appropriate consultation, will make recommendations for the appointment of the Chair. Such recommendations will be forwarded to the IUPUI Chancellor or the Chancellor's designee, who shall appoint the Chair of the IRB biannually. The Chair may be reappointed for an unlimited number of terms.

5.2.8 **Appointment of IRB Vice Chairs**

5.2.8.1 **IUPUI Policy**: The IUPUI Chancellor or Chancellor's designee shall appoint one or more Co- or Vice Chairs biannually, who shall preside over IRB meetings in the absence of the Chair. The Co- or Vice Chair(s) may be reappointed for an unlimited number of terms.

5.2.8.2 **Methodist Policy.** The Executive Vice President of Academic Affairs at Clarian, with appropriate consultation, will make a recommendation for the appointment of the Director of the Methodist Research Institute to serve as the Vice Chair. Such recommendation will be forwarded to the IUPUI Chancellor or the Chancellor's designee who shall appoint the Vice Chair, who shall preside over meetings in the absence of the Chair. The Vice Chair may be reappointed for an unlimited number of terms.

5.2.9 **Appointment of IRB Members**

5.2.9.1 **IUPUI Policy.** Based on recommendations from IUPUI department chairs, IRB members shall be appointed by the IUPUI Chancellor or

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the Chancellor's designee. A reasonable number of alternates who may serve in the place of absent members will also be appointed. The Chair, or the Chair's designee, shall select an alternate for an absent member so as to assure, insofar as possible, that the professional diversity of the members and alternates in attendance at the meeting reflects that of the IRB membership.

5.2.9.2 **Methodist Policy.** The Chair will make recommendations for the appointment of the regular members of the IRB. The Chair shall also make recommendations for the appointment of a reasonable number of alternates who may serve in the place of absent members. These appointment recommendations will be then forwarded to the IUPUI Chancellor or Chancellor's designee, who will appoint regular and alternate members. The Chair, or the Chair's designee, shall select an alternate for an absent member so as to assure, insofar as possible, that the professional diversity of the members and alternates in attendance at the meeting reflects that of the IRB membership.

5.2.10 **IRB Members Designated by the Chair.** Individuals who are appointed as regular or alternate members of an IRB will be designated by the Chair to review study actions which qualify for review under expedited procedures.

5.2.10.1 **IRB Reviewers for Exempt and Expedited New Studies**. IRB members designated to review new study applications which qualify for review under expedited procedures (e.g., new exempt or expedited studies) will be mentored by experienced IRB members during the review of 8 new studies. After such mentoring, IRB members will be considered designated by the IRB Chair as experienced IRB reviewers. Qualified mentors have either satisfactorily provided review for at least 8 new studies or have been IRB reviewers for at least one year.

5.2.10.2 **IRB Reviewers for Minor Amendments, Expedited Continuing Reviews, Provisionally Approved Studies, and General Information Qualifying for Expedited Review**. IRB members designated to review other study actions that qualify for review under expedited procedures (e.g., minor amendments, expedited/completed continuing reviews, etc.) will be mentored by experienced IRB members during the review of 20 full-board study actions at convened IRB meetings. After such mentoring, IRB members will be considered designated by the IRB Chair as experienced IRB reviewers.

5.2.11 **VA Representation on the IRB.** Prior to the appointment of each IRB for the coming 2-year appointment cycle, the Director, Research Compliance Administration and the Administrative Officer (AO) for Research and

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Development (R&D) shall review the IRB membership for all IRBs under the auspices of the MOU.

5.2.11.1 Pursuant to Paragraph 5 (a) (3) (a) of the VHA Handbook 1200.5: (i) two or more VA employees will be appointed as voting members of the IRB on each IRB that reviews VA research; (ii) at least one of these members must be a licensed physician with scientific expertise; (iii) VA members must serve as full members of the IRB; this includes reviewing non-VA research matters coming before the IRB; (iv) at least one of the VA members of the IRB must be present during the review of VA research. Any vacancies and/or specialties required to fulfill the obligations of the IRBs shall be noted and forwarded to the chief of the department or division housing that specialty. The chief nominates a candidate to be the VA representative. The Administrative Officer forwards that name to the Director, Research Compliance Administration, then takes the membership to the R&D Committee, where it is reviewed and approved. The minutes including the approval of IRB members are forwarded to the VA Medical Center Director for approval. Other VA personnel may also submit names to the AO.

5.2.11.2 Pursuant to Paragraph 7 (f) (1) of the VHA Handbook 1200.5, if research involving an FDA-regulated article is involved, a licensed physician must be included in the IRB quorum. This physician is not required to be the VA representative.

5.2.11.3 Pursuant to Paragraph 6 (k) of the VHA Handbook 1200.5, the Medical Center Director must officially appoint members in writing."

5.2.11.4 Pursuant to Paragraph 6 (l) of the VHA Handbook 1200.5, members of VA IRBs and VA representatives to affiliate IRBs must be appointed by the Medical Center Director for a period of 3 years and may be re-appointed indefinitely."

5.2.11.5 Pursuant to Paragraph 5(i) of the VHA Handbook 1200.5, Research & Development (R&D) administration officials including, but not limited to the Associated Chief of Staff for R&D and the Administrative Officer for R&D, are prohibited from serving as voting members of the IRB.

5.2.12 **IRB Member Requirements**. All IRB members are required to read the Belmont Report, take and pass the IUPUI/Clarian Protection in Human Subjects in Research test prior to reviewing any research studies. IRB members shall also review the resources located on the IRB Member Education website, including the IRB Member Education Presentation and/or the Exempt/Expedited New Study Review Procedures.

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5.2.13 **Evaluation of IRB Members During Appointment Period**. In evaluating IRB members during the appointment period, consideration will be given to meeting attendance, quality of reviews, contributions at IRB meetings, timeliness of reviews, and evidence of understanding of applicable regulations, policies, and procedures. If, at any time, issues are raised regarding an IRB member's performance, RCA will seek resolution with the involvement of the IRB Chair, department Chair, Vice Chancellor for Research, IUPUI and/or IRB member directly, as appropriate. Potential outcomes can range from further education for the IRB member to removal from the IRB.

5.2.14 **Evaluation of IRB Members at Time of Re-Appointment**. When IRB members are formally evaluated at the time of reappointment, evaluations that occurred during their service on the IRB will be considered, as well as, input from members of the RCA staff, IRB Chairs and/or Vice Chairs, and department Chairs.

5.2.15 **COI at Time of (Re)Appointment**. Prior to (re)appointment, consideration will be given to potential conflicts of interests (COI) that would preclude an IRB member from reviewing particular studies and/or necessitate their absenting themselves from numerous discussions and voting. In this way, individuals who would not make good IRB candidates would be identified.

5.2.16 Pursuant to Indiana University's federalwide assurance, changes in IRB membership are reported to the Office for Human Research Protections (OHRP).

5.3 IRB Meetings

5.3.1 **IRB Meeting Schedules**. Each IRB ordinarily meets once per month. Meeting schedules are set annually and provided to IRB members well in advance of the meetings. The IRB Chair may, however, call additional meetings at any time if necessary.

5.3.2 **IRB Meeting Quorum**. Decisions made by the IRB are made by a majority vote of the voting members in attendance at the IRB meeting. A majority of the IRB constitutes a quorum, which must include at least one member whose primary concerns are in nonscientific areas. Frequent absence of non-affiliated (community) members is not acceptable. If quorum fails during a meeting, for example, due to lack of a majority of IRB members being present or an absence of a nonscientist member, the IRB cannot take action or vote until the quorum is restored. An IRB can also lose its quorum when members with a conflict of interest leave the room for deliberation and voting.

5.3.3 **IRB Meetings Via Telephone or Video Conference**. IRB meetings are usually held in a face-to-face manner. However, they may be conducted completely or in part by telephone or video conference, if necessary, for example, when an IRB member is unable to be present at a convened IRB meeting. In such cases, IRB

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members participating via telephone or video conference shall receive a complete set of meeting materials to be reviewed at the meeting. The majority of the IRB must participate and discussion must occur in real-time. Such IRB members are counted as part of the quorum and may vote.

5.3.4 A regular or alternate member or consultant present at the meeting having conflicting interest (e.g. involved in the study) in a matter can not vote on that matter and must be absent from the meeting during the deliberation and voting. They can, however, be in attendance to present information or answer questions if the IRB requests it.

5.4 Participation of Non-Members

5.4.1 Individuals who are not members of the IRB may attend the meetings with the consent of the IRB Chair. However, if these individuals are part of a protocol being discussed, they must excuse themselves from the meeting prior to the IRB voting.

5.4.2 **Consultants.** The IRB may invite individuals with competence in special areas to assist in the review of complex issues, which require expertise beyond or in addition to that available on the IRB. These individuals (i.e. consultants) will be independent of both the investigator and the protocol and will communicate their results of the review to the IRB either in the form of written comments or by attending the IRB meeting, as part of the process for review and approval. Such individuals may not be counted toward the quorum or participate in or vote with the IRB. The IRB cannot delegate its responsibility to judge whether the criteria for approval are met to non-members/consultants.

5.5 IRB Subcommittees

5.5.1 Subcommittees may be appointed on an ad hoc basis and must meet the following requirements:

5.5.1.1 The Chair of an IRB may appoint subcommittees or ask IRB members to execute various duties related to the objectives and policies of the IRB.

5.5.1.2 Subcommittees are composed of any number of IRB members or alternates, and other appropriate individuals or consultants.

5.5.1.3 Subcommittees do not have the authority to require any action or impose any sanction based on their findings. Their purpose is to make recommendations to the IRB for its consideration.

5.6 Other Research Review Committees

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5.6.1 **Research Review Committee:** A committee formed by the Methodist Research Institute charged to determine the scientific merit and comprehensiveness of a protocol and other submitted documents to be reviewed by the IRB. The Research Review Committee does not hold veto power. It is an informational service for the Methodist Institutional Review Board (IRB-03) whereby findings are reported to the IRB.

5.6.2 **Consent Review Committees**. A committee formed by the Methodist Research Institute charged to review the informed consent statement for completeness and accuracy to reflect the protocol and adequately inform subjects of the study. The Consent Review Committee does not hold veto power. It is an advisory service for the Methodist Institutional Review Board (IRB-03).

5.6.3 **IU Cancer Center Scientific Review Committee:** A committee formed by the IU Cancer Center to review protocols involving cancer patients. This is a requirement of the IU Cancer Center and approval from this committee must be obtained before a protocol can be submitted to the IRB.

5.6.4 Where any of the above research review committees are not required to review a protocol before it comes before the IRB, the IRB will provide scientific review for that protocol.

5.7 IRB Review Process

5.7.1 IRB members are expected to conduct an in-depth review of all materials for which they are a primary or secondary reviewer. IRB members are expected to be familiar with all other materials in the agenda packet and to be prepared for discussion at the meeting. In order to make appropriate determinations on a proposal, the IRB should be knowledgeable about the local research context in terms of where it is proposed that the research will be conducted. Knowledge of the community from which the subjects are drawn is essential to ensure the protection of subjects' rights and appropriateness of the informed consent process. Therefore, the IRB may request additional information from the investigator or consult with other individuals (i.e. consultants), if necessary, at anytime during the review process. These individuals may be contacted directly, attend the IRB meeting, or provide written information to the IRB for consideration in their review.

5.7.2 **Requirements for IRB Approval.** Based on the IRB's review of documentation provided by the investigator, and in accordance with appropriate regulations and IUPUI/Clarian policies, the IRB may grant approval of a research study or study action (e.g. amendment, continuing review, general information) if it determines that all of the following requirements are satisfied:

5.7.2.1 Risks to subjects are minimized (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever possible, by

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using procedures already being performed on the subjects for diagnostic or treatment purposes;

5.7.2.2 Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview its responsibility;

5.7.2.3 Selection of subjects is equitable. In making this assessment the IRB should consider the inclusion/exclusion criteria and take into account the purposes of the research and the setting in which the research will be conducted and being particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;

5.7.2.4 Informed consent will be prospectively obtained from each subject or the subject's legally authorized representative and appropriately documented and carried out, unless the IRB has waived this requirement;

5.7.2.5 When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. The IRB will review the safety/risk assessment and research oversight plan submitted by the PI in determining the adequacy of data monitoring and subject safety. Additional information on the safety risk assessment and research oversight plan can be found in the IUPUI/Clarian SOP for Safety Monitoring Plan;

5.7.2.6 When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data;

5.7.2.6.1 **Privacy** refers to *individuals* and to their interest in controlling access of others to themselves. Individuals have an interest in controlling the time, place, and nature of the information they give to others and controlling the information or experiences that are proffered to them. Privacy considerations can be affected by gender, ethnicity, age, socio-economic status, education, ability level, health status, relationship to researcher, legal status, etc.

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5.7.2.6.2 **Confidentiality** refers to *data* (e.g. identifiable information about a person) and about agreements and procedures for limiting the access of others to that data. Methods to protect confidentiality should be described both to the IRB (via the study application) and to subjects (via the informed consent process). There can be many different methods employed to protect confidentiality, including making efforts to store and dispose of data securely, sharing data appropriately, obtaining Certificates of confidentiality, etc. Confidentiality expectations may differ for quantitative vs. qualitative research.

5.7.2.7 When some or all the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the research proposal to protect the rights and welfare of these subjects.

5.7.2.8 The amount, method, and timing of compensation is neither coercive, nor presents undue influence to potential subjects. In addition, this would include consideration of the influence of payments to subjects. This also includes that any bonus payments proposed for study completion are reasonable and not so large as to unduly induce subjects to remain in the study when they otherwise would have withdrawn;

5.7.2.9 The proposed subject recruitment methods, advertising materials, and participation payment arrangements are fair, honest, and appropriate. The IRB will use policies listed in the IUPUI/Clarian SOP for Recruitment of Human Participants to assist in its review of advertisements.

5.7.3 **Specific VA Requirements**

5.7.3.1 Pursuant to the VHA Handbook 1200.5, Appendix C 3(c), the IRB must determine if the subject's medical record (electronic or paper) should be flagged to protect the subject's safety by indicating the subject's participation in the study, and the source of more information on the study. Typically, all full Board studies, i.e. studies greater than minimal risk, would require that the subject's medical record be flagged; however, the IRB may not make this a requirement if: 1) the subject's participation in the study involves only one encounter, only the use of a questionnaire, or the use of previously collected biological specimens; or 2) the identification of

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the patient as a subject in a particular study (if the study is not greater than minimal risk) would place the subject at greater than minimal risk.

5.7.3.2 Pursuant to the VHA Handbook 1200.5 16, non-veterans may be entered into VA-approved research studies only when there are insufficient veterans available to complete the study in accordance with 38 CFR 17.45 and 38 CFR 17.92. All regulations pertaining to the participation of veterans as research subjects including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

5.7.4 **IRB Actions**. The IRB may approve, provisionally approve, table, or disapprove a research study. This includes new studies, as well as general information items, amendments, and continuing reviews. All determinations made by the IRB shall be conveyed to the investigator in writing.

5.7.4.1 **Provisional Approval**. The IRB may provisionally approve a study or study action when specific revisions requiring simple concurrence by the investigator can be stipulated. In this case, subsequent review by the convened IRB is not required. The IRB Chair or another IRB member designated by the Chair may approve the investigator's response on behalf of the IRB under an expedited review procedure. This approval will be reported to the IRB at its next meeting.

5.7.4.2 **Table**. The IRB may table a study or study action when substantive clarifications or modifications regarding the protocol or informed consent document that are directly relevant to the determinations required by the IRB are necessary. In this case, subsequent review by the convened IRB is required.

5.7.4.3 **Disapprove**. If the IRB disapproves a research study or study action, written notification will be provided to the investigator, which will include the reasons for the determination.

5.7.4.4 When the IRB approves a new research study, it must determine the study's approval period, which is set at intervals appropriate to the degree of risk, but not less than once per year. In some circumstances, a shorter review period (e.g. biannually, quarterly, or after accrual of a specific number of subjects) may be required. The IRB will require review more frequently than annually for those studies deemed "high-risk" per Appendix P.

5.7.5 **Reopening a Study**. The investigator may request the IRB to reopen a research study that was prematurely closed/expired as long as the request is made within six months of the study's closure/expiration. In reviewing this request, the IRB may require modifications to the research prior to reopening and/or enrolling

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subjects, as necessary. After six months, the investigator must resubmit a new study to reopen the study.

5.7.6 The Board may, upon the request of an investigator or on its own initiative, reconsider any proposal and reverse its own determination or that of a subcommittee.

5.7.7 **Exempt Studies**.

5.7.7.1 At IUPUI: The IRB has granted authority to RCA staff to grant exemptions and accept non-research student projects or research not subject to FDA or Common Rule definitions for human subjects research. However, if RCA staff have questions as to whether or not the project appropriately meets the required criteria, they may request an IRB member designated by the Chair to review and grant such an exemption or acceptance, as appropriate. EXCEPTION: Exemptions for studies conducted at or funded by the VA can only be exempted by an IRB Chair or IRB member designated by the Chair.

5.7.7.2 At Methodist: Exempt applications, non-research student projects, and research not subject to FDA or Common Rule definitions of human subjects research are sent to the IRB Chair or designee for review and acceptance.

5.7.8 **Expedited Studies**. Expedited research applications are reviewed and approved by an IRB member designated by the Chair. At IUPUI, if the investigator is requesting a waiver of informed consent or assent, an additional IRB member designated by the Chair will also review the research study. If these IRB reviewers do not agree on the appropriateness of the waiver, the study will then be reviewed at a convened IRB meeting for resolution. IRB members designated by the Chair to review expedited research applications may not disapprove a research study. Instead, they can deny it as meeting the requirements for an expedited study and request that it be submitted to the full IRB for review.

5.7.9 **Special Consideration for Research Involving Vulnerable Populations**. The IRB must consider additional protections for vulnerable populations participating in research to protect their rights and welfare. Please see the Vulnerable Populations SOP for specific information related to prisoners, children, pregnant women, human fetuses, and fetal material, and persons with cognitive-impairment.

5.7.10 **IRB Reviewer System** (Refer to Appendix J for a list of material provided to IRB members)

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5.7.10.1 **New Studies**. At both IUPUI and Methodist a primary and secondary reviewer system is used for the review of new study submissions.

5.7.10.2 **General Information**. At IUPUI a primary reviewer system is used for the review of general information items, including unanticipated problems involving risk to subjects or others, noncompliance, DSMB reports, etc. sent to the full IRB. At Methodist, all members review the information.

5.7.10.3 **Major Amendments**. At IUPUI and Methodist a primary reviewer system is used for the review of amendments sent to the full IRB.

5.7.10.4 **Continuing Reviews**. At IUPUI and Methodist a primary reviewer system is used for the review of full board continuing reviews.

5.7.10.5 A reviewer may object to reviewing a particular item if he/she feels the material is out of his/her expertise and/or if he/she identifies a conflict with reviewing the item. If this occurs, the IRB member should contact the RCA office as soon as possible so a replacement or an additional reviewer may be identified.

5.7.10.6 Complete IRB study files will be made available for review by any member of the IRB at the meeting, and any member of the IRB may, upon request, review the full protocol.

5.7.11 Except for life-threatening emergencies which meet very specific requirements as outlined in the IUPUI/Clarian SOP for Emergency Use of Investigational Agents, review of all protocols that qualify for full review will be performed at a convened meeting of the IRB.

5.7.12 **Continuing Reviews**

5.7.12.1 Oversight by the IRB is required as long as investigators are either interacting or intervening with subjects or accessing identifiable private information for research purposes. This includes research studies that remain active only for data analysis or for long-term follow-up, even when the research is permanently closed to the enrollment of new subjects and all participants have completed all research-related interventions. For multi-site research, it is acceptable to close the study at the local site if investigators are neither interacting with subjects nor accessing subjects' identifiable information.

5.7.12.2 **Review Interval**: Pursuant to 45 CFR 46.109(e), the IRB will conduct continuing review of research at intervals appropriate to the

degree of risk, but not less than once per year. In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of subjects) may be required. The IRB will require review more frequently than annually for those studies deemed "high-risk" per Appendix P.

5.7.12.3 The regulations make no provisions for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Additionally, where the convened IRB specifies conditions for approval of a protocol that are to be verified as being satisfied by the IRB Chair or by one or more experienced reviewers designated by the Chair (i.e. provisional approval), continuing review must occur no more than one year after the date the protocol was reviewed by the convened IRB.

5.7.12.4 **Verification**. The IRB will determine which projects need verification from sources other than the investigators that no material changes have occurred since the previous IRB review. Specific criteria that may be used include: 1) randomly selected projects; 2) complex projects involving unusual levels or types of risks to subjects; 3) projects conducted by investigators who previously have failed to comply with the requirements of the HHS regulations or the requirements or determinations of the IRB; and (4) projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or from other sources.

5.7.12.5 **Review of the Informed Consent Document(s)**. When the IRB reviews the current informed consent document(s) at the time of continuing review, it shall ensure that it is still accurate and complete. If any significant new findings are identified that may relate to the subject's willingness to continue participation in the study, the IRB shall require that they be provided to subjects in accordance with regulations. The IUPUI/Clarian IRBs do not allow revisions to be made to the informed consent document(s) at the time of continuing review, except those required specifically by the IRB.

5.7.12.6 **Expedited Review Procedure**. An expedited review procedure may be used for the continuing review of research originally approved under an expedited review procedure; that is, the research still meets one or more of the acceptable 7 expedited categories. An expedited review procedure may also be used for the continuing review of research previously approved by the convened IRB as follows:

5.7.12.6.1 Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions (i.e. there

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are no active subjects); and (iii) the research remains active only for long-term follow-up of subjects. OR

5.7.12.6.2 Where no subjects have ever been enrolled at the local site and no additional risks have been identified at any research site (e.g. for multi-center protocols); OR

5.7.12.6.3 Where the remaining research activities are limited to data analysis; OR

5.7.12.6.4 Where the research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) and the IRB has determined and documented at a convened meeting that (i) the research involves no greater than minimal risk; and (ii) no additional risks have been identified.

5.7.12.7 For multi-center protocols, an expedited review procedure may be used by the IRB at the local site whenever the above conditions are satisfied for that site.

5.7.12.8 Research studies that were originally submitted to the full IRB for review, where the investigator wishes to continue the research and at least one subject remains active or is in long-term follow-up must be reviewed by the convened IRB. Additionally, if there is indication that a significant increase in risk exists from the last review, even when no subjects remain active or are in long-term follow-up, the continuing review must be reviewed by the convened IRB.

5.7.12.9 If the investigator fails to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the study's current expiration date (i.e. continuing review due date) previously specified by the IRB, research activities must cease, including enrollment of new subjects, interventions on/interactions with current subjects, and analysis of identified data. However, if the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue is involved such that it is in the best interest of individual subjects, the IRB may permit the study to continue for a brief time required to complete the review process. Enrollment of new subjects cannot occur after the expiration of IRB approval. This lapse in IRB approval need not be reported to OHRP as a suspension of IRB approval under DHHS regulations.

5.7.12.10 Pursuant to the VHA Handbook 1200.5.g.(2), studies conducted at or on behalf of the VA that do not receive continuing review with the timeframe set by the IRB is automatically suspended. Only if the

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IRB or IRB Chair, in consultation with the Chief of Staff (COS), finds that it is in the best interest of individual subjects, can already enrolled subjects continue with research interventions or interactions.

5.7.12.10.1 Once the investigator is notified of the suspension by the local VA research office, he/she must immediately submit to the IRB Chair, a list of research subjects for whom suspension of the research would cause harm. The IRB Chair, with appropriate consultation with the COS, will determine if the subjects may continue in the research. If the study is FDA-regulated, the COS and IRB Chair must follow FDA requirements in 21 CFR 56.1018(b)(3) in making their decision. Additionally, any sponsoring agency, private sponsor, ORD, ORO, or other Federal agencies will be informed, as appropriate, by the local VA research office.

5.7.13 **Modifications to Previously Approved Research**. The IRB requires that any proposed changes in approved research, during the period for which IRB approval has already been given, be reviewed and approved prior to implementing these changes to determine whether the modified research continues to fulfill the criteria for approval, except where necessary to eliminate apparent immediate hazards to the human participants. Investigators may request approval of proposed changes by the completion and submission of an Amendment form. Whenever possible the IRB will require each revision to an IRB-approved research protocol to be incorporated into the written protocol.

5.7.13.1 Pursuant to 45 CFR 46.110(b)(2), minor changes in previously approved research may be reviewed and approved under an expedited review procedure. These are known as "Minor Amendments." Substantive changes and changes that involve increased risks or discomforts must be reviewed and approved at a convened IRB meeting before the changes can be implemented. These are known as "Major Amendments." The IRB has developed guidelines for determining whether proposed changes are "minor" or "major." See IRB Guidelines to Minor and Major Amendments for examples. New primary objectives or significant changes in the statistical design constitute a new study and are not justified as amendments.

5.7.13.2 Change(s) in research activity taken by the investigator without prior IRB approval in order to eliminate apparent immediate hazards must be promptly reported to the IRB using the IUPUI/Clarian Reporting Form for Events that Require Prompt Reporting to the IRB form. The IRB will determine if the changes

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made are consistent with ensuring subjects' continued safety and welfare. Information about protocol changes will be provided to subjects when it might relate to their willingness to continue in the research.

5.7.13.3 **Additional VA Requirements**: Amendments to VA research studies involving issues related to biosafety or radiation safety must first be approved by the appropriate committee or subcommittee prior to granting final IRB approval.

5.7.14 **Device Determinations**. The assessment of whether or not a device study presents a nonsignificant risk (NSR) is initially made by the sponsor. If the sponsor considers that a study is NSR, the IRB will consider the explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. The IRB may agree or disagree with the sponsor's initial NSR assessment. The risk determination should be based on the proposed use of a device in an investigation and not on the device alone. In deciding if a study poses a significant risk (SR), the IRB will consider the nature of the harm that may result from use of the device. If the IRB determines that the device study is SR, the investigator will be notified and the study cannot be approved and/or conducted until the investigator has provided the IRB with documentation of FDA approval of an IDE application.

5.7.14.1 **Significant Risk (SR) Device Study**: A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and (1) is intended as an implant; or (2) is purported or represented to be for use in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

5.7.14.2 **Nonsignificant Risk (NSR) Device Study:** A study that does not meet the definition for a significant risk study. A NSR device study should not be confused with the concept of "minimal risk" as defined in 45 CFR 46.102(i) and 21 CFR 56.102(i) to identify certain studies that may be approved through an "expedited review" procedure.

5.7.14.3 Both SR and NSR device studies require IRB approval prior to conducting the clinical trial.

5.7.14.4 The FDA considers studies of all significant risk devices to present more than minimal risk; thus, full IRB review for all studies involving SR devices is required. Generally, full IRB review is required for NSR studies; however, some NSR studies may qualify

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as minimal risk and the IRB may choose to review those studies under its expedited review procedures.

5.7.14.5 The FDA has the ultimate decision in determining if a device study is SR or NSR.

5.7.15 **IRB Administration and Support**. The functions of the IUPUI/Clarian IRBs are administered and supported by Research Compliance Administration (RCA) at IUPUI and the Methodist IRB Office at Methodist Hospital.

5.7.15.1 The IRBs have given staff in these two offices the authority to conduct preliminary review of all materials submitted to the IRBs in order to ensure that they are in an acceptable form for the IRB.

5.7.15.2 RCA and Methodist IRB office staff also certify the review and approval of human subjects research to external funding agencies, as required.

5.7.15.3 The IRB's have delegated authority to RCA and Methodist IRB office staff to provide guidance to investigators as to whether or not an activity meets the definition of human subjects research and thus requires IRB review and approval. However, staff may consult with IRB Chairs and/or Vice Chairs with any questions.

5.7.16 RCA and the Methodist IRB office will write investigators of IRB actions taken on research. If research is approved by the IRB, but not permitted by RCA, the institution, or the division of Academic Affairs at Clarian, RCA will promptly convey notice to the investigator and the IRB that the research cannot be conducted, including the reasons for that determination. Neither RCA nor any other office of these institutions may approve a research activity that has been disapproved by the IRB. An investigator may appeal a decision made by the IRB if, in his/her opinion, the proposed research does not pose serious harm to the subjects and he/she responds in writing to concerns posed by the IRB. The investigator has an opportunity to appear in person before the IRB, upon request. These appeals should be addressed to RCA or the Methodist IRB office, which will provide this information to the IRB. The IRB may choose to invite the investigator to a meeting to address the concerns or may reject the investigator's appeal based on initial concerns with the research. No external body or official may override IRB disapprovals, nor apply undue pressure on the IRB to reverse a decision. The IRB may, upon the request of an investigator or on its own initiative, reconsider any proposal and reverse its own determination or that of an IRB subcommittee. However, research studies that are tabled or disapproved by the IRB cannot be resubmitted to a different IRB in an attempt to bypass the original IRB's decision.

5.7.17 Deliberations, decisions, findings, and actions of the IRB associated with research activities shall be considered confidential, except as appropriate. This

information is reported to appropriate institutional officials as required by law and/or policies of the IRB. Failure to adhere to this provision may be cause for removal of a member from the IRB. See Public Access Counselor (http://www.state.in.us/pac/) for additional information regarding open door law and open records act.

5.7.17.1 IRB minutes will be written and made available for review with 3 weeks of the meeting date.

5.7.17.2 Once IRB minutes are approved at a subsequent IRB meeting, they may not be altered by anyone, including a higher authority. IRB minutes are distributed and/or made accessible to the following individuals/institutional officials:

5.7.17.2.1 Vice Chancellor for Research, IUPUI

5.7.17.2.2 Veterans Affairs Medical Center, R&D Committee

5.7.17.2.3 Wishard Health Services, Executive Director & CEO

5.7.17.2.4 General Clinical Research (GCRC), Administrative Manager

5.7.17.2.5 Clarian Health Partners, Executive VP of Academic Affairs

5.7.17.2.6 Dean, IU School of Medicine

5.7.17.2.7 Media Relations

5.8 **Cooperative Research**. Cooperative research projects are those projects covered by the human subjects regulations which involve more than one institution. Pursuant to 45 CFR 46.114, in the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with the application regulations. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint reviewer arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. IUPUI and Clarian collaborate with other institutions and engage in multicenter studies. For additional information on cooperative research procedures, including the reliance on another institution's IRB approval, please see Section III of the IRB Instruction Packet.

5.9 **Assurance of Compliance**

5.9.1 Pursuant to 45 CFR 46.103(a), each institution engaged in research which is governed by this policy (45 CFR 46) and which is conducted or supported by a

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federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in the regulations. IUPUI, Clarian, and their affiliates provide this assurance in the form of a Federalwide Assurance approved by the Office for Human Research Protections (OHRP).

5.9.2 Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under 45 CFR 46.101(b) or (i). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by 45 CFR 46.103 has been reviewed and approved by the IRB.

5.9.3 Research Compliance Administration will provide certification of human subjects approval for any research project supported by a federal department or agency upon request.

5.10 IRB Executive Committee Membership

5.10.1 The membership of the IRB Executive Committee consists of the chairs and vice chairs of each IUPUI/Clarian IRB. Other IRB members or consultants may be included to achieve diversity and expertise to carry out the activities of the Committee, as needed.

5.10.2 The Chair is the Vice Chancellor for Research, IUPUI. S/he may appoint another member to perform the functions of the Chair, as necessary.

5.11 IRB Executive Committee Meetings

5.11.1 The committee has periodic meetings as required to perform its duties and responsibilities. There will be at least one meeting per year. Each member is appropriately notified in advance of the date, time, and place of each meeting.

5.11.2 The Chair may call meetings in addition to regularly scheduled meetings, as necessary.

5.11.3 The majority of the Committee members present at a meeting constitutes a quorum.

5.11.4 Committee decisions are made by a majority vote of the members present at the meeting. Members having a conflict of interest in a matter may not vote, but will be counted towards a quorum. Voting will occur only after there has been a full, open discussion.

5.11.5 IRB Executive Committee meetings are usually held in a face-to-face manner. However, they may be conducted completely or in part by telephone or video conference, if necessary.

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5.11.6 The Chair may invite or allow a non-member to attend a meeting, as needed.

5.12 **IRB Executive Committee Subcommittees**

5.12.1 The Chair of the IRB Executive Committee may appoint subcommittees to execute various duties related to the objectives and policies of the committee.

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Title:	**Recruitment of Human Participants**			
Current Version:	**07/07**		Previous Versions:	**02/05**

1. INTRODUCTION

Identifying, approaching, selecting, recruiting and enrolling subjects in a research study must be done in a planned fashion, considering guidelines, with the supervision of the Principal Investigator. If not done properly, a study can fail due to improper subject selection with subsequent early termination of subjects who did not meet entry criteria. There must be fair procedures and outcomes in the selection of research subjects.

A sound recruitment plan should be described and justified and should consider the following points:

- Number of subjects;
- Identification of potential subjects
- Assess the need for approval from treating health care providers
- How best and who to approach for community projects
- Whether subjects may be employees or students of the research staff
- Plan for contacting potential subjects (e.g. methods, medium, communication, advertisement)
- Compensation
- Whether other approvals are needed.

2. OBJECTIVES

The objectives of this SOP are:

2.1. To clarify the minimal requirements, including reporting to the Institutional Review Board (IRB), for selection, recruitment, and enrollment[4.1] of human subjects in research studies at IUPUI/Clarian.

2.2. To clarify the campus resources for selection and recruitment of human subjects into research studies at IUPUI/Clarian.

3. SCOPE

These requirements apply to all studies involving human subjects that are approved by the IUPUI and Clarian IRB(s). The Principal Investigator (PI) is responsible for the oversight and adherence to this policy.

4. RELEVENT DEFINITIONS

(section intentionally left blank)

5. POLICY AND ASSOCIATED PROCEDURES:

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5.1 Recruitment

5.1.1 When approaching or recruiting participants, information must be presented in a language that is understandable to the participant or the representative.

5.1.2 Methods, materials and modes used to approach or recruit subjects must be submitted to the IRB for review, and cannot be used until IRB approval is given. Any advertisements or brochures to be seen or heard by prospective subjects to solicit participation in research must be included with an explanation of the mode of communication at the time of protocol submission. Methods of recruitment may include, but are not limited to, print, radio or, television advertisements, personal contact, database searches, letters to potential subjects, internet listings, newsletters, community talks or booths, etc.

5.1.2.1 Campus resources available to assist with recruitment include:

- Office of Clinical Research volunteer registry: http://www.clinicalresearch.medicine.iu.edu/body.cfm?id=3592.
- Regenstrief Institute (database searches and Gopher prompt system): 630-7070.
- IU Primary Care Research Network (res-Net): http://clinicaltrials.iupui.edu/res_net.html or send e-mail to Res-net@iupui.edu.
- IU School of Medicine Public and Media Relations Office: 274-7722.

5.1.3 Should recruitment or advertising methods be changed or added, the methods and materials to be used must be submitted to the IRB via an amendment form. These recruitment methods and materials must be reviewed and approved by the IRB prior to their use. Once IRB approved, any written materials such as advertisements will include an IRB approval stamp. When advertisements are easily compared to an approved informed consent document, they may be reviewed and approved using an expedited procedure. However, if the IRB reviewer has doubts or other complicating issues are involved, s/he may request that the advertisement be reviewed at a convened IRB meeting.

5.1.4 Materials given to health care providers intended to solicit research subjects which are not given to or seen by the potential subject (e.g. “dear doctor” letters), do not require IRB approval. However, the process (e.g. contacting health care providers for referrals) is required to have IRB approval.

5.1.5 Contacting potential subjects should be carefully considered. If a potential subject is to be identified by protected or confidential information (e.g. medical record, legal files), the procedures for identifying and contacting potential subjects and the methods for disclosing this information, should be clearly delineated in the IRB application. This may include review of existing patient

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information. These procedures will be reviewed by the IRB on a case-by-case basis.

When subjects are to be recruited for participation in research as a result of pre-screening existing health care data, initial contact, whether via telephone or letter, should be by someone involved in the patient's care (e.g. potential subject's physician, nurse, or designee). (For additional information see Guidelines on Research Involving Existing Health Care Data (http://www.iupui.edu/%7Eresgrad/irbpacket/irbpacket12-03.htm#Section8) and the IUPUI/Clarian SOP for Confidentiality and Privacy).

5.1.6 When doing research within a community group or organization, the person authorized to speak for the group should be approached for permission to recruit from that group or organization.

5.1.7 When appropriate, potential subjects should be encouraged to consult their physician prior to enrollment. Before any study findings are reported to the subject's physician, permission for information to be released must be obtained from the subject.

5.1.8 **Recruitment or approaching subjects may not begin** until IRB approval has been obtained for the study, as well as the recruitment process, method, mode and material(s). Additionally, there can be no subject recruitment once a study has been suspended by or terminated with the IRB.

5.1.8.1 Selection of subjects must be based on the IRB approved protocol inclusion and exclusion criteria. Any change in these criteria must first be approved by the IRB.

5.1.8.2 Subjects may be considered for the study (pre-screened), prior to the full informed consent execution, if no procedures are performed. See Sample Telephone Screen form.

5.1.8.3 If subjects are purposely placed into different study groups, the method of assignment (or randomization) must be predetermined.

5.1.8.4 Screening procedures (if applicable) that are not standard of care but rather are being conducted solely for the purposes of the research project must be completed only after the consent has been fully executed. The subject must meet the inclusion and exclusion criteria before he/she is enrolled into the study. If the subject is screened but he/she does not meet the inclusion and exclusion criteria then this is considered a screen failure. However, an exception may occur when permission of the sponsor is obtained as a "waiver" on a case-by-case basis.

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5.2 Additional Sites and/or Sponsoring Organizations

There may be additional approvals necessary depending on where subjects will be recruited from (e.g. VA, GCRC). It is the obligation of the principal investigator to secure these approvals.

5.3 Sponsor Requirements

The sponsor may require approval of the recruitment process (including advertising), e.g., methods, materials, mode of communication, in addition to obtaining IRB approval. The sponsor may or may not provide recruitment tools.

5.4 Media Relations

Use of official University or Department logos may require special approval through the School or Department. For investigators in the School of Medicine, contact Media Relations at 274-7722 for additional guidance.

5.5 Review of Advertisements

5.5.1 The IRB must review all direct advertising for research participants. This refers to advertising that is intended to be seen or heard by prospective participants to solicit their participation in a study.

5.5.2 When advertisements are to be taped for broadcast, the IRB must review the final audio/video tape.

5.5.2.1 The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording.

5.5.2.2 The review of the final taped message prepared from IRB-approved text may be accomplished through expedited procedures.

5.5.3 Advertisements to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

5.5.3.1 The name and address of the investigator and/or research facility;

5.5.3.2 The location of the research and person or office to contact for further information;

5.5.3.3 The condition under study or the purpose of the research;

5.5.3.4 In summary form, the criteria that will be used to determine eligibility for the study;

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5.5.3.5 A brief list of participation benefits, if any (e.g. a no-cost health examination);

5.5.3.6 The time or other commitment required of participants (e.g. number of visits and total duration of participation).

5.5.4 The IRB will review advertising to assure that advertisements do NOT:

5.5.4.1 Make claims, either explicitly or implicitly, that the drug, biologic, device, or other type of intervention is safe or effective for the purposes under investigation;

5.5.4.2 Make claims, either explicitly or implicitly, that the test article or intervention is known to be equivalent or superior to any other drug, biologic, device or intervention;

5.5.4.3 Use terms such as "new treatment," "new medication," or "new drug" without explaining that the test article or treatment is investigational (e.g. not FDA-approved);

5.5.4.4 Promise "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the study;

5.5.4.5 Include proprietary information or the product name, unless it is approved by the sponsor.

5.5.4.6 State or imply certain favorable outcomes or other benefits beyond what is outlined in the informed consent document and the protocol;

5.5.4.7 Include any exculpatory language.

5.5.5 Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid by such means as larger or bold type.

5.5.6 Advertisements submitted to the IRB must be indicative of the size of type and other visual effects that will be employed in the final product.

5.5.7 IRB review and approval of listings of clinical trials on the internet is not required when the system format limits the information provided to the basic trial information, such as the title, purpose of the study, protocol summary, basic

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eligibility criteria, study site location(s), and how to contact the site for further information.

See Recruiting Study Subjects (http://www.fda.gov/oc/ohrt/irbs/recruiting) from the FDA Information Sheets for additional information.

5.6 Review of Payment Arrangements to Participants

5.6.1 Payment to research participants for participation in studies is not considered a benefit, but a recruitment incentive.

5.6.2 The amount and schedule of all payments should be presented to the IRB at the time of initial review.

5.6.3 The IRB shall review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive nor present undue influence.

5.6.4 Any credit for payment should accrue as the study progresses and not be contingent upon the participant completing the entire study.

5.6.5 Unless it creates undue inconvenience or a coercive practice, payment to participants who withdraw from the study may be made at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, the IRB may find it permissible to allow a single payment date at the end of the study, even to participants who had withdrawn before that date.

5.6.6 While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive is not coercive.

5.6.7 The IRB shall determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.

5.6.8 All information concerning payment, including the amount and schedule of payment(s) should be set forth in the informed consent document.

5.6.9 Compensation for participation in research offered by a sponsor may not include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

5.6.10 Pursuant to the VHA Handbook, 1200.5, 12, payment to human subjects to participate in research is prohibited when the research is integrated with a

patient's medical care and when it makes no special demands on the patient beyond those of medical care. Payment may be permitted, with IRB approval, in the following circumstances:

5.6.10.1 **Others Being Paid**. In multi-institutional studies, when human subjects at a collaborating non-VA institution are to be paid for the same participation in the same study at the same rate proposed.

5.6.10.2 **Comparable Situations**. In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.

5.6.10.3 **Transportation Expenses**. When transportation expenses are incurred by the subject that would not be incurred in the normal course of receiving treatment and which are not reimbursed by any other mechanism.

5.6.10.4 Investigators wishing to pay VA research subjects must address in their proposal the specific criteria outlined in the VHA Handbook 1200.5, 12(b).

5.6.10.5 The IRB and R&D Committee must review all proposals for payment of subjects to ensure conformity with VA policies.

5.6.10.6 The VA research office is responsible for ensuring the IRB-approved payment to subjects is made from a VA approved funding source for research activities.

5.7 Tracking

The number of subjects screened and the number of subjects consented should be tracked for reporting purposes. The IRB Continuing Review form requires that reporting of the number of consented subjects and, for VA and NIH-sponsored studies, gender and race information must also be reported.

5.8 Recruitment Incentives

5.8.1 Research staff may not personally accept payments, gifts, or any other types of compensation for recruitment or enrollment, which may constitute an inducement to modify standard practice, benefit a single employee, or give preferential treatment to one sponsor over another. In contrast, compensation offered as acknowledgment for legitimate additional work or effort required by a specific project possibly unanticipated during initial budget negotiations may be accepted; however, it must be appropriately routed as a budget revision for the project.

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However, this does not preclude the receipt of gifts from sponsors (unrelated to a specific research project); however, the institution has clear policy distinguishing "gifts" from "sponsored research projects."

5.8.2 "Gifts" which are unrelated to a specific research project, are unconditional and voluntary and the donor does not directly benefit.

5.8.3 "Sponsored research projects" have a particular intent and the recipient incurs certain obligations. Sponsored research projects involve legal agreements or legal duties related to expectations, risks, rights, indemnifications, and/or time limits. Legal and financial management is different for grants versus gifts.

An explanation of the differences in definition, intent, obligations, documentation, and management of gifts versus sponsored research projects may be found in the following institutional references:

- http://www.fms.indiana.edu/cg/imp_notice/01-4.asp
- http://www.iupui.edu/~resed/giftintro.htm

5.8.4 Referring health care providers are not allowed to be given financial incentives such as "finder's fees."

5.9 **Employee, Colleague, or Student Recruitment**

5.9.1 If recruitment among employees, colleagues, or students is anticipated, it must be explained and justified. It is recommended the persons with the following study-related responsibilities NOT participate as subjects in the research study: data collection or other direct access to study data; direct subject contact and/or care; distribution and/or monitoring of the investigational agent or study intervention.

5.9.2 The investigator should consider and address the possibility of coercion or undue influence and any equivalent alternatives (e.g. for classroom research).

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Title:	Reporting			
Current Version:	03/08		Previous Versions:	02/05, 05/06

1. INTRODUCTION

Pursuant 45 CFR 46.103(b)(5) and 21 CFR 56.108(b), IRBs must establish procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (1) any unanticipated problems involving risks to subjects or others; (2) any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB; or (3) any suspension or termination of IRB approval.

2. OBJECTIVES

The objective of the SOP is to outline the procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, sponsor, coordinating center, appropriate regulatory agencies, and others events determined to be unanticipated problems involving risks to subjects or others, noncompliance determined to be serious or continuing, and suspensions and terminations of approved research by the IRB.

3. SCOPE

These policies and procedures apply to all research activities of faculty, staff, students, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVENT DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1. Pursuant 45 CFR 46.103(b)(5) and 21 CFR 56.108(b), the IRB will review reports of unanticipated problems and serious or continuing noncompliance. If the IRB determines that a report does in fact represent an unanticipated problem, serious or continuing noncompliance, or suspends or terminates approval of research, appropriate institutional officials, regulatory agencies, and others will be notified. Please note that this policy does not apply to administrative holds.

5.2. RCA staff will prepare minutes from the IRB meeting in which the report and the IRB's determination of the report was discussed. Included in the minutes will be the following information:

5.2.1. Description of the event/circumstance;

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5.2.2. Summary of the IRB's deliberations, including any provisions;

5.2.3. Actions taken by the IRB;

5.2.4. Reasons for the IRB's actions;

5.2.5. Plans for continued investigation or action.

5.3. After review and approval by an RCA Director, a copy of the minutes will be distributed to:

5.3.1. the principal investigator; and

5.3.2. the IRB.

5.3.3. Unless already made aware of the report, a copy of the minutes will also be distributed to the following individuals, as applicable:

5.3.3.1. The Chair of the VA Research and Development Committee (or designee), if the research is conducted at or funded by the VA. The Chair will in turn forward the report to the VA Office of Research Oversight Regional Office.

5.3.3.2. Director, Contract & Grant Administration, who will forward the report to the sponsor or contract organization, if the research is funded and the study was suspended or terminated.

5.3.3.3. Department chair or supervisor of the principal investigator, as appropriate.

5.3.3.4. University counsel, if the report raises issues of legal liability or there is a threat or perceived threat of a lawsuit.

5.3.3.5. The Privacy Officer of the covered entity, if the event involved unauthorized use, loss, or disclosure of PHI from that covered entity.

5.3.3.6. The Information Security Officer of the organization, if the event involved violations of information security requirements of that organization.

5.4. A formal report will be prepared by an RCA Director or designated RCA staff member and sent as applicable to:

5.4.1. Office for Human Research Protections (OHRP), if the study is subject to DHHS regulations;

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5.4.2. Food and Drug Administration (FDA), if the study is subject to FDA regulations. A study is considered to be FDA-regulated if any of the following are true:

5.4.2.1. The research procedures include the administration or use of any foods, including dietary supplements, which bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.

5.4.2.2. The research is being done as part of an IND or IDE submission.

5.4.2.3. The data may be submitted to the FDA.

5.4.2.4. The data may be held for inspection by the FDA.

5.4.3. Other federal agencies, for example NIH, DOD, if suspension or termination.

5.4.4. Chancellor for IUPUI and Vice Chancellor for Research, IUPUI.

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5.5. **Specific VA Reporting Requirements**: Pursuant to VA Guideline for Reporting Research Related Issues (adopted by R&D Committee 4/19/07), all allegations of noncompliance, conflict of interest, or unethical behavior reported to Research Compliance Administration must be reported to the VA Research Office within 1 business day. Likewise, all allegations of noncompliance reported to the VA Research Office must be reported to Research Compliance Administration within 1 business day. Initial reports may be made via telephone.

5.6. Reports of serious or continuing noncompliance may be brought to the IRB Executive Committee if it is determined that information regarding the noncompliance could benefit the group.

5.7. All reports will be completed within 30 days of the IRB's action.

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Title:	Research Personnel Requirements			
Current Version:	07/07		Previous Versions:	09/04, 02/02

1. INTRODUCTION

Research with human subjects requires appropriate safety measures, compliance to regulatory requirements, and a staff well versed in the proper conduct of human subjects research. Multiple training[4.4] opportunities exist to educate staff on the protocol-specific and general regulatory requirements for human subjects research. Agency and sponsor inspections almost always seek to assure that the research team is appropriately qualified and trained for the demands of the protocol.

2. OBJECTIVE(S)

The objectives of this SOP are to:

2.1. Ensure that employees have appropriate training and qualifications[4.3] (per job description[4.1]).

2.2. Identify appropriate training mechanisms for research staff.

2.3. Provide examples of appropriate documentation of training.

3. SCOPE

This SOP applies to all personnel involved in the implementation and coordination of investigations involving human subjects by all departments of IUPUI/Clarian. It covers all human subjects research approved by the IUPUI/Clarian IRBs.

4. RELEVANT DEFINITIONS

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5. POLICIES AND RELATED PROCEDURES

5.1. All members of the research team should have adequate knowledge of ethical principles, professional standards, federal regulations, and other applicable law.

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5.2. Personnel involved in research with human subjects must have appropriate education, background, and experience for the research.

5.3. It is the responsibility for the principal investigator to ensure that all co-investigators, research coordinators, and applicable support staff are educated on the appropriate IUPUI/Clarian SOPs, HIPAA Privacy and Security regulations, proper conduct of human subjects research and protocol specific activities.

5.4. Research studies subject to the IUPUI/Clarian SOP for Auditing of Research Involving Human Subjects must maintain a training file with current records of study staff for a research area or specific research protocol for auditing purposes. Suggested contents include CV, licensure, SOP training log, continuing education, and experience. This training file should be updated annually.

5.5. All principal investigators, co-investigators, (anyone involved in the design, conduct, or reporting of the research, or having significant interaction with subjects) including personnel obtaining informed consent listed on the IUPUI/Clarian IRB application must take and pass the IUPUI human subjects protection test.

5.5.1 Protection of Human Subjects in Research Course:
www.iupui.edu/%7Eresgrad/Human%20Subjects/HumanSubjectsCourse.html

5.5.2 Human Subjects Protection Test
www.indiana.edu/~rcr/hsp01reg.phtml

5.6. The administrative personnel in the office of Research Compliance Administration will keep a record of those successfully completing this test and confirm, prior to final IRB approval, that all listed personnel have passed the test.

5.7. In exceptional circumstances where the test requirement may not be appropriate, other methods of ensuring understanding may be proposed to the IRB (via the RCA office) for review and approval.

5.8. It is the responsibility of the principal investigator to ensure that all research staff who will be assisting in the conduct of the research have seen and read the IRB-submitted protocol and have agreed to participate.

5.9. All individuals distributing and/or dispensing investigational drugs/devices/radiologics must be educated on the appropriate IUPUI/Clarian SOPs (Investigational Drug and Device Accountability) and must be appropriately qualified.

5.10. The individual who is the point of contact for federal, sponsor, or IUPUI/Clarian inspections must be adequately prepared.

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Title:	Responsibilities of Principal Investigators			
Current Version:	12/07		Previous Versions:	03/02, 09/04, 02/05, 04/05

1. INTRODUCTION

Principal Investigators (PIs) share with the Institutional Review Board (IRB) and Funding Organizations the responsibility for ensuring that research with human subjects is properly conducted such that participants are adequately protected. The environment in which investigators conduct research and the type of research they conduct influence their roles and responsibilities. Competent, informed, conscientious, compassionate and responsible investigators provide the best possible protection for research subjects. Additionally, there are many regulatory agencies to guide the PI in the proper conduct of research involving human subjects. Investigators must be properly qualified and trained and have adequate experience to undertake this type of research. The PI is ultimately responsible for the adequate conduct of research involving human subjects; however, he/she may delegate research-related responsibilities to other members of the research, provided these individuals are appropriately qualified and trained.

2. OBJECTIVE

To delineate the roles and responsibilities of Principal Investigators (PIs) in conducting human subjects research.

3. SCOPE

These requirements apply to all studies involving human subjects that are approved by the IUPUI and Clarian IRB(s). The Principal Investigator (PI) is *ultimately* responsible for the oversight and adherence to this policy.

4. RELEVANT DEFINITIONS

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5. POLICIES AND RELATED PROCEDURES FOR ALL RESEARCH

5.1. GENERAL RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)

5.1.1 The PI is personally responsible for conducting and/or supervising the research according to the IRB-approved protocol.

5.1.2 The PI is responsible for ensuring that the research is conducted according to the investigational plan, any conditions of approval imposed by the IRB and applicable regulations for protecting the rights, safety, and welfare of human subjects involved in research. This involves ensuring that:

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5.1.2.1 the study design protects the safety and welfare of research subjects;

5.1.2.2 the personal dignity and autonomy of the research subjects are respected;

5.1.2.3 subjects are protected from harm by maximizing anticipated benefits and minimizing possible risks; and

5.1.2.4 the benefits and risks of the research are distributed fairly.

5.1.3 The PI must be familiar and comply with the ethical principles of human subject research (The Belmont Report), the requirements of the federal regulations, including The Common Rule, FDA, and HIPAA regulations, applicable state laws, including state privacy laws, relevant professional standards, institutional policies, and any other applicable regulations. Compliance with the federal regulations will in no way render inapplicable pertinent state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

5.1.4 The PI is responsible for reviewing and fully understanding the definition of a "human subject" and when activities are subject to IRB review and/or when to seek guidance. Additionally, the PI must review and fully understand the relevant IUPUI/Clarian Standard Operating Procedures (SOPs) and pass the Human Subjects Protection test. These principles, regulations, laws, and policies are located on or linked from the RCA website.

5.1.5 New PIs (those who have not conducted research since March 2004) involved in research with human subjects are required to complete the Investigator 101 Course and pass the test, which was developed by the Office of Human Research Protections on the appropriate conduct of clinical and non-clinical research. This includes both behavioral and medical protocols and all levels of submission (exempt, expedited, and full review).

5.1.6 The PI is responsible for ensuring that all members of the research team, including all associates, colleagues, or employees assisting in the conduct of the research, are appropriately qualified and trained.

5.1.6.1 For IU employees, the PI must follow and notify members of the research team of applicable Human Resource policies.

5.1.6.2 The PI must also inform members of the research team about their role-related responsibilities as they pertain to the conduct of the research in order to comply with applicable regulations and policies, such as those concerning IRB review, informed consent, reporting, maintenance and retention of records, and supervision of research

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conduct. This includes ensuring that members of the research team also review and fully understand the relevant IUPUI/Clarian SOPs and pass the Human Subjects Protection test.

5.1.6.3 The PI must also be in continual communication with members of the research team, including co-investigators, laboratories, nursing units, etc., to ensure the proper conduct of the research.

5.1.7 When the conduct of the research relies on entities within the organization not under the control of the investigator (e.g. pathology, nursing, pharmacy, radiology, counseling), and where participant protections require those entities to be prepared for their involvement, the PI must communicate with those entities accordingly.

5.1.8 The PI is responsible for assessing the safety and risk of the research and ensuring an appropriate research oversight plan is in place for monitoring the research. Additional guidance related to safety/risk assessment can be found in the IUPUI/Clarian SOP for Safety Monitoring Plan.

5.1.9 The PI makes the initial determination of whether or not an activity meets the definition of "human subjects research," and if it does, must obtain appropriate IRB approval of the research, including informed consent (or waiver), authorization for the release of health information (or waiver), and other study-related documents, as required. Additional guidance in making the determination of whether or not an activity meets the definition of "human subjects research" is provided in the Checklist for Determining Whether an Activity Requires IRB Review document or by contacting the Research Compliance Administration office.

5.1.10 The PI is responsible for the adequate and accurate retention and maintenance of research records, including signed informed consent documents, signed release of health information authorization forms and other HIPAA-specific documentation, in accordance with all agency regulations and in a manner which will facilitate reconstruction of study events by the IRB, should the necessity for an audit and/or and in-depth review arise. Additional guidance on record retention and maintenance can be found in the IUPUI/Clarian SOP for Data Management.

5.1.11 The PI must cooperate fully with and be adequately prepared for all internal and external (e.g. sponsor, federal agency) auditing and monitoring activities. Please see the IUPUI/Clarian SOP for Auditing of Human Subjects Research for additional guidance.

5.1.12 The PI must ensure the quality and authenticity of the research data.

5.1.13 The PI must maintain the privacy of research participants and the confidentiality of their data. Persons can be wronged even if they are not physically harmed,

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such as if sensitive or embarrassing personal information is made public, either intentionally or unintentionally. Thus, a breach of subject confidentiality is considered a significant risk. The PI must ensure that the study design adheres to these principles. Additional guidance related to privacy and confidentiality can be found in the IUPUI/Clarian SOP for Confidentiality and Privacy.

5.1.14 The PI must ensure that all study subjects meet the inclusion and exclusion criteria set forth by the study protocol. The PI is also responsible for notifying subjects of any significant new findings during the study that may affect their willingness to participate.

5.1.15 The PI must respond appropriately to questions, concerns, complaints or requests for information that come from potential subjects, subjects in the recruitment process, current research subjects, and/or past research subjects.

5.1.15.1 If a question, concern, complaint, or request is made from a subject, and the PI or other member of the research team cannot readily supply an answer or resolution, the subject should be given a short timeframe in which to receive a reply. During this time, the PI or other member of the research team may obtain necessary information from other research staff, department heads, institutional administrators, RCA or the Methodist IRB office, or others as needed to address the issue.

5.1.15.2 In situations where a subject is asking about his/her rights as a research participant, the PI or other member of the research team should provide the subject with the RCA contact number (included on the informed consent template) to call.

5.1.15.3 Subject complaints received in this manner should be reported to the IRB at the time of continuing review, unless they require prompt reporting to the IRB as per the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.

5.1.16 The PI is responsible for determining that appropriate resources needed to protect human subjects are available. This may include personnel, space, equipment, time, and in some cases, provisions to transport subjects to the ER or provide for psychological support. PI's shall not commence a research study without ensuring adequate resources are available and shall stop a research study if resources become unavailable. If the PI stops a research study for this reason, he/she should contact the appropriate person within the organization (e.g. pharmacy, IRB, department head) depending on the resource issue that caused the study to be stopped.

5.1.17 The PI must comply with conflict of interest policies as outlined in the IUPUI/Clarian SOP for Conflict of Interest Reporting to the IRB and institutional policies related to financial conflicts of interest.

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5.1.18 The PI must employ the following practices when students will be recruited as subjects:

5.1.18.1 Informed consent for participation must be sought only under circumstances that minimize the possibility of coercion or undue influence. For example, in general it is not acceptable for professors to recruit their own students for a research project due to the inherent potential for coercion the student might feel to participate.

5.1.18.2 The PI should include genuinely equivalent alternatives for those students who wish not to participate. For example, it would not be appropriate to provide as an alternative to participating in a simple questionnaire project, the option of writing a 5-page paper.

See Appendix N for additional guidance on recruiting students as subjects.

5.1.19 The PI is responsible for obtaining all appropriate approvals before commencing the research. This includes, but may not be limited to, IRB, VA Research & Development, Scientific Review (SRC), and General Clinical Research Center (GCRC) approvals.

5.1.20 **Research at the VA**. Investigators conducting research at or receiving funding from the VA have additional responsibilities. Refer to the VHA Handbook 1200.5 for additional requirements.

5.2. STUDY STATUS AND PROGRESS RESPONSIBILITIES OF THE PI

5.2.1 The PI is required to prospectively request any changes to the research study in the appropriate manner (submission of an amendment), and implement those changes only after receiving written approval from the IRB, except where necessary to eliminate apparent immediate hazards to human participants. If this occurs, the investigator must promptly report the exception to the FDA by protocol amendment and the IRB using the **IUPUI/Clarian Prompt Reporting Form**. The IRB will determine if the changes made are consistent with ensuring subjects' continued safety and welfare. If appropriate, the sponsor and other regulatory agencies must also be notified.

5.2.2 The PI must promptly notify the IRB when a research study is to be withdrawn from further IRB review.

5.2.2.1 If this occurs prior to IRB approval, the PI should submit a letter to the IRB making this request.

5.2.2.2 If this occurs after IRB approval has been granted for a research study (e.g. study termination, study completion, study never

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initiated), the request must be made using the standard continuing review form provided by the RCA or Methodist IRB office.

5.2.2.3 To report a status change (e.g. closed to subject enrollment) of an ongoing study that occurs off the study's continuing review cycle, the PI may submit a memo to the IRB making this request. If, however, the PI wishes to terminate or "complete" an approved research study prior to it's continuing review due date, the PI may request a continuing review form from the RCA or Methodist IRB office, as appropriate, to report this change in study status to the IRB.

5.2.2.4 Study completion should be promptly reported to the IRB. This is done by contacting the RCA or Methodist IRB office to request that a continuing review report be generated for completion.

5.2.3 The PI is responsible for reporting progress of approved research (e.g. continuing review) to the IRB and if required, the sponsor and/or monitor, as often as required and in a manner prescribed by the IRB on the basis of risks to subjects, but not less than once per year for expedited and full review studies.

5.2.3.1 Oversight by the IRB is required as long as investigators are either interacting or intervening with subjects or accessing identifiable private information for research purposes. This includes research studies that remain active only for data analysis or for long-term follow-up, even when the research is permanently closed to the enrollment of new subjects and all participants have completed all research-related interventions. For multi-site research, the investigator may close the study at the local site if investigators are neither interacting with subjects nor accessing subjects' identifiable information

5.2.3.2 The RCA or Methodist IRB office will generate a continuing review form for the PI to complete in advance of the study's continuing review due date. The PI must complete this form, even if a study will not be initiated or is being terminated or discontinued for any reason in the interim.

5.2.3.3 The regulations make no provisions for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Thus, if a PI fails to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research, including research interventions or interactions, enrollment of new participants, and analysis of identified data, must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or

interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

5.2.3.4 **Research Conducted at the VA.** If research is conducted at the VA and expires because the IRB did not grant continuing review, either because the IRB did not receive the required materials or because the IRB received the materials but did not grant continuing approval, the following additional requirements must be met:

5.2.3.4.1 The PI must submit immediately to the IRB Chair, a list of research subjects for whom stopping research procedures would cause harm.

5.2.3.4.2 The PI must notify the sponsor.

5.2.4 The PI must promptly report to the IRB any unanticipated problems involving risk to subjects or others and noncompliance as defined in the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance and, if appropriate, to the sponsor and other appropriate regulatory agencies. The determination of the relationship of the event to the study and/or test article rests with the PI.

5.2.5 The PI must notify the IRB if he/she is leaving the institution and must either terminate ongoing studies or arrange for appropriate transfer of authority of all ongoing studies to another qualified investigator.

5.2.6 If a suspension or termination involves the withdrawal of current subjects from the research, the PI is responsible for notifying and withdrawing the subjects in a manner that considers their safety, rights and welfare. Subjects must also be notified if follow-up for safety reasons is required or permitted. Events requiring prompt reporting to the IRB must continue to be reported as defined in the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.

5.3. INFORMED CONSENT AND AUTHORIZATION RESPONSIBILITIES

5.3.1 Pursuant to 45 CFR 46.116 and 21 CFR 50.20, unless waived or altered, no investigator may involve a human being as a participant in research covered by these policies unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative (LAR).

5.3.2 An investigator shall seek such consent only under circumstances that: (i) provide the prospective subject or the LAR sufficient opportunity to consider whether or not to participate and (ii) minimize the possibility of coercion or undue influence.

5.3.3 Pursuant to 45 CFR 46.117(a) and 21 CFR 50.27(a), unless waived by the IRB, informed consent shall be:

5.3.3.1 Documented by the use of a written consent form approved by the IRB.

5.3.3.2 Signed and dated by the subject or the subject's legally authorized representative.

5.3.3.3 A copy shall be given to the person signing the form.

5.3.4 The investigator is responsible for ensuring that informed consent is obtained from each research subject before that subject participates in the research study; unless the informed consent requirement has been waived by the IRB.

5.3.5 The investigator is ultimately responsible, even when delegating the task of obtaining informed consent, to another individual knowledgeable about the research.

5.3.6 The investigator is also responsible for ensuring that a release for health information authorization form is obtained from each subject at the time of consent, unless the authorization requirement has been waived by the IRB.

5.3.7 The investigator is responsible for ensuring that appropriate informed consent is obtained from each research subject who withdraws from a study when the investigator wishes to continue to follow the subject's health and collect clinical data.

5.3.8 The PI is required to obtain and document informed consent from each subject or subject's legally authorized representative in accordance with the Informed Consent SOP.

5.4. CERTIFICATION FOR RESEARCH SUPPORTED BY A FEDERAL DEPARTMENT OR AGENCY

5.4.1 Pursuant to 45 CFR 46.103(f), the investigator is required to submit the certification of human subjects review and approval ("certification") with the application or proposal or by such later date as may be prescribed by the Department or Agency to which the application or proposal is submitted. If the certification is not submitted within the appropriate time limits, the application or proposal may be returned to the institution.

5.4.2 Under no condition shall research covered by 45 CFR 46.103 of the policy be supported prior to receipt of the certification that the research has been reviewed and approved by an IRB.

5.5. ADDITIONAL RESPONSIBILITIES FOR RESEARCH INVOLVING INVESTIGATIONAL DRUGS

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5.5.1 Pursuant to 21 CFR 312.53(c)(1), before participating in an investigation, the PI must provide a commitment (Form FDA-1572) to the sponsor that he/she:

5.5.1.1 Will conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of participants;

5.5.1.2 Will comply with all requirements regarding the obligations of clinical investigators and all other pertinent requirements;

5.5.1.3 Will personally conduct or supervise the described investigation(s);

5.5.1.4 Will inform any potential participants that the drugs are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent and IRB review and approval are met;

5.5.1.5 Will report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with §312.64;

5.5.1.6 Has read and understands the information in the investigator's brochure, including the potential risks and side effects of the drug; and

5.5.1.7 Will ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

5.5.2 In addition to the investigational plan, conditions of approval imposed by the IRB, and applicable regulations, the PI is also responsible for ensuring that an investigation is conducted according to the signed investigator statement and any conditions of approval imposed by the FDA.

5.5.3 The PI is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.

5.5.3.1 Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes.

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5.5.3.2 The case history for each individual shall document that informed consent was obtained prior to participation in the study.

5.5.4 The PI is required to retain records required to be maintained under 21 CFR 312 for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and the FDA is notified.

5.5.5 **Investigator Reports**

5.5.5.1 **Progress Reports**. The PI is required to furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.

5.5.5.2 **Safety Reports**. The PI is required to promptly report to the sponsor any adverse effect that may reasonable be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately.

5.5.5.3 **Final Report**. The PI is required to provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.

5.5.5.4 **Financial Disclosure Reports**. The PI is required to provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statement as required under 21 CFR 54. The investigator is required to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

5.5.6 **Inspection of Investigator Records and Reports**

5.5.6.1 The investigator is required, upon request from any properly authorized officer or employee of FDA, at reasonable time, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 21 CFR 312.62, Investigator Recordkeeping and Record Retention.

5.5.6.2 The investigator is not required to divulge participant names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

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5.5.7 **Research involving investigational drugs conducted at the VA**. Research involving investigational drugs that is conducted at the VA must follow these additional requirements:

5.5.7.1 Inform the pharmacy service through the use of VA Form 10-1223 when IRB and R&D approvals have been obtained.

5.5.7.2 Provide the pharmacy with a signed copy of VA Form 10-1086 to document each subject's consent to participate in the study.

5.5.7.3 Inform the Chief, Pharmacy Service, and the R&D Committee when a study has been terminated.

5.6. ADDITONAL RESPONSIBILITIES FOR RESEARCH INVOLVING INVESTIGATIONAL DEVICES

5.6.1 Pursuant to 21 CFR 812.43(c)(4), the PI must provide the sponsor with a signed agreement that includes a statement of the PI's commitment to:

5.6.1.1 Conduct the investigation in accordance with the signed agreement, the investigational plan, applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;

5.6.1.2 Supervise all testing of the device involving human participants; and

5.6.1.3 Ensure that the requirements for obtaining informed consent are met.

5.6.2 Pursuant to 21 CFR 312.140(a), the PI shall maintain the following accurate, complete, and current records relating to his/her participation in an investigation:

5.6.2.1 All correspondence with another investigator, the IRB, the sponsor, a monitor or FDA, including required reports.

5.6.2.2 Records of receipt, use, or disposition that relate to:

5.6.2.2.1 The type and quantity of the device, the dates of its receipt, and the batch number or code mark;

5.6.2.2.2 The names of all persons who received, used, or disposed of each device; and

5.6.2.2.3 Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

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5.6.2.3 Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

5.6.2.3.1 Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study;

5.6.2.3.2 All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests; and

5.6.2.3.3 A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

5.6.2.4 The protocol, with documents showing the dates of reasons for each deviation from the protocol.

5.6.2.5 Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

5.6.3 **Investigator Reports.** Pursuant to 21 CFR 812.150(a), the PI shall prepare and submit the following complete, accurate, and timely reports:

5.6.3.1 **Unanticipated Device Effect**. The PI shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation per the reporting requirements described in the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.

5.6.3.2 **Withdraw of IRB Approval**. The PI shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

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5.6.3.3 **Progress Reports**. The PI shall submit progress reports on the investigation to the sponsor, the monitor and the IRB at regular intervals, but in no event less often than yearly. For reporting to the IRB, this is done at the time of continuing review.

5.6.3.4 **Protocol Deviation**. The PI shall notify the sponsor and the IRB of any deviation from the investigational plan to protect the life or physical well-being of a participant in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and the IRB, in accordance with §812.35(a) is also required. For reporting requirements, please see the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.

5.6.3.5 If the PI uses a device without obtaining informed consent, the PI shall report such use to the sponsor and IRB within 5 working days after the use occurs. For reporting requirements, please see the IUPUI/Clarian SOP for Unanticipated Problems and Noncompliance.

5.6.3.6 **Final Report**. The PI shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the IRB.

5.6.3.7 **Financial Disclosure Reports**. The PI is required to provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statement as required under 21 CFR 54. The investigator is required to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study

5.6.3.8 The PI shall, upon request by the IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

5.6.4 **Device Risk Assessment**. This investigator must provide to the IRB the sponsor's initial assessment of whether or not a device study is considered significant risk (SR) or nonsignificant risk (NSR).

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5.6.4.1 **Nonsignificant Risk Determination**. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to the FDA.

5.6.4.2 **Significant Risk Determination**. If, however, the IRB disagrees with the sponsor's initial NSR assessment, the investigator must notify the sponsor, who must notify the FDA that a SR determination has been made. The study can be conducted as a SR study once FDA approval of an IDE application has been provided to the IRB, and the study has been granted final IRB approval.

5.6.4.3 The FDA has the ultimate decision in determining if a device study is SR or NSR. If the FDA does not agree with an IRB's decision that a device study presents a NSR, the sponsor must submit an IDE application to the FDA. Alternately, if a sponsor files an IDE application with the FDA because it is presumed to be a SR study, but the FDA classifies the device study as NSR, FDA will return the IDE application to the sponsor and the study would be presented to the IRB as a NSR device study.

5.6.5 If the IRB determines that it cannot approve a clinical investigator because the investigation does not meet the criteria in the exception provided 21 CFR 50.24(a) or because of other relevant ethical concerns, the IRB will document its findings and provide them promptly in writing to the investigator, who is required to notify the sponsor of the clinical investigation.

5.6.6 **Inspection of Investigator Records and Reports**

5.6.6.1 The PI (or other investigator who has authority to grant access) shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, process, packed, installed, used, or implanted or where records of results from use of devices are kept.

5.6.6.2 The PI shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

5.6.6.3 The PI shall permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the PI to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

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5.7. ADDITIONAL RESPONSIBILITIES FOR BOTH INVESTIGATIONAL DRUG AND DEVICE STUDIES

5.7.1 The PI is responsible for informing any patient or subject, or any person used as a control, that the drug(s) or device(s) are being used for investigational purposes and assuring that the requirements relating to obtaining informed consent and IRB approval, as required by federal regulations, are followed.

5.7.2 If applicable, the PI must ensure that the toxicology and pharmacokinetics/ pharmacodynamics or safety data of a test article (e.g. device, drug, biologic) to be given to a human subject have been fully evaluated such that it is safe for use in human subjects.

5.7.3 If the research involves an investigator-held IND or IDE, the investigator assumes all of the responsibilities of the sponsor per 21 CFR 312, Subpart D or 21 CFR 812, Subpart C, including adverse event reporting to the FDA and participating sites (multi-center trials) and submission of annual reports. Because of the additional responsibilities of a sponsor, the PI must meet with individuals in the Office of Clinical Research (OCR) to discuss these responsibilities prior to study approval.

5.7.4 The PI must maintain compliance with institutional, hospital, clinic, OSHA, and other special committee regulations and policies (e.g. radiation safety, Scientific Review Committee, General Clinical Research Center, or other institutional committees) as well as Medicare/Medicaid billing, and HIPAA requirements (see IUPUI/Clarian SOP for Confidentiality and Privacy).

5.7.5 The PI must provide to the IRB the IND and/or IDE number issued by the FDA, if applicable for investigational drugs or devices before final IRB approval can be granted.

5.7.6 The PI is responsible for reading and understanding all of the information, including the potential risks and side effects, of any drug(s) and/or device(s) used in a research study.

5.7.7 If applicable, the PI must submit updated clinical investigators brochures to the IRB as they occur. In addition, any progress or final reports must be provided to the IRB with the PI's written assessment.

5.7.8 For studies involving investigational drugs, the PI must appropriately complete FDA form 1572. Additionally, FDA form 3455 must be completed by all investigators completing or listed on the 1572 form. FDA 3455 discloses financial arrangements between study sponsor and study investigator, significant payments from study sponsor, proprietary interest in the tested product, significant equity interest in the tested product or study sponsor, steps taken to

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minimize the potential for bias, and any other additional information required by the sponsor. These forms are not submitted to the IRB.

5.7.9 If applicable, the PI must ensure appropriate disposition/accountability of drugs and devices and ensuring that the information obtained from the sponsor is accurate. (See IUPUI/Clarian SOPs for Investigational Drug Accountability and Investigational Device Accountability.)

Note: The PI may delegate specific tasks to members of the research team. However, the PI assumes ultimate responsibility for these tasks.

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Title:	Safety Monitoring Plans			
Current Version:	07/07		Previous Versions:	09/01, 09/04, 02/05, 04/05

1. INTRODUCTION

The federal regulations governing human subjects research state that 1) the research plan, when appropriate, shall make adequate provisions for monitoring of the collected data to ensure the safety of research subjects; and 2) there shall be adequate provisions to protect the privacy of subjects and to maintain the confidentiality of research data. The specifics of each study must be thoroughly evaluated and consideration given to a number of factors pertaining to each research study in order to determine the risk/benefit ratio for a given research study. Based on such assessed risk, safety checkpoint indicators should be built into the study protocol to continually monitor subjects' safety. Periodic oversight should also be applied to assure that the safeguards built into the protocol are effective and followed and the research team is working effectively to maintain subject safety. Therefore, IUPUI/Clarian, as well as other national organizations (e.g. NIH), require a safety/risk assessment and research oversight plan for every human subjects research study requiring full board review (and in some cases, expedited) endorsed.

In general, these research plans, also called data safety monitoring plans, should provide for a regular review of accrued research data and other relevant information so as to ensure the validity and integrity of the data and that there is no change to the anticipated risk/benefit ratio of the research study. Additionally, there should be an ongoing review of study procedures so as to ensure that the privacy of research subjects and the confidentiality of their research data have not been violated.

2. OBJECTIVE

The objectives of this SOP are to provide:

2.1. Investigators with guidelines for assessing the safety and risk of a research study and for developing a research oversight plan for continually monitoring the research; and

2.2. IUPUI/Clarian IRBs with guidelines for evaluating a proposed safety/risk assessment and research oversight plan for various types of human subjects research.

3. SCOPE

These policy and procedures apply to all research activities of faculty, staff, student, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVENT DEFINITIONS

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5. POLICY AND RELATED PROCEDURES

5.1. For the IRB to grant approval of a research project, it must ensure that the safety and welfare of human subjects are adequately protected. As part of it's assessment, it shall determine that all of the criteria for IRB approval of research outlined in §46.111 (and 5.7.2 of the IRB Operations SOP) are satisfied.

5.2. As part of the IRB's review to assess whether the safety and welfare of subjects is adequately protected in a given research study, it may evaluate a research oversight plan outlined and submitted by the investigator.

5.3. **PI Responsibilities for Developing a Safety/Risk Assessment and Research Oversight Plan**

5.3.1 For all research studies that are considered "greater than minimal risk" and require full IRB review, the PI will be responsible for developing a DSMP[4.3] to assure that subject safety will be monitored. In some cases, the IRB may also request that an expedited study (a study considered "less than minimal risk") develop a DSMP if it is felt to be necessary.

5.3.2 This plan will be required for all new research submissions meeting the criteria above (in 5.3.1) before the IRB can grant final approval

5.3.3 Because of the wide variety of types of research that is conducted within the IUPUI/Clarian system, the risk assessment and research oversight plan can also vary widely. Rather than a specific policy, the investigator should consider the following when developing a safety/risk assessment and research oversight plan:

5.3.3.1 What is the nature of the research study? Does it involve the administration of a substance (e.g. drug or biologic) or an investigation device? For additional information on device risk requirements for investigational devices, see the IRB Operations SOP.

5.3.3.2 Is the subject population vulnerable? (e.g. cognitively impaired, prisoners, pregnant women, minors, unconscious)? These populations require additional protections. See the IUPUI/Clarian SOP for Vulnerable Populations for additional information on the requirements.

5.3.3.3 Where is the study being conducted? (e.g. hospital, public area)

5.3.3.4 How complex is the study? (e.g. multi-dose, multi-drug dose-escalation, double-blinded, altered pharmacokinetics, early study phase, investigator-initiated, multi-site).

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5.3.3.5 How experienced is the research team? (e.g. first study vs. experienced)

5.3.3.6 What is the duration of the study (e.g. two days vs. two years) and duration of subject participation (e.g. 1 visit vs. many visits), and how many subjects will the research involve?

5.3.3.7 Is there any oversight by other organizations? (e.g. pharmaceutical company, NCI, etc.).

5.3.3.8 What kind of security safeguards exist for individually identifiable research data? Elements to consider:

- Does the study involve sensitive information (e.g. HIV, mental health, etc.)?
- Is it a multi-site study with sharing and/or accessing of data, video, or photography amongst many sites/individuals?
- Will databases be accessed or developed?
- How will subjects be recruited?

5.3.3.9 What kinds of safeguards exist for protecting the privacy of subjects? Elements to consider:

- Where are interviews or other face-to-face encounters taking place and what measures have been taken to protect subjects' privacy?
- Are there any signs or other revealing information visible at the research site that might "stigmatize" subjects?

5.3.4 The oversight could be done using a variety of different individuals or entities, for example a pharmaceutical sponsor, contract research monitor, others within the department, General Clinical Research Center (GCRC), or a granting organization (e.g. NCI). In some situations a Data Safety Monitoring Board (DSMB[4.2]) may be required (e.g., NIH). Considerations in designing a safety monitoring plan, review process, safety reports, interim analysis, independence of review, steps emanating from review, statistical considerations, and stopping rules are outlined in Generic Monitoring Plan for Trials Requiring a Data Safety Monitoring Board.

5.3.5 For some sponsored-research studies, the DSMP may already be explained within the protocol. This DSMP may even include an independent DSMB. If this is the case, the PI can simply reference that plan in response to this DSMP requirement.

5.3.6 If, however, the protocol does not contain its own DSMP, the PI is required to develop his/her own plan while taking into consideration the elements listed above. The PI should use the DSMP template and additional guidelines and

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surveys provided in the appendices of this document to assist in the plan's development.

5.4. IRB Responsibilities in Evaluating a Proposed Safety/Risk Assessment and Research Oversight Plan

5.4.1 Based on the IRB's review of required documentation provided by the investigator, including the safety/risk assessment and research oversight plan, in accordance with appropriate regulations and IUPUI/Clarian policies, and with consideration of the guidance provided in this SOP, the IRB will determine the adequacy of and have final approval authority regarding the research oversight plan. It may add, revise, or delete elements from the research oversight plan for each study, as necessary, to ensure the safety of subjects.

5.4.2 Evidence of execution of and adherence to the research oversight plan (e.g. dates of oversight checks, reports) will be requested by the IRB at interim or continuing updates. In some cases, the HSR Auditor[4.4] or other designee might perform an audit to determine the adherence to the oversight plan and/or observe or monitor the informed consent process. Also, based on new information on the safety aspects of the research the oversight process may be modified, based on the investigator's or the IRB's recommendation. This information should be retained and kept current. These documents will be useful during sponsor or regulatory agency inspections, i.e., to show due diligence concerning subject safety.

5.4.3 As part of the research oversight plan, the IRB will determine the continuing review cycle for each study. Typically, the IRB reviews each study on an annual basis. However, for studies that are considered "high-risk" as outlined in Appendix P, the IRB may set the review cycle to occur more frequently (e.g. every 3-6 months or after 10 subjects have been enrolled). This review cycle may change during the course of the study if at any time the IRB determines that the risks to subjects have either increased or decreased.

5.4.4 With information provided in continuing review reports or from other sources, the IRB will determine which studies require verification from sources other than the investigator that no material changes have occurred since the last continuing review and may result in a change to the research oversight plan. The following criteria will be used to make this determination:

5.4.4.1 Randomly selected studies;
5.4.4.2 Complex studies involving unusual levels and types of risk to subjects;
5.4.4.3 Studies conducted by investigators who previously failed to comply with federal regulations and institutional policies; and
5.4.4.4 Studies where concern about possible material changes occurring without IRB approval have been raised.

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Title:	Security of Research Data			
Current Version:	07/07		Previous Versions:	12/04

1. INTRODUCTION

Safeguarding the confidentiality, integrity and availability of research data is critically important to maintaining a successful research program. Good security ensures and builds research subject confidence that their personal information will be kept confidential, and also ensures that valuable research data is protected and accessible when needed.

Schools/departments/practice plans are responsible for managing the security of their systems, computers, networks and other computer resources**.** Principal Investigators (PIs) also play an important role in addressing the security of research data. This SOP describes some of the key responsibilities that PIs and researchers have in safeguarding research data.

2. OBJECTIVES

The objectives of this SOP are:

2.1. To define expectations regarding Principal Investigator and research team member responsibilities in appropriately safeguarding all basic and clinical research data, whether or not it includes Protected Health Information (PHI) in all forms – electronic, paper and verbal; and

2.2. To define procedures and guidelines to help the IUPUI research community and its partners (Clarian, VA, Wishard, etc.) understand what is expected under Indiana University (IU) and Indiana University School of Medicine (IUSM) policy, as well as state and federal laws and regulations, including the Health Insurance Portability and Accountability Act (HIPAA.)

For more details regarding Indiana University and Indiana University School of Medicine security policies, visit http://www.itpo.iu.edu and http://technology.iusm.iu.edu/. For more details regarding HIPAA research requirements, see the IUPUI/Clarian SOP for Subject Confidentiality and Privacy.

3. SCOPE:

This Standard Operating Procedure (SOP) applies to the following:

3.1. All personnel who conduct research, assist in the performance of research or otherwise collect, use or disclose data in connection with human subjects research activities at IUPUI/Clarian.

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3.2. All human subjects research including exempt, expedited, and full review protocols reviewed and approved by the IUPUI/Clarian Institutional Review Board (IRB).

3.3. All data used or accessed for human subjects research purposes, including experimental data of all forms and data involving Protected Health Information (PHI). This includes data maintained in all forms, including paper, electronic or verbal form.

4. RELEVANT DEFINITIONS:

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5. POLICY REFERENCE AND ASSOCIATED PROCEDURES:

5.1. **Roles and Responsibilities of Principal Investigator and Research Team in Safeguarding Research Data**

Policy References: IU Guidelines for Handling Electronic Institutional and Personal Information, IU Best Practices for Handling Electronic Institutional and Personal Information, IU Policy on Security of University IT Resources

5.1.1 In general, all members of the research team are responsible for correctly and sufficiently using research computers, databases and records to ensure security and confidentiality of the data stored and transmitted using those resources.

5.1.2 Principal Investigators (PI) are responsible for ensuring research data remains secure when under the research team's control by:

5.1.2.1 Using appropriate safeguards to maintain the confidentiality, integrity and availability of data that is collected, used, shared and/or stored for research purposes, including Protected Health Information (PHI);

5.1.2.2 Establishing appropriate security oversight for a research project and identifying whether certain aspects should be delegated and to whom.

5.1.2.3 Identifying all on-site and off-site research personnel who have or need access to research data in any form and ensuring they employ appropriate safeguards and follow all university policies regarding access to data.

5.1.2.4 Ensuring all members of the research team in contact with the data understand their responsibilities and that access to this data is appropriately restricted.

5.1.2.5 Ensuring that for human subject research, the Summary Safeguard

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Statement in the IRB application appropriately explains the safeguards used to protect the data, including the Data Source (i.e. the types of records that are used to gather the data) and the Data Recording/Collection method.

5.1.2.6 Immediately reporting any suspected or known security breaches that compromise research data to the Information Technology Security Office (ITSO) and the appropriate Security Office (e.g. IU School of Medicine, Clarian, VA, Wishard, IUMG, etc.). See *Section 5.7 Responding to Security Incidents Procedure below for details.*

5.2. **Security Plan**

Each research project or center requires an appropriate security plan designed to safeguard the security of research data. This may be project specific, team specific or lab or location specific.

5.2.1 This may be delegated to an appropriate person within a Department, School, or Division but the PI is ultimately responsible for communicating needs and for ensuring an appropriate security organizations plan exists. Please note: in some situations, this could involve multiple organizations. As a result, this delegation may need to cross multiple organizational policies (i.e. Clarian, Wishard, VA, etc.)

5.2.1.1 The PI is responsible for identifying which security policies are applicable to their specific project and for oversight of the delegate.

5.2.1.2 The PI is responsible for identifying the need for the addition of any piece of equipment to the IU network (e.g. hardware, software, wireless devices, etc.)

5.2.1.3 The PI is responsible for coordinating security planning for the delegate and any third party outside the university (e.g. other institutions, investigators, companies, sponsors, labs, etc.) involved in supplying electronic resources used to collect, store or share research data for a research project.

5.2.2 If the PI chooses not to delegate this responsibility, the PI is responsible for developing their own security plan (See Appendix Z for security plan outline) that provides the following:

5.2.2.1 Description of the local environment, including:

- Identification of data inputs;
- Locations of collections of data;
- Explanation of the type of data collected and a data flow diagram; and

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5.2.2.2 Explanation of the security controls that will be employed to ensure compliance with this policy.

5.3. Acceptable Use of Research Data and University Computer Resources

Policy References: IU Computer Users Privileges and Responsibilities, Interim Policy on Use of IU IT Resources (IT-01), and IUPUI/Clarian SOP for Data Management

5.3.1 Research team members may only access or use Computer Resources for approved research purposes when:

5.3.1.1 They are authorized to access the resource for research purposes and the research is approved by the appropriate research oversight committee (i.e. IRB, IACUC, IBC, VA R&D, etc.); and

5.3.1.2 Use of the data is for legal and ethical purposes that comply with university policy, as well as state and federal laws and regulations.

5.3.2 Data should only be collected, used, stored, shared, disposed of in accordance with the IUPUI/Clarian SOP for Data Management.

5.4. Secure Collection and Storage of Research Data

Policy References: IU Best Practices for Handling Electronic Institutional and Personal Information and IUSM SEC-02, Disposition of IUSM Electronic Media

5.4.1 Collected data should be securely gathered and stored.

5.4.1.1 **Electronic data:** Data collected using a computer resource (e.g. a laptop, hard drive, local shared drive, web-based system, CDs, floppy disks, etc.) or a PDA should be stored in a secure location. Following are general guidelines:

- Keep all computer resources, including diskettes, CDs and other removable media in a secure location such as a locked office, a locked cabinet, or a room with limited access by unauthorized personnel, etc.
- Ensure that security features on the computer or PDA are enabled, particularly if connected to a network or to the Internet. For instance, access should require a password before allowing a user entry to a computer and/or electronic files.
- Secure electronic surveys or questionnaires. The survey should be restricted to only authorized personnel, using passwords to protect the survey, encrypting data when in transit, etc.
- If data is reviewed electronically (e.g. CareWeb or Regenstrief Medical Record System, VA CPRS, patient care database, etc.)

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do so from a secure computer.

- Position computer monitors to minimize viewing by others.
- If diskettes, CDs and other removable media are transported, reasonable measures should be taken to ensure they are delivered securely to the intended recipient. (For instance, ensuring that media are not left unattended in public places or places where they could easily be compromised.) In addition, data stored on diskettes, CDs or other removable media should not be taken home or transferred to a personally-owned computer. For more details regarding remote access procedures, see Section 5.9 of this document.
- Research data collected for a study should be stored on a designated secure server whenever possible. The PI should identify an appropriate location for storing research data in the project's approved security plan. Storing data on workstations should be minimized wherever possible.

5.4.1.2 **Printed Data**: Data referenced or collected from paper records must also be properly safeguarded. Following are general guidelines:

- Keep the records in a secure location, such as a medical records room or a locked private office.
- If practical, original records should not be removed from the source location or from an approved research location.
- If original records are removed from the source or from an approved research location, to another approved research location, then records must be securely transported. Secure transport includes a fully enclosed folder, locked briefcase, US Mail or courier service. Reasonable measures should be taken to limit the amount of original data removed from the source location.
- Under no circumstances should paper records be left unattended in a public area.
- Paper surveys or questionnaires should be gathered and organized in a manner to minimize potential loss of the information. In addition, the data collection instruments should be stored in a secure location such as a locked cabinet or office that has limited access by unauthorized personnel (i.e. anyone who is not part of the research team).
- Paper records / data recorded in a researcher's notes, on a case report form or in other documents, must be kept in a secure location, such as a locked office, locked cabinet or other area with limited public access.

5.4.1.3 **Phone or In-Person Interviews**: If data are collected during interviews (either phone interviews or those conducted in person), consider the physical proximity of the subject and interviewer and

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the manner in which the data are collected during the interview:

- Interviews should be conducted in a private location when possible so that the subject's information would not likely be overheard by individuals who are not members of the research team.
- In addition, records created from these interviews (e.g. notes, surveys or other documentation or recordings) should be kept in a secure location or on a secure computer.

5.4.1.4 **Video and Audio Data:** Data collected using video, audio or other media must be safeguarded when recorded and stored.

- Data should be collected in a private location when possible so that the subject's information would not likely be overheard by individuals who are not members of the research team.
- Once the video or audio recording is completed, the tapes, CDs or other media should be stored in a secure location (e.g. a locked cabinet or office.)

5.4.1.5 **Long-Term Storage / Archival**: Data that are archived or placed into long-term storage should be securely stored.

- Printed, audio and video records or files should be securely stored off-site where possible, or at a minimum stored in a locked room or cabinet. Access to the records should be limited to authorized personnel.
- Electronic files should be encrypted where possible.
- PIs should maintain an inventory of records or files maintained in long-term storage.
- When professional storage facilities or archival companies are utilized contractual agreements should adequately protect the data.

5.5. Secure Disposition, Disposal or Destruction of Research Data and Electronic Media

Policy References: IU Best Practices for Handling Electronic Institutional and Personal Information, the Department of Defense 5220.22-M National Industrial Security Program Operating Manual (NISPOM, dated January 1995) and IUSM SEC-02, Disposition of IUSM Electronic Media

5.5.1 PIs must ensure that data transferred outside the immediate control of the research team are sent to authorized parties and that data are stored securely. This applies to organizations that handle storage or ongoing management of the data (e.g. off-site storage facilities or research sponsors.)

5.5.2 Records, electronic media (such as CDs, diskettes, etc.) or computer equipment on which research data are stored, must be physically destroyed or sanitized according to the following guidelines before that resource is sold, donated or

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discarded:

5.5.2.1 **Printed research data:** Printed data may be destroyed by burning, shredding or other approved measures.

- The process for destruction should ensure that the information cannot be reconstructed; and
- If shredding is used, crosscut shredders are preferred.

5.5.2.2 **Data stored on computers and other electronic devices**: Permanently delete or overwrite data stored on computers, laptops, PDAs and other electronic devices before transferring the equipment, or destroy discarded equipment.

- Simply deleting data from a computer's hard drive does not permanently delete the data. In other words, data must be removed at the physical level or appropriately overwritten before transferring the equipment to someone else. This generally involves the use of special software designed to cleanse or overwrite the data. For assistance with permanently deleting or overwriting data, please contact the Information Technology support person for your Department, or school location.
- Within the School of Medicine, you may contact the Information Services Technology Management Office at http://technology.iusm.iu.edu/.

5.5.2.3 **Reusable media such as CDs and diskettes:** Files that will no longer be used must be permanently deleted from reusable media before transferring the media outside the researcher's control. In addition, diskettes and CDs must be destroyed when discarded. Any of the following means may be used for destroying electronic media: shredding, burning, melting, or other approved methods.

5.5.2.4 **Other Media:** Permanently destroy video or audio tapes, files or other media, including data contained in microform when discarded (e.g. microfilm, microfiche, or similar high data density material). These media may be destroyed by shredding, burning or other approved methods.

5.5.2.5 **Disposal of equipment:** If equipment will be discarded, contact the information technology support person in your Department or Office to coordinate the proper destruction of the equipment. The IUPUI Purchasing Department and IUSM SEC-02, Disposition of IUSM Electronic Media and its associated procedures outline the requirements for properly disposing of equipment.

5.5.3 IUPUI/Clarian policy specifies certain timeframes required for retaining data. For more details, see the IUPUI/Clarian SOP for Subject Privacy and

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Confidentiality and the IUPUI/Clarian SOP on Data Management.

5.5.4 For additional information on securely removing data from storage media, see the Securely Remove Data Guide at: http://www.itso.iu.edu/howto/secure-delete.epl.

5.6. Back-up and Disaster Recovery

Policy References: IU Guidelines for Handling Electronic Institutional and Personal Information

Principal Investigators are responsible for ensuring that research team members understand and follow proper backup procedures. All research data must be backed up and fully recoverable in the event the primary copy is damaged or unavailable.

5.6.1 Back-Up Electronic Data

5.6.1.1 All electronic research data should be placed on a network server maintained by the University wherever possible. It is the PI's responsibility to verify where data are stored and confirm that it is, in fact, a university-maintained network server. The details of the back-up process should be included in the approved security plan.

- Data stored on such network servers will automatically be backed up on a routine basis. As a result, researchers should not have to maintain a separate back-up copy of these data.
- Electronic research data, such as Protected Health Information, should NOT be permanently stored on computers, laptops or personal devices if at all possible. Data collected on these devices should be transferred to University-maintained network servers as soon as possible for permanent storage to avoid potential loss of data.

5.6.1.2 If data are stored locally (on a computer's hard drive – e.g. c:\ drive), backups should be done on a monthly basis at a minimum until the data can be transferred to a network server for permanent storage. It is highly recommended that more frequent backups are made.

- At a minimum, one fully recoverable version of electronic research data must be stored off-site. It is also recommended that weekly, monthly and yearly backups also be stored off-site.

5.6.2 Back-Up Printed Data

5.6.2.1 Researchers should assess the likelihood that paper records could be destroyed or damaged and assess whether backup copies of printed data should be made.

5.6.2.2 Copies of printed research data, such as questionnaires, reports and

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forms as well as source documents should be made whenever possible and stored at a secure off-site location to avoid loss of critical research and supporting data.

5.6.3 **Disaster Recovery:** Principal Investigator should ensure that the research team understands the process for retrieving backed up data if the primary copy becomes unusable. The retrieval process should be tested at least annually to ensure that data can be recovered from the back-up copy.

5.7. **Responding to Security Incidents**

Policy References: IU Policy on Security of University IT Resources (IT-12) and IUSM Incident Response Policy

5.7.1 Known or suspected breaches of security of computer or technology research resources must be reported to the appropriate security contact for that office or location as soon as the incident is discovered:

5.7.1.1 For Indiana University and IU School of Medicine:
- IT Security Office (ITSO) at it-incident@iu.edu
- Office of Compliance Services Hotline: **877-526-6759**

5.7.1.2 Clarian Health – **IS Security Officer 962-3175**

5.7.1.3 Wishard Health Services – **IS Security Officer 630-7880**

5.7.1.4 VA Hospital – **Information Security Officer, 554-0000, ext. 3118**

5.7.2 If the incident pertains to compromise of research data in other forms (e.g. paper records, video, audio, etc.), notify the appropriate compliance office as follows:

5.7.2.1 Office of Research Compliance (IRB Office) – resrisk@iupui.edu; and/or

5.7.2.2 For IU School of Medicine (IUSM): Office of Compliance Services Hotline: **877-526-6759**

5.7.3 The Principal Investigator and the research team must assist the Incident Response Team as needed with security incident investigations.

5.7.4 ITSO and/or IUSM may remove or disconnect any computer resource that presents a risk to the university or the IUSM security. ITSO and/or IUSM will determine, in consultation with the Principal Investigator whether to restore & resume operation of a computer or whether additional measures should be pursued following investigation of an incident. The PI's Department will be responsible for all costs needed to investigate, cleanup & recover from a security

incident.

5.7.5 Pursuant to Indiana code 4-1-11, whenever a security breach of electronic data is experienced that is reasonably believed to have exposed unencrypted "personal information" to unauthorized third party access, individuals whose data was exposed must be notified. For additional information, please refer to IC 4-1-11 (http://www.ai.org/legislative/ic/code/title4/ar1/ch11.html).

5.8. Sanctions for Misuse or Abuse of Research Resources

Policy Reference: IU Interim Policy on Sanctions for Misuse or Abuse of IU Technology Resources (IT-02)

Abuse or misuse of resources that contain research data will be investigated by the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC) and other appropriate offices. These offices have the authority to take disciplinary action, up to and including confiscation of equipment, termination of network connectivity and/or termination of a research study.

5.9. Remote Access to the IUSM Network

Policy References: IU Policy on Extending the Network (IT-19), IU Policy on Wireless Networking (IU-20)

5.9.1 Researchers are not permitted to independently install remote access devices, Virtual Private Networks, or wireless networks or dial-in modem services.

5.9.2 If a new or wireless network (e.g. installing a wireless router to connect several computers that have wireless cards) is being considered for the study, the PI must coordinate with the information technology support person in their Department and obtain written approval from the UITS Network Operations Center. This does not include computers with wireless cards that utilize the institution's (e.g. IU, Clarian, etc.) existing wireless network.

5.9.3 IU, Clarian, VA and Wishard all have stringent requirements that must be met before any new networks or remote access devices may be installed.

5.10. Electronic Mail Security

Policy References: IU Best Practices for Handling Electronic Institutional and Personal Information, IU Policy on Use of Electronic Mail (IT-21)

5.10.1 IU e-mail users must comply with state and federal law, institutional policies and normal standards of professional and personal ethics, courtesy & conduct related to e-mail use.

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5.10.2 When an individual is provided an IUPUI e-mail address solely for the purpose of a research study (i.e. a sponsored e-mail account), the person who sponsored the account must notify actadmin@iupui.edu when a researcher no longer needs access for that study.

5.10.3 Email accounts and account passwords shall not be shared.

5.10.4 Sensitive research data should not be sent via e-mail unless specific steps are taken to confirm the transmission is secure. (Routine e-mail within Indiana University (Outlook) or purchased services are generally not secure and their use for transmitting sensitive data should be minimized).

5.10.4.1 Consult with the information technology support person to determine whether the Department or office can implement a secured e-mail transmission.

5.10.4.2 Indiana state law has very specific requirements regarding the use of e-mail for provider to patient communications. For more details, contact the IUSM Compliance Office.

5.10.5 Use of subject e-mail lists to communicate with subjects or potential subjects must respect subject confidentiality and comply with all appropriate IUPUI/Clarian Standard Operating Procedures. Note that IRB approval of email content may also be required.

5.10.6 PIs are responsible for determining when research communications sent via e-mail should be retained for a particular study and for communicating these requirements to the research team.

5.10.7 E-mails that are sent with confidential information should include the following disclaimer:

CONFIDENTIALITY NOTICE: This email message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, you must not forward, copy, print, save, use or disseminate this message or any attachments. Please contact the sender by reply email and delete and/or destroy all copies of the original message. Thank you.

5.11. **Anti-Virus**

Policy Reference: IU Computer Users Privileges and Responsibilities

5.11.1 Principal Investigators are responsible for ensuring that a current version of a virus control program (e.g. Symantec's Norton Antivirus (NAV))is in place on

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all computers used for research purposes, and for updating the virus detection program on a routine basis.

5.11.2 Users should be aware of computer viruses and other destructive programs and take steps to avoid them. For instance:

5.11.2.1 Avoid opening emails from an unrecognized sender; and

5.11.2.2 Avoid installing programs or files from unknown sources.

5.11.2.3 Routinely update virus protection program.

5.12. **Access to Research Data**

Policy Reference: IU Policy on Access to Institutional Data

5.12.1 Research data may only be accessed for approved research studies according to the information's sensitivity and the level of risk should the data be disclosed. *(For more details regarding information sensitivity categories, see Exhibit A).*

5.12.2 Principal Investigators are responsible for ensuring that appropriate measures are employed so that only authorized research personnel have access to research data for that study. This includes databases, records, software or other sources used for research purposes that are within the PI's or research team's control.

5.12.3 The PI should ensure that researchers understand appropriate procedures for requesting access to data maintained by other parties.

5.12.4 In order for a non-IU Research Collaborator to access & use IU computer, network and e-mail resources, the Principal Investigator must provide written certification of need and submit this certification to ITPO by completing the form found at https://itaccounts.iu.edu/. Directions for filling out the form are found at: http://kb.indiana.edu/data/akll.html . Periodic renewal is required with ITPO.

Access to research data and University resources should be appropriately terminated for research team members who end their involvement with the study by notifying acadmn@iupui.edu when a researcher no longer needs access.

5.13. **Managing User Computer Accounts**

Policy References: IU Guidelines for Handling Electronic Institutional and Personal Information, IU Policy on Network and Computer Accounts Administration (IT-18)

5.13.1 **Setting Up Access to Systems or Computers:** If new computers, systems, software or databases are created or obtained for a study and these resources are

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not accessed through a secure IU Network connection, then additional security measures apply. For more details, see the IU Policy on Network and Computer Accounts Administration (IT-18) at http://www.itpo.iu.edu/IT18.html.

5.13.1.1 Each user must be assigned an individual logon (i.e. user ID and password).

- Passwords should be assigned to restrict access to Limited and Restricted information whenever possible.
- Passwords should be obscure (i.e. not common dictionary words or words that are easily derived). This applies only when a new computer, system, or database are installed for a study. Passwords are otherwise maintained by the Information Technology representative within your Department or by UITS.
- User logons should be tracked and documented (such as maintaining an active user list for new resources developed for a research study).

5.13.2 **Procedures for Providing Access to University Systems:**

5.13.2.1 Provide access only to those who legitimately require it.

5.13.2.2 Require users to be identified and authenticated before allowing access.

5.13.2.3 Limit access to needed services and authorized individuals only.

5.13.2.4 Assign accounts only to individuals (i.e., don't use group accounts).

5.13.3 **Using Systems or Computers:**

5.13.3.1 Researchers may not share their logons or passwords with others;

5.13.3.2 Passwords should be changed periodically;

5.13.3.3 Researchers may not assume the identity of another computer user; and

5.13.3.4 Researchers should not leave their logon active and unattended.

5.14. **Data Encryption**

Policy References: IU Guidelines for Handling Electronic Institutional and Personal Information

Unencrypted data, whether stored in a file or transmitted across the network, is vulnerable to disclosure. Data should be encrypted whenever possible, particularly for

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archived data stored off-site and when sending data electronically (through e-mail or file transfer). There is technology available to protect sensitive data contained in stand alone files, e-mail communications, and data passed between a web browser and a web server. For assistance, consult UITS Best Practices or contact your Information Technology support person in your office or location.

5.15. **Computer Security**

Policy References: IU Guidelines for Handling Electronic Institutional and Personal Information

5.15.1 PIs should know whether there are adequate safeguards to protect computers, including laptops and PDAs, the data and files. Computers that are not sufficiently protected should be enhanced with additional appropriate safeguards.

5.15.2 Guidelines for using computers include but are not limited to:

5.15.2.1 Password-protected screen savers should be used whenever possible;

5.15.2.2 Computers should not be left unattended if that could result in unauthorized access;

5.15.2.3 Systems should be logged off and closed when not in use; and

5.15.2.4 Users should prevent others from inadvertently viewing their computer screen when working with sensitive data.

5.15.3 Guidelines for protecting system vulnerabilities:

5.15.3.1 Apply vendor-supplied security fixes (patches) to protect against system compromise.

5.15.3.2 Regularly scan computers for security vulnerabilities.

5.15.3.3 Remove unneeded services and software.

5.15.3.4 Stay informed of security issues. One way to do this is to routinely check the University IT Security Office website at: http://www.itso.iu.edu for current security issues and security guides.

5.16. **Faxing Research Data**

5.16.1 Researchers should use the following guidelines when faxing research data:

5.16.1.1 Include a fax cover sheet with a confidentiality statement, particularly when faxing restricted data such as Protected Health

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Information (PHI);

5.16.1.2 Use reasonable measures to ensure the receipt of fax transmissions is protected from general viewing; and

5.16.1.3 Fax machines utilized to transmit or receive research data should be located in areas with restricted access or limited to authorized personnel only whenever possible.

5.17. **Research Security Audits: Applies only to School of Medicine**

5.17.1 Principal Investigators will cooperate with security audits and will maintain appropriate documentation needed for security audit purposes, including but not limited to:

5.17.1.1 A list of all researchers working on a given research project that have access to data used for that project;

5.17.1.2 A copy of the security plan for that project, lab or location; and

5.17.1.3 A copy of a security audit log when required by regulation (e.g. FDA, HIPAA, etc.) For instance, this could include a list of researchers who accessed a research database or system, including the date and time of the access.

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Title:	SOP Process			
Current Version:	07/07		Previous Versions:	09/01, 11/04

1. INTRODUCTION

The Belmont Report established three basic ethical principles – autonomy/respect for persons, beneficence, and justice – which are the cornerstone for regulations involving human subjects. It is these three basic ethical principles that Indiana University Purdue University Indianapolis (IUPUI) and Clarian Health Partners (Clarian) follow to govern the conduct of human subjects research. To this end, the policies and Standard Operating Procedures (SOPs)[4.5] were established for the Human Research Protection Program (HRPP). Through well thought-out policies, clear and concise definitions, and standard procedures that fit well into the actual work process, an operation can function with regularity, efficiency, and good quality. (SOPs) provide the basis for orienting and educating new staff. The SOPs are the first place regulatory agencies[4.3] and study sponsors[4.6] go when seeking to assure themselves that a research department or investigator and their staff are operating appropriately in their field of expertise. Recently, IUPUI[4.2] and Clarian[4.1] have merged their existing SOPs into a series of joint documents to guide research operations.

2. OBJECTIVES

The objectives of this SOP are to describe the ways in which SOPs will be written, reviewed, approved, and implemented. SOPs will be used in the day-to-day functioning of the researchers and departments of IUPUI/Clarian to assure subject safety and protocol/regulatory compliance. They will be utilized to help ensure data integrity.

3. SCOPE

This SOP applies to all personnel involved in the implementation and coordination of investigations involving human subjects by all departments of IUPUI/Clarian. Personnel responsible: Principal Investigator/Co-investigator(s) and, *when delegated by the investigator*, sub-investigator(s), research coordinators, and other appropriately experienced and trained designated site personnel.

4. DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1. It is the policy of IUPUI/Clarian that research involving human subjects will be conducted according to high ethical and professional standards and in line with current research practices in the field.

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5.2. SOPs will be written by individuals with specific technical expertise regarding quality and compliance in human subject research. The writing of SOPs will be overseen by the Director, Research Compliance Administration[4.4]. New SOPs will be reviewed and approved by the IRB Executive Committee and the Vice Chancellor for Research and Graduate Education.

5.3. To that end, standard operating procedures (SOPs) will be followed by those conducting or supporting research.

5.4. The SOPs will be the basis for educating new people on the conduct of human subjects' research.

5.5. SOPs will be used to guide regulatory agency inspectors, sponsor company monitors or auditors, and IUPUI/Clarian oversight staff as they examine and evaluate the conduct of human subjects' research.

5.6. SOPs will be reviewed annually in the office of Research Compliance Administration to assure they accurately reflect research processes within IUPUI/Clarian. Research Compliance Administration will seek designated topic experts to assist them in their reviews.

5.7. No revisions of the SOPs are allowed, except by the office of Research Compliance Administration. If revisions appear to be needed, requests for change should be made to the Director, Research Compliance Administration.

5.8. A record (official) copy of the SOPs will be maintained in the Research Compliance Administration office.

5.9. SOPs will be available on-line at http://www.iupui.edu/~respoly/human-sop/human-sop-menu.htm.

5.10. For training purposes and day-to-day use, SOPs may be printed off-line, but, when notified by the office of Research Compliance Administration that new versions have been created, it is the responsibility of Deans' offices and all research individuals who have printed copies to collect and destroy old versions.

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Title:	Student Projects			
Current Version:	07/07		Previous Versions:	04/05, 02/05

1. INTRODUCTION

For research to be reviewed by the Institutional Review Board (IRB), it must meet the definition of "human subjects research" as defined by the regulations (45 CFR 46, the Common Rule). In some courses students collect data by using professional research methods, even though the student's work is not expected to contribute to generalizable knowledge. Some of the methods involve human subjects, and in some instances subjects may be placed at risk. For this reason, student research projects involving human subjects should be reviewed and approved prior to initiation of the research project to assure that the rights and welfare of human subjects are protected. Students also need to learn the principles and policies governing research involving human subjects as a part of instruction in research methods.

2. OBJECTIVE

The objective of this SOP is to explain the criteria and submission requirements for student projects.

3. SCOPE

These policies and procedures apply to all student projects that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. DEFINITIONS

(section intentionally left blank)

5. POLICY AND ASSOCIATED PROCEDURES

5.1. Pursuant to Indiana University's and Clarian's federalwide assurances (FWAs), all human subjects research conducted at or on behalf of these institutions or their affiliates must be reviewed, prospectively approved, and subject to continuing review at least annually, as applicable by the IRB. This applies whether research is conducted by faculty or students or by individuals or a group.

5.2. **Graduate Thesis**. Thesis and dissertation projects involving human subjects are considered research and will require review by the IRB.

5.3. **Assignments for Class**. Class work assignments are usually not intended to or likely to lead to generalizable results, and, as such are not considered "research." However, there are some circumstances that require review and approval by the IRB.

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5.4. **Guidelines**. Student projects, excluding thesis and dissertation projects, which 1) are research practica (usually in the form of course-related research projects and/or directed studies; and 2) do not involve physically or psychologically invasive, intrusive, or stressful procedures; and 3) in the judgment of the faculty sponsor, do not have the potential for placing individuals at more than minimal risk do not require review and approval by the IRB. However, student projects that 1) may place individuals at more than minimal risk; and 2) involve vulnerable populations, such as children or adolescents, pregnant women, prisoners, people who are mentally disabled or those with impaired decision-making capacity, or human in vitro fertilization, are subject to prospective review and approval by the IRB. Additionally, if the results of a study project will be published, presented, or otherwise disseminated beyond the IUPUI/Clarian community, the project must be prospectively reviewed and approved by the IRB.

5.5. **Faculty Oversight.** Per IUPUI/Clarian policy, students cannot serve as Principal Investigators (PIs) of research projects. As such, student projects require that a Faculty Sponsor serve in this role.

5.6. **Responsibilities of Faculty Sponsors.** Faculty Sponsors have the ultimate responsibility for assuring that the rights and welfare of human subjects are not violated. This responsibility includes:

5.6.1 informing students of the ethical principles for the protection of human subjects in research and applicable policies and procedures;

5.6.2 reviewing and monitoring student projects to ensure they are in accordance with applicable policies and procedures;

5.6.3 assessing whether risk is more than minimal; and

5.6.4 ensuring that student projects involving protected health information comply with HIPAA requirements.

5.6.5 Faculty Sponsors must be listed as principal investigators for all student projects requiring exempt, expedited, or full IRB review. Otherwise, they may be listed as the faculty sponsor on the application.

5.7. **Submission Requirements for Student Projects**

5.7.1 If the student project meets the definition of "human subjects research" as defined in the regulations and in this document, then…**IRB review is required**. Consult the IRB Instruction Packet to determine the required level of review (i.e. exempt, expedited, or full) and submission requirements.

5.7.2 If the student project is subject to FDA regulations, then… **IRB review is required.** Consult the IRB Instruction Packet to determine the required level of review (i.e. exempt, expedited, or full) and submission requirements.

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5.7.3 If the student project does not meet the definition of "human subjects research," but may place individuals at more than minimal risk and involves a vulnerable population (i.e. children or adolescents, pregnant women, prisoners, people who are mentally disabled or those with impaired decision-making capacity, or human in vitro fertilization), then…**IRB review is required**. Complete and submit an Application for Non-Research Student Projects.

5.7.4 If the student project involves research with one or more deceased individuals, then…**IRB review is required.** Complete and submit an Application for Research Not Subject to FDA or Common Rule Definitions of Human Subjects Research.

5.7.5 If the student project involves research with data derived from a limited data set or is de-identified data created from PHI from a HIPAA covered entity, then…**IRB review is required**. Complete and submit an Application for Research Not Subject to FDA or Common Rule Definitions of Human Subjects Research.

5.7.6 If the student project involves research with coded private information or biological specimens, then…**IRB review is required**. Complete and submit an Application for Research Not Subject to FDA or Common Rule Definitions of Human Subjects Research.

5.7.7 If the student project involves 1) only learning and research techniques; 2) no more than minimal risk; 3) data that is recorded anonymously by the students (i.e., no names, social security numbers, or any other codes that can be linked to a list of names, or the recorded data will not identify the individuals through their behavior; 4) data gathered for the instructor and students of the course; and 5) will not be published or otherwise distributed, then…**IRB review is NOT required.**

5.8. **Blanket Acceptance/Approval**. In instances where a class of students will be conducting group or individual research projects as a part of the classroom instruction, and the instructor believes that, under the guidelines, IRB approval is required, the instructor may request a "blanket" acceptance or approval from the IRB. This involves the submission of one application that sets forth the parameters of the research being conducted by the students. Individual forms are completed for each student researcher as long as the research falls within the parameters described in the "blanket" application. If, however, the student research does not fall within the described parameters, separate approval is required. This does not apply to research activities requiring expedited or full IRB review. Contact the RCA office before any such requests are made.

5.9. **IRB Review of Student Projects**

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5.9.1 At IUPUI: The IRB has granted authority to RCA staff to accept the following student projects:

5.9.1.7 Non-research student projects;

5.9.1.8 Research projects not subject to FDA or Common Rule definitions of human subjects research; and

5.9.1.9 Exempt research projects. EXCEPTION: Exemptions for studies conducted at or funded by the VA can only be exempted by an IRB Chair or IRB member designated by the Chair.

5.9.2 At Methodist: Non-research student projects and research not subject to FDA or Common Rule definitions of human subjects research applications are sent to the IRB Chair or designee for review and acceptance.

5.9.3 **Ethical Principles**. The IRB will not accept any student project that does not fulfill ethical principles reflected in the Belmont Report. These basic ethical principles are:

5.9.3.7 Respect for Persons (Autonomy) – individuals should be treated as autonomous agents and persons with diminished autonomy are entitled to protection.

5.9.3.8 Beneficence – Human subjects should not be harmed and the research should maximize possible benefits and minimize possible harms.

5.9.3.9 Justice – the benefits and risks of research must be distributed fairly.

5.9.4 The will not accept any student project that does not comply with HIPAA requirements.

5.9.5 RCA staff may consult with members of the IRB designated by the Chair if there are questions as to whether or not the project appropriately meets the ethical principles or complies with HIPAA requirements.

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Title:	Unanticipated Problems and Noncompliance			
Current Version:	03/08		Previous Versions:	08/05, 06/05, 04/05, 02/05

1. INTRODUCTION

All members of the Indiana University Purdue University Indianapolis (IUPUI)/Clarian Health Partners (Clarian) research community involved in human subjects research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional policies governing the conduct of research involving human subjects.

Federal regulations 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) require Institutional Review Boards (IRBs) to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the federal department or agency head of any unanticipated problems involving risks to subjects or others (hereafter referred to as "unanticipated problems"), any serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB, and any suspension or termination of IRB approval. In keeping with this regulatory requirement, investigators are required to promptly report to the IRB unanticipated problems, serious or continuing noncompliance, and suspensions or terminations. The IUPUI/Clarian IRBs will review these reports and fulfill reporting requirements to the appropriate institutional officials, federal departments or agencies, and appropriate other entities. This document focuses on the reporting responsibilities of the investigator. Additional reporting responsibilities required by the federal regulations can be found in the Reporting SOP.

2. OBJECTIVES

2.1. Define the events that require prompt reporting to the IRB;

2.2. Outline the procedures for investigators for promptly reporting unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval;

2.3. Explain the IRB's potential actions in response to reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval.

3. SCOPE

These policies and procedures apply to all research activities of faculty, staff, student, or others who are involved in human subjects research that fall under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVENT DEFINITIONS

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5. POLICY AND ASSOCIATED PROCEDURES

5.1. In accordance with Federal regulations, the IUPUI/Clarian IRBs have established the following policies and procedures for the reporting of unanticipated problems and noncompliance as a means of ensuring (i) the relationship of the risks and benefits to subjects participating in research studies remains acceptable throughout the conduct of the study; and (ii) the consent document contains the information necessary for subjects to make an informed decision about their participation or continuation in the study.

5.2. Reports of unanticipated problems or noncompliance can come from a number of different sources, including investigators, members of the research team, study sponsor, regulatory body (e.g. OHRP, FDA), subjects and/or their families, institutional personnel or committees, the media, the public, or anonymous sources. Additionally, the IRB can identify unanticipated problems and noncompliance during its review of research studies.

5.3. **A Discussion of Unanticipated Problems and Adverse Events.** HHS regulations (45 CFR 46) do not define or use the term "adverse event," nor is there a common definition of this term across government and non-government entities. However, the regulations do address the need to report "unanticipated problems." Only a small subset of adverse events occurring in human subjects participating in research will meet the definition of an unanticipated problem. Because the federal regulations require that IRBs have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and any supporting department or agency head of any ***unanticipated problems***, and not ***adverse events***, not all adverse events will require prompt reporting. In fact, the vast majority of adverse events occurring in human subjects are not unanticipated problems. Only if the adverse event meets the three criteria of an unanticipated problem (i.e., unexpected, related or possibly related to participation, and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized) and requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others, does it require prompt reporting.

Diagram taken from OHRP Guidance on Unanticipated Problems and Adverse Events (January 15, 2007)

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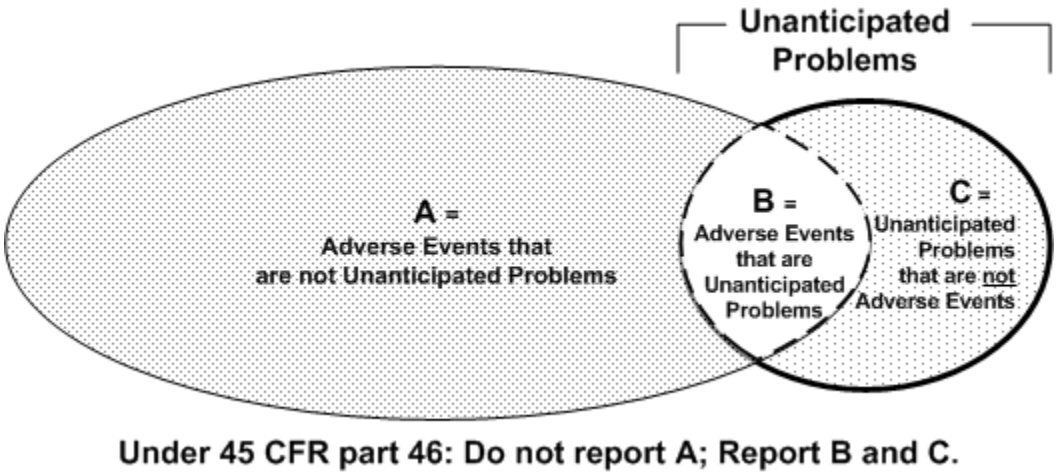

The diagram illustrates three key points:

1. The vast majority of adverse events occurring in human subjects are not unanticipated problems (Area A).
2. A small portion of adverse events are unanticipated problems (Area B).
3. Unanticipated problems include other incidents, experiences, and outcomes that are not adverse events (Area C).

5.3.1. **Assessing whether an adverse event is *unexpected.*** See the definition of "unexpected adverse event." Consider that the vast majority of adverse events occurring in the context of research are *expected* in light of 1) the known toxicities and side effects of the research procedures; 2) the expected natural progression of subjects' underlying diseases, disorders, and conditions; and 3) subjects' predisposing risk factor profiles for the adverse event. Thus, most individual adverse events do not meet the first criterion for an unanticipated problem and do not require prompt reporting to the IRB.

5.3.2. **Assessing whether an adverse event is *related or possibly related to participation*.** See the definition of "related or possibly related to participation." In general, adverse events that are determined to be at least partially caused by the procedures involved in the research would be considered related to participation in the research, whereas adverse events determined to be solely caused by an underlying disease, disorder, or condition of the subjects or other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject would be considered unrelated to participation in the research. Many individual adverse events occurring in the context of research are not related to participation in the research and, therefore, do not meet the second criterion for an unanticipated problem and do not require prompt reporting to the IRB.

5.3.3. **Assessing whether an adverse event *suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized*.**

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The first step in assessing whether an adverse event meets the third criterion for an unanticipated problem is to determine whether the adverse is ***serious***. See the definition of "serious adverse event." Adverse events that are unexpected, related or possibly related to participation in research, and *serious* are considered to be the most important subset of adverse events representing unanticipated problems because such events suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized and routinely warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects. However, other adverse events that are unexpected and related or possibly related to participation in the research, but not serious, would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

5.4. **Reporting Internal Adverse Events to the IRB**. For an internal adverse event, a local investigator typically becomes aware of the event directly from the subject, another collaborating local investigator, or the subject's healthcare provider. Upon becoming aware of an internal adverse event, the investigator should assess whether the adverse event represents an unanticipated problem following the guidelines described above. If the investigator determines that the adverse event does in fact represent an unanticipated problem **and** requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others, the investigator must report it to the IRB using the Prompt Reporting Form within five business days of the investigator becoming aware of the event. Unless determined to not represent an unanticipated problem by RCA staff or the IRB Chair or Chair's designee, the report will be reviewed at a convened IRB meeting for possible action.

Reporting Timeframe: Five (5) business days from becoming aware of the event.

5.5. **Reporting External Adverse Events to the IRB**. The majority of adverse event reports received by investigators are reports of external adverse events experienced by subjects enrolled in multicenter clinical trials. Reports of individual external adverse events often lack sufficient information to allow the investigators or IRBs at each institution engaged in a multicenter clinical trial to make meaningful judgments about whether the adverse events are unanticipated problems. As such, external adverse events should *only* be reported to the IRB when a determination has been made that the events meet the criteria for an unanticipated problem and requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others. Individual external adverse events are expected to rarely meet these criteria. Note that, in general, investigators and the IRB are not appropriately situated to assess the significance of individual external adverse events. These adverse events are better submitted for review and analysis to a monitoring entity (e.g. research sponsor, DSMB/DMC) in accordance with the monitoring plan described in the IRB-approved protocol. When an investigator receives a report of an external adverse event, he/she should review the report and assess whether it satisfies the criteria of an

unanticipated problem. If the external adverse event is determined to represent an unanticipated problem **and** requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others, the investigator must report it to the IRB using the Prompt Reporting Form within five business days of the investigator becoming aware of the event. Unless determined to not represent an unanticipated problem by RCA staff or the IRB Chair or Chair's designee, the report will be reviewed at a convened IRB meeting for possible action.

Reporting Timeframe: Five (5) business days from notification of the event.

5.6. **Reporting Other Unanticipated Problems (not related to adverse events) to the IRB**. There are other types of incidents, experiences, and outcomes that occur during the conduct of human subject research that represent unanticipated problems but are not considered adverse events. These unanticipated problems are those events (other than adverse events) listed in the prompt reporting list (found at 5.8 of this document) and include major internal protocol deviations, internal changes to the IRB-approved protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant(s), internal complaints of a participant that indicate unexpected risks or that cannot be resolved by the research team, publications in the literature, safety monitoring reports, interim results, or other findings that indicate an unexpected change to the risks or potential benefits of the research, in terms of severity or frequency, changes in FDA labeling or withdrawals from marketing of a drug, device, or biologic used in a research study, unanticipated adverse device effects, and investigator- or sponsor-initiated study suspensions or holds. If the event is determined to represent an unanticipated problem **and** requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others, the investigator must report it to the IRB using the Prompt Reporting Form within five business days of the investigator becoming aware of the event. Unless determined to not represent an unanticipated problem by RCA staff or the IRB Chair or Chair's designee, the report will be reviewed at a convened IRB meeting for possible action.

Reporting Timeframe: Five (5) business days from notification of or becoming aware of the event.

5.7. **Reporting Noncompliance to the IRB**. The IRB, as part of its oversight responsibilities must establish procedures for the evaluation of noncompliance with human subject protection regulations and the prompt reporting of serious or continuing noncompliance with the federal regulations and institutional policies. All noncompliance must be reported to the IRB. This section discusses two types of noncompliance reporting. One involves observed or apparent noncompliance and the other involves allegations of noncompliance.

5.7.1. Reports of Observed or Apparent Noncompliance

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5.7.1.1. Reports of observed or apparent noncompliance are to be reported to the IRB using the Noncompliance Reporting Form within five (5) business days of knowledge of the noncompliance.

5.7.1.2. Upon receipt of the report, it will be reviewed by an RCA Director or designee to determine whether the report represents noncompliance. If the report is found **not** to represent noncompliance, the RCA Director or designee will sign the report and return it to the investigator, retaining a copy of the report in the study file. No further action is required.

5.7.1.3. If the RCA Director or designee determines the report to represent noncompliance, he/she may involve the IRB Chair or designee in determining whether the report represents serious or continuing noncompliance. If the RCA Director, IRB Chair, or designee determines that the noncompliance is neither serious nor continuing, the RCA Director, IRB Chair, or designee will work with the investigator on a corrective action plan. If the investigator fails to respond or a reasonable negotiation cannot be accomplished, the noncompliance is handled as continuing noncompliance and will be reviewed at a convened IRB meeting.

5.7.1.4. If the RCA Director, IRB Chair or designee determines the report to likely represent serious or continuing noncompliance, the matter will be referred to the convened IRB for review. Only the convened IRB can make a determination of serious or continuing noncompliance.

5.7.1.5. The RCA Director, IRB Chair or designee, or convened IRB reserve the right to request additional information and/or to require a specific action as a result of the noncompliance report.

Reporting Timeframe: Five (5) business days from knowledge of observed or apparent noncompliance.

5.7.2. Reporting Allegations of Noncompliance to the IRB

5.7.2.1. Allegations of noncompliance may be received by the IRB at any time and from a number of sources including, but not limited to, a member of the research team, a study participant, a concerned third party.

5.7.2.2. The RCA Director or designee will gather information regarding the allegation, conduct an investigation, if necessary, and determine whether the allegation is true.

5.7.2.3. If the RCA Director or designee is unable to make a determination, he/she will involve the IRB Chair to make a determination of whether the allegation is true.

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5.7.2.4. If the RCA Director, IRB Chair or designee determines the allegation to be false, the findings and outcomes will be documented, filed, and communicated to the complainant, respondent, and investigator, as appropriate.

5.7.2.5. If the RCA Director, IRB Chair or designee determines the noncompliance to be true and potentially serious or continuing, it will be handled per 5.7.1.

5.7.2.6. If the RCA Director or IRB Chair or designee cannot determine whether the allegation of noncompliance is true, the matter will be referred to the convened IRB for review and determination.

5.7.2.7. The RCA Director, IRB Chair or designee, or convened IRB reserve the right to request additional information or require suspension of IRB approval as a result of the noncompliance allegation.

5.7.2.8. If, at any point during the investigation, the RCA Director, IRB, IRB Chair or designee believes the allegation raises issues of legal liability or there is a threat or perceived threat of a lawsuit, the IRB staff will involve the IUPUI University Counsel office.

5.8. **List of Events that Require Prompt Reporting to the IRB:** Any of the following:

5.8.1. Any adverse event (including internal and external adverse events, injuries, side effects, deaths, or other problems), which in the opinion of the local principal investigator:

5.8.1.1. was unexpected;

5.8.1.2. was related or possibly related to participation in the research;

5.8.1.3. suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized; and

5.8.1.4. requires changes to the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others.

5.8.2. Major internal protocol deviation (as defined under this policy).

5.8.3. Any internal change to the IRB-approved protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant(s).

5.8.4. Any internal complaint of a participant that indicates unexpected risks or that cannot be resolved by the research team.

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5.8.5. Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risks or potential benefits of the research, in terms of severity or frequency.

5.8.6. Any change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research study.

5.8.7. Any unanticipated adverse device effect (as defined in this policy).

5.8.8. Investigator- or sponsor-initiated study suspension or hold.

5.8.9. Internal serious or continuing noncompliance (as defined in this policy).

NOTE: The above should be reported regardless of whether they occur during the study, after participant withdrawal or completion, or after study completion if they are profound or they demonstrate long-term risks that would necessitate notifying participants.

5.9. IRB Responsibilities When Reviewing Unanticipated Problems and Noncompliance Reports

5.9.1. When the IRB receives a report of an unanticipated problem or noncompliance, it must review the report to determine whether the affected research protocol still satisfies the requirements for IRB approval under §46.111. In particular, the IRB shall consider whether risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result.

5.9.2. Pursuant to §46.109(a), the IRB has the authority to require, as a condition of continued approval by the IRB, submission of more detailed information by the investigator(s), the sponsor, the study coordinating center, or the DSMB/DMC about any unanticipated problem or noncompliance occurring in a research protocol.

5.9.3. If the IRB determines that a report does in fact represent an unanticipated problem or serious or continuing noncompliance, it must report it to appropriate institutional officials, regulatory agencies (e.g. OHRP, FDA), and others, as applicable. (For additional information regarding the IRB's reporting requirements, please see the Reporting SOP). If the IRB determines that the report does not represent an unanticipated problem or serious or continuing noncompliance, no further reporting is required.

5.9.4. Upon review of a report of an unanticipated problem or noncompliance, the IRB will determine if any action must be taken as a result of the report. The IRB will consider the rights and welfare of participants when taking any action or imposing any sanction. Possible actions or sanctions include, but are not limited to:

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5.9.4.1. No action taken, protocol continues as previously approved.

5.9.4.2. No further action required, investigator's proposed corrective action plan is adequate.

5.9.4.3. Refer to or consult with other institutional entities (Dean, University Counsel, Ethics Committee, IRB Executive Committee, subcommittee appointed by the IRB).

5.9.4.4. Restrict use of or destroy research data collected.

5.9.4.5. Audit the research study(ies).

5.9.4.6. Modification to the research protocol and/or informed consent process/document.

5.9.4.7. Notify or reconsent past and/or current participants if the report may relate to their willingness to continue to take part in the study.

5.9.4.8. Withdraw currently enrolled participants if it is determined to be in their best interest.

5.9.4.9. Require additional training of the investigator and/or research team.

5.9.4.10. Modify the continuing review schedule.

5.9.4.11. Require increased reporting by the investigator and/or increased monitoring of the research and/or informed consent process.

5.9.4.12. Restrict privileges of investigator to conduct human research.

5.9.4.13. Suspend or terminate research or suspend specific research activities (e.g. recruitment, enrollment, interaction/intervention, and/or follow-up).

5.9.4.14. Other actions deemed appropriate.

5.10. IRB-Imposed Suspensions and Terminations Due to Unanticipated Problems and Serious or Continuing Noncompliance

5.10.1. Pursuant to §46.113, the IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements, institutional policies, federal or state regulations, or has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional

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officials, and the department or agency head. (For additional information regarding the reporting of suspensions and terminations, please see the Reporting SOP).

5.10.2. Suspensions and terminations cannot be overturned by Institutional Officials.

5.10.3. Suspensions of research are typically made at a convened IRB meeting; however, they can also be made on an urgent basis by either the IRB Chair or designee, if necessary. Suspensions can only be lifted by the convened IRB. If the IRB Chair or designee suspends research, it will be reported to the full IRB for consideration and possible action. Termination of research can only be made by the convened IRB.

5.10.4. When the IRB Chair or designee suspends or the convened IRB suspends or terminates a research study, any unanticipated problems or outcomes resulting from the suspension or termination must be reported to the IRB in accordance with this policy.

5.10.5. When the IRB suspends or terminates a research study, it will consider whether the suspension or termination requires that subjects be withdrawn from the study and/or places them at risk of harm.

5.10.6. When subjects must be withdrawn from a study, the IRB will consider the safety, rights, and welfare of subjects and determine necessary termination procedures (e.g. drug tapering, final visit, lab tests, other follow-up, and/or arrangements for continued care).

5.10.7. If the IRB determines that the suspension or termination will place subjects at risk of harm and/or follow-up of subjects for safety reasons is permitted or required, the IRB will determine which subjects are to be notified, e.g. current or past participants, and the manner in which they are to be notified, e.g. in writing or by telephone. Depending upon the reasons for the suspension or termination and the design of the study, the IRB may require that any of the following individuals be notified of the suspension or termination:

5.10.7.1. All subjects who have been or who are currently enrolled;

5.10.7.2. Only subjects who are currently enrolled and active; or

5.10.7.3. Only subjects who participated in a certain aspect of the study.

5.10.8. **VA Research**. If research conducted at or funded by the VA is suspended by the IRB, the investigator must submit to the IRB Chair a list of VA subjects for whom the suspension would cause harm. The IRB Chair will consult with the VA Chief of Staff to determine whether the subjects could continue receiving intervention.

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5.10.9. Investigators may request to attend an IRB meeting to discuss a suspension or termination in order to provide clarification of the issues. Additionally, investigators may request in writing that the IRB reconsider a suspension or termination, within 10 days of such action.

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Title:	Vulnerable Populations			
Current Version:	03/08		Previous Versions:	

1. INTRODUCTION

Pursuant to 45 CFR 46.111, the IRB must determine that specific requirements are satisfied in order to approve research with human subjects. One such requirement is that the selection of subjects is equitable (§46.111(a)(3)). In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Because of the special vulnerability of these populations, the federal regulations, state and local laws, and institutional policies require additional protections for these individuals.

2. OBJECTIVES

2.1. Explain the additional protections required when involving vulnerable population in research

2.2. Explain investigators' responsibilities when involving vulnerable populations in research

2.3. Explain the IRB's responsibilities when reviewing proposed research involving vulnerable populations

3. SCOPE

These policies and procedures apply to all research activities of faculty, staff, students, or others who are involved in human subjects research that falls under the jurisdiction of the IUPUI/Clarian IRBs.

4. RELEVENT DEFINITIONS

(section intentionally left blank)

5. POLICY AND ASSOCIATED PROCEDURES

5.1. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (Subpart B)

5.1.1. Research involving women who are or may become pregnant should receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when

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informed consent of the father is required for the research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society.

5.1.2. **Research Involving Pregnant Women or Human Fetuses**. Pursuant to 45 CFR 46.204, pregnant women or human fetuses may be involved in research if all of the following conditions are met:

5.1.2.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

5.1.2.2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

5.1.2.3. Any risk is the least possible for achieving the objectives of the research;

5.1.2.4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A;

5.1.2.5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46, Subpart A, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

5.1.2.6. Each individual providing consent under paragraph (5.1.1.4) or (5.1.1.5) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

5.1.2.7. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46, Subpart D;

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5.1.2.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

5.1.2.9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; **and**

5.1.2.10. Individuals engaged in the research will have no part in determining the viability of a neonate.

5.1.3. **Research Involving Neonates**. Pursuant to 45 CFR 205(a), neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

5.1.3.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

5.1.3.2. Each individual providing consent under §46.205(b)(2) or §46.205(c)(5) is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

5.1.3.3. Individuals engaged in the research will have no part in determining the viability of a neonate.

5.1.3.4. The requirements of §46.205(b) or §46.205(c) have been met as applicable.

5.1.4. Pursuant to 45 CFR 46.205(b), until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless the following additional conditions have been met:

5.1.4.1. The IRB determines that: (i) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, **or** (ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; **and**

5.1.4.2. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of 45 CFR 46, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

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5.1.5. **Research Involving Nonviable Neonates**. Pursuant to 45 CFR 46.205(c), after delivery, a nonviable neonate may not be involved in research covered by Subpart A of 45 CFR 46 unless all of the following additional conditions are met:

5.1.5.1. Vital functions of the neonate will not be artificially maintained;

5.1.5.2. The research will not terminate the heartbeat or respiration of the neonate;

5.1.5.3. There will be no added risk to the neonate resulting from the research;

5.1.5.4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; **and**

5.1.5.5. The legally effective informed consent of both parents of the neonate is obtained in accord with Subpart A of 45 CFR 46, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

5.1.6. Pursuant to 45 CFR 46.205(d), a neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46, Subparts A and D.

5.1.7. Pursuant to 45 CFR 46.206, research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. If information associated with the material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable

5.1.8. In evaluating the inclusion of pregnant women, human fetuses, and neonates in research, the IRB will consider the protocol-specific findings provided by the investigator in the Request Form for the Inclusion of Pregnant Women, Human Fetuses, and Neonates in Research and document its determination in the IRB minutes.

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5.1.9. Pursuant to 45 CFR 46.207, the Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if:

5.1.9.1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; **and**

5.1.9.2. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either: (1) That the research in fact satisfies the conditions of §46.204, as applicable; or (2) The following: (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; (ii) The research will be conducted in accord with sound ethical principles; and (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

5.1.10. Research in Which Pregnancy is Coincidental to Subject Population. Any research in which women of childbearing potential are possible subjects may inadvertently include women already pregnant or women who may become pregnant. DHHS regulations, specifically 45 CFR 46.116(b)(1), requires that, when appropriate, the informed consent document include a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable. The IRB must then judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to ensure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the investigator immediately should they become pregnant. In some instances there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

5.1.11. Investigator Responsibilities When Involving Pregnant Women, Human Fetuses, and/or Neonates in Research

5.1.11.1. When research proposes to enroll pregnant women, human fetuses, or neonates, the investigator must obtain approval from the IRB before any such subjects may be enrolled in the research.

5.1.11.2. For a new study proposing to enroll such subjects, the investigator must complete and submit the Request Form for the Inclusion of

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Pregnant Women, Human Fetuses, or Neonates in Research with the new study application.

5.1.11.3. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with the completed Request Form for the Inclusion of Pregnant Women, Human Fetuses, or Neonates in Research.

5.1.12. **Additional VA Requirements**. Pursuant to Appendix D.4 of the VHA Handbook 1200.5, research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue) or research related to in vitro fertilization must not be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities.

5.1.13. For research involving the participation of pregnant women as research subjects, in addition to finding and documenting that the conditions of 45 CFR 46.204 and 205 are met, as applicable, the IRB must also:

5.1.13.1. Determine that adequate provision has been made to monitor the risks to the subject and the fetus;

5.1.13.2. Determine that adequate consideration has been given to the manner in which potential subjects are going to be selected;

5.1.13.3. Determine that adequate provision has been made to monitor the actual consent process by procedures such as: (1) overseeing the process by which individual consents are secured either by approving enrollment of each individual or verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity are being followed; and (2) monitoring the progress of the activity and intervening, as necessary, through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

5.2. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (Subpart C)

5.2.1. Pursuant to 45 CFR 46.306(a)(2), biomedical or behavioral research may involve prisoners as subjects only if the IRB determines that the proposed research involves solely the following:

5.2.1.1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk (per minimal risk definition for prisoners found in Section II, Applicable SOP Definitions) and no more than inconvenience to the subjects;

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5.2.1.2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk (per minimal risk definition for prisoners found in Section II, Applicable SOP Definitions) and no more than inconvenience to the subjects;

5.2.1.3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; **or**

5.2.1.4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.

5.2.2. The exemptions outlined at 45 CFR 46.101(b) do not apply to prisoners.

5.2.3. **Additional Duties of the Institutional Review Boards**. In addition to all other responsibilities prescribed for IRBs under 45 CFR 46, the IRB shall review and approve research involving prisoners only if it finds that:

5.2.3.1. The research under review represents one of the categories of research permissible under §46.306(a)(2);

5.2.3.2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

5.2.3.3. The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

5.2.3.4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control

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subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

5.2.3.5. The information is presented in language which is understandable to the subject population;

5.2.3.6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; **and**

5.2.3.7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

5.2.3.8. In evaluating the inclusion of prisoners in research, the IRB will consider the protocol-specific findings provided by the investigator in the Request Form for the Inclusion of Prisoners in Research and document its determination in the IRB minutes.

5.2.4. Additional Considerations When Research Proposes to Involve Prisoners.

5.2.4.1. When a prisoner is also a child (e.g. an adolescent detained in a juvenile detention facility), appropriate additional requirements must be satisfied for the inclusion of children in research as outlined in 5.3 below.

5.2.4.2. Expedited review of research involving prisoners is not permitted; it must be reviewed at a convened IRB meeting.

5.2.4.3. Research that would otherwise be exempt according to §46.101(b), cannot be exempt when it involves prisoners.

5.2.5. Composition of the IRB Where Prisoners are Involved. Pursuant to 45 CFR 46.304, in addition to satisfying the requirements in 45 CFR 46.107, an IRB who regularly reviews research involving prisoners shall also consider the inclusion of one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. The composition of the IRB must satisfy the following requirements found at 45 CFR 46.304(a) and (b):

5.2.5.1. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; **and**

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5.2.5.2. At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB only one IRB need satisfy this requirement.

5.2.5.3. In the absence of choosing someone who is a prisoner or has been a prisoner, the IRB will choose a prisoner representative who has a close working knowledge, understanding, and appreciation of prison conditions from the perspective of a prisoner. Suitable individuals could include prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

5.2.6. When the convened IRB reviews research involving prisoners (including initial review, continuing review, amendments, and unanticipated problems), the prisoner representative must be present as a voting member.

5.2.7. Additional Requirements for Conducting Research within a Federal Prison Facility

5.2.7.1. The Bureau of Prisons (BOP) accepts for review well-designed research proposals; however, medical and pharmaceutical experimentation are prohibited. For research conducted within a federal prison facility, in addition to the IRB's requirements for the involvement of prisoners, the BOP also requires that investigators:

5.2.7.1.1. Read the Belmont Report.

5.2.7.1.2. Read the BOP Program Statement of Research.

5.2.7.1.3. Be familiar with Department of Justice regulations for protecting human subjects (28 CFR 46).

5.2.7.1.4. Complete a Researcher Statement (one for each researcher listed in the proposal).

5.2.7.1.5. Prepare a research proposal as described in the Program Statement (see additional instructions regarding informed consent).

5.2.7.1.6. Submit the complete proposal and Researcher Statement(s) to the appropriate BOP office (for more information, see the process described in the Program Statement).

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5.2.7.2. For additional information regarding research applications to the BOP, please click: Apply to Conduct Research In the Bureau of Prisons.

5.2.8. Additional Requirements for Conducting Research Within a Department of Corrections (DOC) Facility

5.2.8.1. Research with human subjects involving medical testing, chemical, experimental drugs, etc. is prohibited by the DOC's Health Care Services Directives.

5.2.8.2. Pursuant to 210 IAC 1-6-7, all requests for access to offender or juvenile records for research purposes shall be made to the director of planning services in written form. Such requests shall include the name of the agency or organization performing the research and the names of the persons directly responsible for the following:

5.2.8.2.1. Conducting such research.

5.2.8.2.2. The purpose of such research.

5.2.8.2.3. How the research is to be performed.

5.2.8.2.4. What measures will be taken to assure the proper protection of classified information.

5.2.8.3. Approval of such requests will be granted or denied consistent with provisions of IC 4-1-6-8.6 and department procedures. IC 4-1-6-8.6 states that in cases where access to confidential records containing personal information is desired for research purposes, the agency shall grant access if:

5.2.8.3.1. the requestor states in writing to the agency the purpose, including any intent to publish findings, the nature of the data sought, what personal information will be required, and what safeguards will be taken to protect the identity of the data subject;

5.2.8.3.2. the proposed safeguards are adequate to prevent the identity of an individual data subject from being known;

5.2.8.3.3. the researcher executes an agreement on a form, approved by the oversight committee on public records, with the agency, which incorporates such safeguards for protection of individual data subjects, defines the scope of the research project, and informs litigation by the data subject or subjects;

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5.2.8.3.4. the researcher agrees to pay all direct or indirect costs of the research; **and**

5.2.8.3.5. the agency maintains a copy of the agreement or contract for a period equivalent to the life of the record.

5.2.9. Investigator Responsibilities When Involving Prisoners in Research

5.2.9.1. Investigators may not screen for, recruit into, or enroll any individual involuntarily confined or detained in a penal institution to a research study without prior IRB approval.

5.2.9.2. Investigators are responsible for obtaining and providing documentation to the IRB of approval from detention or correctional facilities involved in the research.

5.2.9.3. For a new study proposing to enroll such subjects, the investigator must complete and submit the Request Form for the Inclusion of Prisoners in Research with the new study application.

5.2.9.4. For an existing study proposing to enroll such subjects, the investigator must submit an amendment along with the completed Request Form for the Inclusion of Prisoners in Research.

5.2.10. Procedures When a Current Subject Becomes a Prisoner During the Research

5.2.10.1. When a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research protocol was not previously approved by the IRB in accordance with the requirements for research involving prisoners under 45 CFR 46, Subpart C, the investigator must promptly notify the IRB. Additionally, all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below.

5.2.10.2. If the investigator wishes to have the prisoner-subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of Subpart C. The investigator must submit to the IRB:

5.2.10.2.1. Notification that a previously enrolled research subject has become a prisoner;

5.2.10.2.2. An amendment requesting the inclusions of prisoners; and

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5.2.10.2.3. A completed Request for Prisoners in Research form.

5.2.10.3. The IRB review must occur at a fully convened IRB meeting.

5.2.10.4. **Exception**: The federal regulations allow for one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interest of the prisoner-subject to continue to receive interactions or interventions and/or obtain private identifiable information in the research study while incarcerated, the IRB Chair may determine that the prisoner-subject may continue to participate in the research until the requirements of Subpart C are met. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study.

5.2.10.5. IRB review and approval are not required if research interactions and interventions or obtaining of identifiable private information will not occur during the incarceration period.

5.2.11. Additional Requirements for Research Conducted or Supported by DHHS that Involves Prisoners. Pursuant to 45 CFR 46.306(a), biomedical or behavioral research conducted or support by DHHS may involve prisoners as participants only if:

5.2.11.1. The institution has certified to the Secretary that the IRB has approved the research under §46.305.

5.2.11.2. In the judgment of the Secretary the proposed research involves solely one of the permitted categories of research involving prisoners listed under 45 CFR 46.306(a)(2); or

5.2.11.3. Research that involves epidemiologic studies that meeting the following criteria:

5.2.11.3.1. The sole purposes of the research are one of the following: (i) to describe the prevalence or incidence of a disease by identifying all cases; or (ii) to study potential risk factor associations for a disease.

5.2.11.3.2. The institution certifies to the Office for Human Research Protections (OHRP) that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that: (i) the research presents no more than minimal risks and no more than

inconvenience to the prisoner-participants; and (ii) prisoners are not a particular focus of the research.

5.2.11.4. Except as provided in §46.306, biomedical and behavioral research conducted or supported by DHHS shall not involve prisoners as participants.

5.2.12. **Additional VA Requirements**. Pursuant to Appendix D.5 of the VHA Handbook 1200.5, research involving prisoners must not be conducted by VA investigators while on official duty, or at VA-approved off-site facilities a waiver has been granted by the Chief Research and Development Officer. If the waiver is granted, the research must be in accordance with 45 CFR 46, Subpart C.

5.3. Additional Protections for Children Involved as Subjects in Research (Subpart D)

5.3.1. Pursuant to 45 CFR 46, Subpart D and 21 CFR 50, Subpart D, the IRB can approve research involving children as research subjects only when it satisfies the conditions outlined below.

5.3.1.1. **45 CFR 46.404. Research not involving greater than minimal risk.** To approve research in this category, the IRB must find and document the following determinations:

5.3.1.1.1. the research presents no more than minimal risk to the children; **and**

5.3.1.1.2. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

5.3.1.2. **45 CFR 46.405. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.** To approve research in this category, the IRB must find and document the following determinations:

5.3.1.2.1. the research presents more than minimal risk to the children by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being;

5.3.1.2.2. the risk is justified by the anticipated benefits to the subjects;

5.3.1.2.3. the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; **and**

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5.3.1.2.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

5.3.1.3. **45 CFR 46.406. Research involving greater than minimal risk and no prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.** To approve research in this category, the IRB must find and document the following determinations:

5.3.1.3.1. the research presents a minor increase over minimal risk by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject;

5.3.1.3.2. the intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;

5.3.1.3.3. the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; **and**

5.3.1.3.4. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth at §46.408.

5.3.1.4. A fourth category of research requires a special level of HHS review beyond that provided by the IRB. 45 CFR 46.407. Research not otherwise approvable (i.e. the research does not meet the conditions of §46.404, §46.405, or §46.406), which presents an opportunity to further understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research in this category may only be conducted if:

5.3.1.4.1. The IRB believes that the research does not meet the requirements of §46.404, §46.405, or §46.406, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; **and**

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5.3.1.4.2. The Secretary, HHS or his/her designee, after consulting with a panel of experts in pertinent disciplines (e.g. science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either:

5.3.1.4.2.1. that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406; **or**

5.3.1.4.2.2. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; the research will be conducted in accordance with sound ethical principles; **and** adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in §46.408.

5.3.2. **Adequate provisions for soliciting the assent of children**. Pursuant to 45 CFR 46.408(a) and 21 CFR 50.55(a), the IRB shall determine and document that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

5.3.2.1. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. In general, the IRB will require assent from children, ages seven (7) to seventeen (17); however, the IRB acknowledges there are situations in which it may be appropriate for younger children, depending on their aptitude/ability to provide assent. Alternatively, there may be situations in which older children with higher cognitive ability may be able to read, understand, and subsequently sign the adult consent document. In these instances, the investigator must prospectively justify this scenario in the Request Form for the Inclusion of Children in Research and make the necessary changes to the informed consent document, for example, the inclusion of "you/your child" language and a child signature line.

5.3.2.2. The assent of the children is not a necessary condition for proceeding with the research if the IRB determines that either of the following are true:

5.3.2.2.1. the capability of some or all of the children is so limited that they cannot reasonably be consulted; **or**

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5.3.2.2.2. the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research,

5.3.2.3. To prospectively request a waiver of assent for some or all children, the investigator must complete the Waiver of Child Assent section on the Request Form for the Inclusion of Children in Research.

5.3.2.4. When the IRB approves a waiver of assent for some or all children, it will determine which children are not required to assent.

5.3.2.5. Even where the IRB approves a waiver of child assent, an age appropriate information sheet may still need to be given to the child-subjects.

5.3.2.6. When the IRB determines that assent is required, it shall determine whether and how assent must be documented.

5.3.2.7. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirements under circumstances in which consent may be waived in accord with §46.116.

5.3.3. **Adequate provisions for soliciting the permission of each child's parents or guardian**. Pursuant to 45 CFR 46.408(b), the IRB shall determine and document, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian.

5.3.3.1. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405.

5.3.3.1.1. Although the regulations allow permission of only one parent or guardian for research conducted under §46.404 or §46.405, the IRB must determine that the permission of one parent or guardian is sufficient. For example, it may be inappropriate to allow permission of only one parent or guardian in a standard therapeutic trial for childhood cancer where one has time to obtain permission from both parents, unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent or guardian has legal responsibility for the care and custody of the child, just because the research is conducted under §46.404 or §46.405.

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5.3.3.2. Where research is covered by §46.406 and §46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

5.3.3.3. Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117, Documentation of informed consent.

5.3.4. **Waiver of parental or guardian permission**. The IRB may waive the requirement for obtaining parental or guardian permission if it determines and documents the findings under either §46.116(c) or §46.116(d) and that the research is not FDA-regulated. In addition and pursuant to 45 CFR 46.408(c), if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects, for example, neglected or abused children, it may waive the parental permission requirements provided an appropriate mechanism is in place to protect the children, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate substitute mechanism, for example, appointing a child advocate or an assent monitor, for protecting children participating in research would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition. In addition, the IRB may waive the parental permission requirements in cases involving older adolescents who, under applicable law, may consent on their own behalf for selected treatments, for example, venereal disease, drug abuse, or emotional disorders.

5.3.5. To prospectively request a waiver of parental/guardian permission, the investigator should complete the Waiver of Parental/Guardian Permission (Consent) section on the Request Form for the Inclusion of Children in Research.

5.3.6. **Disagreement between a child and his/her parents about research participation**. If a child is capable of assent and the IRB requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his/her parents or guardian have granted permission, the child's decision prevails, unless the IRB has waived the assent requirement under §46.408(a). Conversely, if a child assents to participate in research and parental permission has not been waived by the IRB, the permission of the parents or guardian is required before the child can be enrolled in the research.

5.3.7. **When a child reaches the legal age of consent while enrolled in a research study**. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no

longer regulated by the requirements of §46.408 regarding parental or guardian permission and subject assent. As such, unless the IRB determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in §46.116, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. The IRB could, however, approve a waiver of informed consent under §46.116(d), if it finds and documents that the required conditions are met. Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subjects.

5.3.8. **Wards of the State or Other Agency.** Pursuant to 45 CFR 46.409(a), children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if the IRB finds and documents that such research is either:

5.3.8.1. Related to their status as wards; or

5.3.8.2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

5.3.8.3. If the research is approved under §46.409(a), the IRB must require appointment of an advocate for each child who is a ward.

5.3.8.3.1. The advocate will serve in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*.

5.3.8.3.2. One individual may serve as advocate for more than one child.

5.3.8.3.3. The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research.

5.3.8.3.4. The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

5.3.9. Investigator Responsibilities When Involving Children in Research

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5.3.9.1. Investigators may not screen for, recruit into, or enroll any child to a research study without prior IRB approval.

5.3.9.2. For a new study proposing to enroll such subjects, the investigator must complete and submit the Request Form for the Inclusion of Children in Research with the new study application. The investigator will make the initial determination regarding the appropriate category in which the research falls, including justification as to why that category was selected. In addition, an explanation regarding how adequate provisions are made for soliciting the assent of the children and the permission (parental/guardian informed consent) of each parent or guardian must be provided.

5.3.9.3. For an existing study proposing to enroll such subjects, the investigator must submit and amendment along with the completed Request Form for the Inclusion of children in Research. The investigator will make the initial determination regarding the appropriate category in which the research falls, including justification as to why that category was selected. In addition, an explanation regarding how adequate provisions are made for soliciting the assent of the children and the permission (parental/guardian informed consent) of each parent or guardian must be provided.

5.3.9.4. If the IRB grants a waiver of child assent, the investigator must still obtain parental/guardian permission (consent), unless a waiver of parental/guardian permission has also been granted.

5.3.9.5. The investigator may only approach the child-subjects to assent to participate in the research after the parents/guardian have given written permission (consent).

5.3.10. IRB Responsibilities When Reviewing Research Involving Children

5.3.10.1. In evaluating the inclusion of children in research, the IRB will consider the protocol-specific findings provided by the investigator in the Request Form for the Inclusion of Children in Research and document its determination in the IRB minutes.

5.3.10.2. In addition to satisfying the requirements in 45 CFR 46.107, an IRB who regularly reviews research involving children shall also consider the inclusion of one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. However, to fulfill this requirement, the IRB may invite consultants (i.e. non-voting individuals) to assist in the review of issues related to this subject population.

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5.3.10.3. When the convened IRB reviews research involving children (including initial review, continuing review, amendments, and unanticipated problems), an individual who is knowledgeable about and experienced in working with children should be present at the meeting.

5.3.10.4. When the convened IRB reviews research involving children funded by the National Institute on Disability and Rehabilitation Research (NIDRR), an individual who is knowledgeable about and experienced in working with children with disabilities should be present at the meeting.

5.3.11. **Additional VA Requirements.** Pursuant to Appendix D.7 of the VHA Handbook 1200.5, research involving children must not be conducted by VA investigators while on official duty or at VA or approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer. If the waiver is granted, the research must be in accordance with 45 CFR 46, Subpart D.

5.4. **Additional Protections for Individuals with Cognitive Impairment.** In the absence of evidence to the contrary, the law assumes competence in adults. However, certain groups of individuals may be suspected of lacking competence. These include persons with mental retardation/developmental disability, dementia, delirium, or major psychiatric disorders, such as schizophrenia. Patient groups that are susceptible to decreased competency include the elderly, terminally ill, and neurology patients. Patients on certain medications may also suffer a lack of competence. Conversely, the presence of cognitive impairment does not automatically disqualify a subject from consenting/assenting to or refusing research participation. The critical issue is whether the cognitive impairment leads to an impaired decisional capacity.

5.4.1. **Assessment of Competence in Potential Research Subjects**. There are no well-established, standardized measures for determining competency to consent to research. Therefore, assessment should be done on an individual basis and should determine the ability of the potential subject to:

5.4.1.1. understand the nature of the research and of his/her participation;

5.4.1.2. appreciate the consequences of the participation;

5.4.1.3. show the ability to consider alternatives, including the option not to participate; and

5.4.1.4. show the ability to make a reasoned choice.

5.4.2. Investigators must not interpret the potential subject's attentiveness and agreeable comments/behavior as evidence of the potential subject's competence

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or willingness; many cognitively impaired persons retain attentiveness and social skills.

5.4.3. IRB Responsibilities When Reviewing Research Involving Cognitively Impaired Individuals.

5.4.3.1. In addition to satisfying the requirements in 45 CFR 46.107, an IRB who regularly reviews research involving cognitively impaired subjects shall also consider the inclusion of one or more individuals who are knowledgeable about and experienced in working with this population to serve as a voting IRB member. However, to fulfill this requirement, the IRB may invite consultants (i.e. non-voting individuals) to assist in the review of issues related to this subject population.

5.4.3.2. When the convened IRB reviews research involving cognitively impaired subjects (including initial review, continuing review, amendments, and unanticipated problems), an individual who is knowledgeable about and experienced in working with cognitively impaired subjects should be present at the meeting.

5.4.3.3. When the convened IRB reviews research involving cognitively impaired subjects, it must find and document:

5.4.3.3.1. That appropriate provisions are made for determining the participant's ability to provide consent or their ability to withdraw. The determination of capacity to consent or ability to withdraw may be made through a standardized measure or consultation with another qualified professional. The IRB must approve the process for making such a determination.

5.4.3.3.2. Because the capacity to consent or the ability to withdraw may fluctuate, the IRB must evaluate the process for continued verification of understanding and willingness to participate. The consent procedures should describe a plan for protecting individuals who may lose their capacity to provide consent or their ability to withdraw while participating in research activities. The IRB may require that an outside witness observe and confirm the consenting process.

5.4.3.3.3. For participants who lack decision-making capacity, the permission of the individual's legally authorized representative is required and assent should be obtained from the participant.

5.4.3.3.4. In research situations where there is the potential for direct benefit to the participant, the IRB may waive the requirement to obtain assent from the participants. However, permission from the legally authorized representative must be obtained.

5.4.3.3.5. Even where the IRB determines that the subjects are capable of consenting or withdrawing, the IRB may still waive the consent requirements under circumstances in which consent may be waived in accord with §46.116 of Subpart A, General requirements for informed consent.

5.4.3.3.6. Because of the obvious vulnerability of individuals who are **institutionalized**, additional protections must be considered. The IRB must consider the rationale and justification for involvement of institutionalized participants, including an explanation as to why non-institutionalized individuals could not be used.

5.4.3.4. In evaluating the inclusion of cognitively impaired individuals in research, the IRB will consider the protocol-specific findings provided by the investigator on the Request Form for the Inclusion of Cognitively Impaired Individuals in Research and document its determination in the IRB minutes

5.4.4. **Additional VA Requirements**. Pursuant to Appendix D.6 of the VHA Handbook 1200.5, research involving cognitively impaired individuals (incompetent persons or persons with impaired decision making capacity) may only be approved when the following conditions apply:

5.4.4.1. Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

5.4.4.2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

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5.4.4.3. Procedures have been devised to ensure that legally authorized representatives (LAR) are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC)), or LARs and next-of-kin, or guardians, must be given descriptions of both proposed research studies and their obligations of the person's representatives. They must be told that their obligation is to try to determine what the prospective subject would do if competent, or if the prospective subject's wishes cannot be determined, what they think is in the subject's best interest.

5.4.4.4. Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.

5.4.4.5. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

Section II – Applicable SOP Definitions

1. **Act**: The Federal Food, Drug, and Cosmetic Act, as amended (§§ 201-902, 52 Stat. 1040 et seq. as amended (21 USC §321-392)).
2. **Administrative Hold:** A voluntary decision made by an investigator, even if prompted by a verbal or written recommendation from the IRB Chair or another institutional official, to suspend or terminate some or all activities being conducted under an IRB-approved research protocol pending further review or investigation by the IRB or other entity with the institution. This is **not** considered a suspension or termination of IRB approval.
3. **Administrative Noncompliance**: Noncompliance that is administrative in nature (for example, submitting a report of an unanticipated problem a day late, submitting incomplete documentation).
4. **Adult**: Defined by Indiana State Law as "of full age," and "person in his majority" meaning person at least eighteen (18) years of age.
5. **Adverse Events**: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms.
6. **Allegation of Noncompliance:** An assertion of noncompliance made by a second party that must be proved or supported with evidence to either confirm or deny its occurrence.
7. **Assent**: An individual's affirmative agreement to participate in research obtained in conjunction with permission of the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
8. **Audit:** An independent review of a research study, (e.g. data, processes, investigator or team involved with human subject research). Audits are conducted by auditors according to set rules. Audits conducted by the IUPUI/Clarian HSR Auditor "sample" information and observe parts of a research study to determine if it is in compliance with federal and state regulations including, but not limited to, HIPAA, the Common Rule, FDA regulations, and University policies, as appropriate.
9. **Audit Plans**: Documents that describe, in general terms and to the degree possible, the types of audit activities that will be undertaken in relation to (1) research compliance and subject safety and (2) HIPAA compliance. The IUPUI/Clarian audit plans describe the process for establishing the audit schedule, and conducting the audits. The Auditor reviews the audit plan every other year, or more frequently if needed, to account for new information or changes in regulations or institutional polices.
10. **Audit Report**: A report, written by an auditor, in which the observations and findings of an audit are documented. The audit report provides key points to counsel, educate and help an auditee self-correct areas of suspected or real noncompliance as well as report to applicable authorities when necessary.
11. **Audit Schedule**: The audit schedule lists all research studies involving human subjects in the IUPUI/Clarian system anticipated to be audited with the rationale for the audits. The audit schedule is developed by the HSR and HIPAA Auditor on a semi-annual basis.

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12. **Audit Trail:** Documentation and/or system that allows reconstruction of the course of events relating to creation, modification, and deletion of data and/or records.

13. **Auditee**: The department, investigator, or research team to be audited.

14. **Auditor**: For purposes of this SOP, an auditor is a person trained in human subjects research that has undergone special training on regulatory agency standards and guidelines, institutional policies, and auditing techniques.

15. **Authorization:** Express written permission that an individual permits the release and use of their individually identifiable health information for a particular purpose. Authorizations are not required to use an individual's health information to treat them, obtain payment or for a provider's health care operations. However, under HIPAA, research is not considered health care operations, and therefore requires an authorization or waiver of authorization with limited exception. The provider (or investigator) is responsible for obtaining an authorization from an individual.

16. **Benefit**: A valued or desired outcome; an advantage.

17. **Biological Specimens:** Cells, blood, urine, tissue, organs, hair or nail clippings, even if the investigator did not collect these materials.

18. **Biologics:** Biologics, in contrast to drugs that are chemically synthesized, are derived from living sources (such as humans, animals, and microorganisms). Most biologics are complex mixtures that are not easily identified or characterized, and many biologics are manufactured using biotechnology. Biological products often represent the cutting-edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have no other treatments available. These agents are under the jurisdiction of the Center for Biologics Evaluation and Research (CBER) under Section 351 of The Public Health Service. CBER is responsible for ensuring 1) The safety of this nation's entire blood supply and the products derived from it; 2) The production and approval of safe and effective childhood vaccines, including any future AIDS vaccines; 3) The proper oversight of human tissue for transplantation; 4) Adequate and safe supply of allergenic materials and anti-toxins; and 5) The safety and efficacy of biological therapeutics, including an exciting new array of biotechnology-derived products used to treat diseases such as cancer and AIDS.

19. **Blinding/Masking:** A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

20. **Certification:** The official notification by the institution to the supporting department or agency, in accordance with the requirements of 45 CFR 46, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

21. **Certified Copy**: A copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original. A paper copy of electronic information is not automatically considered a "certified" copy, but rather must be verified as such.

22. **Children:** Defined by the federal regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research or clinical investigation, under the applicable law of the jurisdiction in which the research or clinical investigation will be conducted."

Section II – Applicable SOP Definitions

Per Indiana State Law, "minors" are defined as "persons less than 18 years of age;" therefore, are considered "children" for purposes of the regulations. EXCEPTION: According to Indiana State Law, a minor may consent for himself/herself if any of the following are true: 1) By law the minor is considered emancipated; 2) The minor is at least fourteen (14) years of age, not dependent on a parent for support, is living apart from parents or from an individual *in loco parentis4.8*; AND is managing his/her own affairs; 3) The minor is or has been married; 4) The minor is in the military service of the United States; OR 5) The minor is authorized to consent to the health care by any other statute.

23. **Clarian Health Partners (Clarian):** A corporation that includes Indiana University Hospital, James Whitcomb Riley Hospital for Children, Methodist Hospital and its wholly owned subsidiaries including Methodist Research Institute and any employee of those hospitals and subsidiaries.

24. **Clinical Investigation:** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under §505(i), §507(d), or §520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by the FDA as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies (21 CFR 50.3(c)). The terms "research," "clinical research," "clinical study," "study," and "clinical investigation" are deemed to be synonymous for purposes of this part.

25. **Clinical Investigator**: A listed or identified investigator or sub-investigator (co-investigator) who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

26. **Coded Samples:** Coded samples are those from which the source of the specimen can be identified by reference to a code rather than a name or other personal identifier. When such samples are obtained from a tissue repository, the repository retains information linking the code to a particular human specimen. Information is sufficient such that the investigator, repository or third party could link the biological sample or information derived from the research using the sample with a particular person or small group of identifiable individuals.

27. **Cognitively Impaired:** Having a psychiatric disorder (e.g. psychosis, neurosis, personality or behavior disorder), and organic impairment (e.g. dementia), or a developmental disorder (e.g. mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.

28. **Colleague**: Another provider or clinician with a covered entity or practice plan, or a co-investigator in a research protocol.

29. **Collector-Investigators:** Persons charged with the responsibility of obtaining specimens from subjects for the purposes of adding to a repository.

30. **Comparable Device:** A device, not necessarily identical to the device that is the subject of the HDE, but one that the FDA considers to meet the needs of the identified patient population. In

making this determination, the FDA will consider the device's intended use, technological characteristics, and the patient population to be treated or diagnosed with the device.

31. **Compensation affected by the outcome of clinical studies**: Compensation that could be higher for a favorable outcome than for an unfavorable outcome, such as compensation that is explicitly greater for a favorable result or compensation to the investigator in the form of an equity interest in the sponsor of a covered study or in the form of compensation tied to sales of the product, such as a royalty interest.

32. **Computer Resources:** All computers and related equipment and electronic communication devices, including but not limited to software, data communications or other tools, instruments, modems, electronic mail, phones, voicemail, facsimile machines, and other multimedia equipment, etc. that are owned by Indiana University or connected to the University's or practice plan's network or that contain research data used for IUPUI research studies.

33. **Computerized System**: Computer hardware, software, and associated documents (e.g., user manual) that create, modify, maintain, archive, retrieve, or transmit in digital form information related to the conduct of a research study.

34. **Conducted at or on behalf of:** Human subjects research that is conducted at these institutions' facilities or property; is sponsored by these institutions, is conducted by or under the direction of any employees or agents of these institutions in connection with their institutional responsibilities, or involves the use of these institutions' non-public information to identify or contact human research subjects or prospective subjects.

35. **Confidentiality:** The assurance that certain information that may include a subject's identity, health, behavior, or lifestyle information, or a Sponsor's proprietary information would not be disclosed without permission from the subject (or sponsor). Confidentiality is a means of protecting one's privacy.

36. **Conflict of Interest:** The following is a general definition of the term **conflict of interest.** It is based on Public Health Service Department regulations, and therefore applies to National Institutes of Health funded research. This general definition also informs and guides the IRB's analysis of non-NIH funded research relationships. In all cases, additional factors not inconsistent with applicable requirements may also be considered in determining whether a conflict of interest exists or whether proactive steps should be taken to avoid conflicting interests. A conflict of interest may exist when a covered person's Significant Financial Interests the interests of outside entities in which a covered person holds a Significant Financial Interest, reasonably would appear to affect or be affected by the covered person's research or sponsored programs. Under State law on conflict of interest it is a crime for a public employee to knowingly or intentionally deriving a pecuniary benefit from transactions between the employee (including employee's spouse and dependents) and the public employer. This law establishes a much lower threshold -- $250 or more of transactions during any twelve month period. To avoid criminal penalties, therefore, university employees should disclose to the Board of Trustees of Indiana University any situations likely to result in a contract involving the purchase, sale, or services or other matters, between the university and the employee or employee's dependents.

37. **Continuing Noncompliance**: A pattern on noncompliance that, in the judgment of the convened IRB, IRB Chair, or IRB Chair's designee, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of participants, would have been foreseen as compromising the scientific integrity of a study such that important conclusions could

no longer be reached, suggests the likelihood that noncompliance will continue without intervention, or frequent instances of minor noncompliance. Continuing noncompliance also includes failure to respond to a request to resolve an episode of noncompliance with human subject protection regulations.

38. **Corrective Action**: Action taken to correct a situation that has occurred.

39. **Covered Entity:** Health plans, health care clearinghouses, and health care providers who transmit any health information in electronic form in connection with a HIPAA required standard transaction–typically providers that bill electronically. Here at IUPUI/Clarian, examples of covered entities include Wishard, Clarian, VAMC, IUMG-PC, and all practice plans within IUMG-SC (e.g. UMDA, etc.). The School of Medicine itself is not a covered entity. For the purposes of research, an Investigator may recruit the patients within their own Covered Entity, as can the clinical nurse or Research Coordinator that is working under the direction of the Investigator. A Covered Entity may elect to form a Business Associate Agreement with another party. Depending upon the agreement between a Covered Entity and a Business Associate, the Business Associate may effectively use and disclose PHI when performing a function on behalf of a Covered Entity. For example, Regenstrief Institute of Medicine provides software and systems to several Covered Entities and is a Business Associate of Clarian Health Partners and Health and Hospital Corporation of Marion County. This permits Regenstrief to use and disclose Protected Health Information collected at University Hospital, Riley Hospital, Methodist Hospital, and Wishard Hospital for those contracted purposes. For the purposes of this SOP, the term "Covered Entity" will be utilized, but Investigators may need to keep in mind additional relationships may also be governed by Business Associate agreements.

40. **Custom Device**: A device that 1**)** necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician or dentist; 2) is not generally available to, or generally used by, other physicians or dentists; 3) is not generally available in finished form for purchase or for dispensing upon prescription; 4) is not offered for commercial distribution through labeling or advertising; and 5) is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

41. **Data Integrity:** A state in which all data values stored in the database are said to be correct. This state can be compromised in a number of ways, for example, human errors when data is entered; errors that occur when data is transmitted from one computer to another; software bugs or viruses; hardware malfunctions such as disk crashes or memory leaks; natural disasters such as fires and floods.

42. **Data Safety/Security:** Allowing only authorized people or systems access to the data. Limiting access to the data by roles, which are granted permissions to view, update, or delete data within the database.

43. **Data Use Agreement:** To use or disclose a limited data set for the purpose of research, public health or healthcare operations, a covered entity must enter into a data use agreement with the recipient of the information. The agreement may take the form of a formal contract if the relationship is with a third party, or could be a simple confidentiality agreement that workforce members sign when a provider wants to create and use a limited data set for its own research purposes. The principal investigator can determine if they will require co-investigators within the

covered entity to sign a data use agreement. The agreement must meet detailed requirements as follows: specify permitted uses and disclosures of the limited data set; identify who may use or receive the limited data set; and restrict further use and disclosure.

44. **Data Validation/Audit:** A method or process where data in its former, current, and future state are accounted for. This includes, but is not limited to, tracking the original data entered, tracking who and when an individual or system viewed or changed any data, and tracking why data was changed.

45. **Dead Fetus**: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

46. **De-Identified:** Health information is de-identified if there is no reasonable basis to believe that the data can be used to identify an individual, or if the provider has no reasonable basis to believe it can be used to identify the individual. The Privacy rule requires one of the two following approaches to de-identify data: If a person with appropriate knowledge and experience applying generally accepted statistical and scientific principles and methods for rendering information not individually identifiable makes a determination that the risk is very small that the information could be used, either by itself or in combination with other available information, by anticipated recipients to identify a subject of the information.

    OR

    If all 18 identifiers have been removed, including name, all geographic subdivisions smaller than a State including street address, city, county, precinct, zip codes and equivalent geocodes,(except for the initial 3 digits of a zip code if more than 20,000 people reside in the area), all dates including birthdays (other than the year) and ages over 89, phone numbers, fax numbers, email addresses, social security numbers, medical record numbers, health plan beneficiary numbers, account numbers, certificate/license numbers, vehicle identifiers and serial numbers (including license plate #), device identifiers and serial #'s, URLs, IP addresses, biometric identifiers, full face photographic images and any comparable images, any other unique identifier, characteristic or code. Note: Other demographic information, such as gender, race, ethnicity, and marital status are not included in the list of identifiers that must be removed.

47. **Delegated authority to consent on behalf of incapable party**: Per Indiana Code 16-36-1-6, an individual authorized to consent to health care for another who for a time will not be reasonably available to exercise the authority may delegate the authority to consent during that time to another individual. The delegation: (1) must be in writing; (2) must be signed by the delegate; (3) must be witnessed by an adult; and (4) may specify conditions on the authority delegated. Unless the writing expressly provides otherwise, the delegate may not delegate the authority to another individual.

48. **Delivery**: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

49. **Department or Agency Head**: The head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

50. **Designated record set**: For purposes of this SOP, the term "designated record set" means any item, collection, or grouping of information that includes protected health information and is maintained, collected, used, or disseminated by or for a covered entity. Each covered entity will have to define its Designated Record Set. Patients have a right to access and propose amendments to their designated record set and to know when their designated record set is disclosed for certain purposes, such as disclosures made under an IRB-approved waiver of authorization.

Section II – Applicable SOP Definitions

51. **Direct Advertising**: Advertising that is intended to be seen or heard by prospective participants to solicit their participation in a study.

52. **Dissent**: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

53. **Divestiture.** Allow arrangements to go forward contingent upon the sale or disposal of specified financial interests to eliminate or reduce the financial conflict of interest by a date certain.

54. **Data Safety Monitoring Board (DSMB):** A formally appointed independent group of experts assigned to conduct interim monitoring of accumulating date from research activities to assure the continuing safety of research subjects, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. A Data Safety Monitoring Committee (DSMC) is synonymous with a DSMB.

55. **Data Safety Monitoring Plan (DSMP)**: A plan established to assure that each research study has a system for appropriate oversight and monitoring of the conduct of the study to ensure the safety of subjects and the validity and integrity of the data. A DSMP is commensurate with the risks involved with the research. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the research study.

56. **Electronic Audit Trail**: A compilation of documentation that allows reconstruction of the course of events relating to the creation, modification, and deletion of records related to the conduct of the research study in general, and the details related to each subject's participation, in particular. An **electronic audit trail** is a secure, computer generated, time-stamped electronic record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic record.

57. **Electronic Data:** Any combination of text, graphics, data, audio, pictorial, or any other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system. This includes any information that has been collected and entered into a software application to move or process. This includes, but is not limited to, information on a handheld device or in an email system.

58. **Electronic Database:** A collection of any data that is organized so that its contents can easily be accessed, managed, updated and stored electronically. This includes, but is not limited to, the storing of information in Microsoft's Word, Excel, or Access, Borland's Paradox, Filemaker's FilemakerPro, or DDH Software's HanDBase.

59. **Electronic Signature:** A method to authenticate the identity of the sender of a message or the signer of an electronic document.

60. **Eligible Domestic Partner:** This person is the same sex as the employee; at least 18 years of age and competent to enter into a contract; not legally married or the domestic partner of another individual; has lived with the employee as a couple for at least six consecutive months; and has submitted documentation to verify an interdependent relationship with the employee that is the functional equivalent of a marriage.

61. **Emancipated Minor**: A legal status conferred by court order upon persons who have not yet attained the age of legal competency, but who are entitled to treatment as legal adults. For additional information, please see Indiana Code 31-34-20-6.

Section II – Applicable SOP Definitions

62. **Emergency Use:** The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

63. **Encryption:** The process of converting information, particularly identifiable information such as social security number and name that identifies individuals, into a code to secure that information from unauthorized access.

64. **Enrollment:** If a subject requires screening tests to determine eligibility, enrollment begins when the informed consent for screening is obtained. If there is no screening, then enrollment begins at the time of consent for the study. In situations where waiver of consent is applicable, enrollment begins when data is collected.

65. **Essential Documents**: Documents which individually and collectively permit evaluation of the conduct of research and the quality of the data produced. These include but are not limited to regulatory and patient specific records. A complete list of these documents can be found in the ICH Guidelines, Section 8.0.

66. **Exclusion Criteria:** A list of requirements, any one of which excludes a potential subject from selection and participation in a study.

67. **Exempt Review Procedure:** A review procedure consisting of a review of research involving human subjects by an RCA staff person or a member of the IRB designated by the Chair.

68. **Expedited Review Procedure:** A review procedure consisting of a review of research involving human subjects by the IRB Chairperson or by one or more experienced reviewers designated by the Chairperson from among members of the IRB.

69. **External**: From the perspective of a multicenter clinical trial, other institutions engaged in the clinical trial.

70. **External Entity:** Any person, trust, organization, enterprise, or other entity (including government agencies) that is not an entity under the control of or under common control with the University.

71. **Faculty Sponsors:** Full or part-time faculty employed by IUPUI/Clarian who engage in classroom instruction, supervise on or off campus internships, clinical experiences or practica, or mentor students who are conducting independent projects.

72. **Family Member**: For purposes of this SOP, this person is not a legally authorized representative, but can be any one of the following legally competent persons: spouses, parents, children (including adopted children), brothers, sisters, and spouses of brothers and sisters, and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

73. **Federalwide Assurance (FWA):** A formal document between an institution and the federal government that commits them to comply with applicable regulations governing the conduct of all research involving human subjects. Indiana University and Clarian Health Partners hold such assurances.

74. **Fetus**: The product of conception from implantation under delivery.

75. **Financial Interest:** Pursuant to the Indiana University Policy on Financial Conflicts of Interest in Research, is anything of monetary value, including, but not limited to, salary, consulting fees, honoraria, equity interests (e.g., stocks, stock options or other ownership interests), interests in real

or personal property, dividends, royalties, rent, capital gains, intellectual property (e.g., patents, copyrights and royalties from such rights, including those paid by Indiana University Research and Technology Corporation/ IURTC), and forgiveness of debt. The term does not include compensation from Indiana University, except royalties or other remuneration from Indiana University (note that royalties or other payments from Indiana University Research Technology Corporation ("IURTC") must be disclosed); income from seminars, lectures, or other educational activities sponsored by public or nonprofit entities; or income from service on advisory committees or review panels for public or nonprofit entities, income from service on advisory committees, or review panels for public or nonprofit entities; any financial interest arising solely by means of investment in a mutual, pension, or other institutional investment fund where the covered person does not exercise control over the management and investments of such fund..

Examples of Financial Interests that must be disclosed include: 1) I receive $10,000 or more a year in consulting fees for RX Company. I am conducting a clinical trial on a product made by RX Company; 2) I am conducting a clinical trial with support from RX Company on a patented product that was developed by me or is licensed to RX and generates some royalties based on my IU license; 3) I have a patent on a product that is licensed to RX Company and I intend to use the product in a research study I am conducting. [Note: Disclosure is required for any proprietary interest. There is no $10,000 threshold]; 4) I hold $3,000 in stock options whose value might increase if the results of the research I want to conduct are positive; 5) My spouse serves on the board of directors of a biotech company and I want to conduct a study sponsored by that pharmaceutical company; 6) I am conducting a research study that could adversely affect a product produced by a company in which I have a Significant Financial Interest; and 7) My spouse works full-time for a pharmaceutical company and I want to conduct a study sponsored by that pharmaceutical company.

76. **For-Cause Audit**: An audit conducted in response to the IRB's (or other authoritative entity) concern about the conduct of a research study, including the process of informed consent or about whether the rights and welfare of subject is adequately protected.

77. **GCP (Good Clinical Practice)**: A standard by which clinical trials are designed, performed, monitored, audited, recorded, analyzed, and reported so that there is public assurance that the data are credible, and that the rights, integrity, and confidentiality of subjects are protected.

78. **Genetic Research:** research (not diagnostic testing) which involves either the analysis of human chromosomes or DNA from an individual and/or family members for the purpose of deriving information concerning the individual or family about the presence, absence or mutation of genes, DNA markers or inherited characteristics or other studies with the intent of collecting and evaluating information about heritable diseases and/or characteristics within a family.

79. **Greater than Minimal Risk**: The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

80. **Guardian**: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. The FDA includes in its definition that this individual can also consent on behalf of a child to participate in research, even when general medical care includes participation in research.

81. **Harm**: A hurtful or adverse outcome of an action or event. Harms incurred by research can occur close in time to the research, or can follow long after it has concluded.

Section II – Applicable SOP Definitions

82. **Health Care**: Defined by Indiana State Law as any care, treatment, service, or procedure to maintain, diagnose, or treat an individual's physical or mental condition, including admission to a health care facility.

83. **Health Care Operations:** Activities that are "compatible with and directly related to" treating an individual and obtaining payment for those services. Protected Health Information may be used or disclosed for health care operations without an individual's authorization. These activities include, conducting quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines, provided that the obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities. Research is NOT health care operations. As a result, if the purpose of the activity is to obtain generalizable knowledge, then the privacy rule's research requirements apply. In addition, health care operations includes reviewing the competence or qualifications and accrediting/licensing of health care professionals and plans, evaluating health care professionals and health plan performance, training future health care professionals, insurance activities relating to the renewal of a contract for insurance, conducting or arranging for medical review and auditing services, and compiling and analyzing information in anticipation of or for use in a civil or criminal legal proceeding.

84. **HIPAA**: The Health Insurance Portability and Accountability Act of 1996. Also referred to as the Privacy Rule.

85. **Human Fetal Material**: Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.

86. **Human Subject:** A living individual about whom an investigator (whether professional or student) conducting research obtains l) data through intervention or interaction with the individual, or 2) identifiable private information (as defined by 45 CFR 46.102f). FDA includes in its definition of "human subject" an individual who is or becomes a participant in research, either as a recipient of an investigational drug, as an individual on whom or on whose specimen an investigational device is used, or as a control. A "human subject" may either be a healthy human or a patient and is synonymous with "subject," "participant," and "volunteer."

87. **Human Subjects Research (HSR) and HIPAA Auditor**: The HSR and HIPAA Auditor is independent from the research area, is employed by RCA and the IU School of Medicine Office of Compliance Services, and reports to the Institutional Review Board. The HSR and HIPAA Auditor performs audits on human subjects research within the IUPUI/Clarian system. The HSR and HIPAA Auditor will consult with and educate IUPUI/Clarian researchers who conduct human subjects research in fulfilling their responsibilities to assure compliance.

88. **Humanitarian Device Exemption (HDE)**: An application that is similar to a premarket approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD).

89. **Humanitarian Use Device (HUD)**: A device that is "intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or that are manifested in fewer than 4,000 individuals (per year) in the United States."

90. **Identified Samples** - Biological samples obtained by an investigator or a 3rd party which have identifiers attached or a link permitting determination of the individual subject source through the use of a code.

Section II – Applicable SOP Definitions

91. **Identifiers**: Identifiers are information that can be used to link a sample or scientific result with a specific person or group of people. Examples of identifiers include name, social security number, hospital number or other unique identifier. It should also be noted that using current information technology, a combination of descriptive data may be sufficient to allow identification of the donor and thereby collectively may be considered identifiers (e.g. zip code, birth date or profession may be sufficient to identify a specific individual). HIPAA recognizes eighteen (18) identifiers that may make health information identifiable to an individual. For details, see the definition for De-Identified above.

92. **Immediate Family Member**: For purposes of this SOP, a person's spouse, dependent and eligible domestic partner.

93. **Immortalized Cell Line:** A culture which is apparently capable of an unlimited number of population doublings.

94. **Implant:** A device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also "implants".

95. ***in loco parentis*:** Someone who acts in the place of a parent.

96. **Inclusion Criteria**: The requirements that prospective subjects must meet to be eligible for selection and participation in a study.

97. **Individually Identifiable Health Information (IIHI):** Information that is a subset of protected health information, including demographic information collected from an individual, and a) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and b) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; and that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

98. **Informed Consent:** An ongoing process by which a subject (or his/her legal representative) voluntarily confirms his or her willingness to participate in a particular research project, after having been informed of all aspects of the research that are relevant to the subject's decision to participate. Informed consent is often, but not always, documented by means of a written, signed, and dated informed consent form with documentation, which is retained in the subject's record.

99. **Institution:** A person, other than an individual, who engages in the conduct of research on subjects or in the delivery of medical services to individuals as a primary activity or as an adjunct to providing residential or custodial care to humans. The term includes, for example, a hospital, retirement home, confinement facility, academic establishment, and device manufacturer.

100. **Institutional Facility:** A public or private entity i.e. Hospital Convalescent Home Nursing Home Extended Care Facility or any other health care facility whose primary purpose is to provide a physical environment for subjects to obtain health care services.

101. **Institutional Review Board (IRB):** Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical and/or behavioral (general) research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. This independent body is constituted of members with varying backgrounds (e.g. medical, scientific, nonscientific, and unaffiliated).

Section II – Applicable SOP Definitions

102. **Institutional Work:** Works created at the instigation of the University, under the specific direction of the University, for the University's use, by a person acting within the scope of his or her employment or subject to a written contract.

103. **Interaction**: Includes communication or interpersonal contact between the investigator (or a member of the research team) and the subject.

104. **Internal**: From the perspective of a multicenter clinical trial, IUPUI/Clarian (or their affiliates) investigators engaged in the clinical trial. .

105. **Intervention**: Includes both physical procedures by which data are gathered (e.g. venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

106. **Investigational Device:** A device that is the object of a clinical investigation or research involving one or more human subjects to determine its safety and effectiveness. This definition also includes "transitional devices," which are devices that had been previously regulated by the FDA as drugs prior to the passage of the Medical Device Amendments. Generally these are not approved by the FDA, or are being tested or studied for indications not previously approved by the FDA.

107. **Investigational Device Exemption (IDE):** The application to the FDA for research involving a device not yet approved by the FDA or research on a product for non-approved indication. In most cases, the Sponsor holds the IDE, but in some studies, the Investigator holds the IDE.

108. **Investigational Drug:** A new drug or biological drug that is used in a clinical investigation. The terms "investigational drug" and "investigational new drug" are synonymous for this SOP.

109. **Investigational Drug Service (IDS):** A pharmacy or pharmacist specializing in the handling, storage, labeling and distribution of investigational agents.

110. **Investigational New Drug Application (IND):** The application to the FDA for research involving a product not yet approved by the FDA or research on a product for a non-approved indication. In most cases, the Sponsor holds the IND, but in some studies the Investigator holds the IND.

111. **Investigational Product:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. Under Indiana Code 25-26-13-2, "Investigational New Drug" means any drug that is limited by state or federal law to use under professional supervision of a practitioner4.7 authorized by law to prescribe or administer such drug.

112. **Investigator:** An individual who actually conducts a clinical investigation, i.e. under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

113. **IRB Executive Committee**: A committee made up of the chairs and vice chairs of each of the IUPUI/Clarian IRBs, along with other members, as needed, to achieve diversity. The committee is responsible for developing and coordinating IUPUI and Clarian IRBs' policy and procedural matters involving the use of human subjects in research. Its operations will be administered through the IUPUI Research Compliance Administration (RCA) department.

Section II – Applicable SOP Definitions

114. **IUPUI/Clarian:** Refers to anyone employed by or using the facilities of IUPUI or Clarian Health Partners or any affiliated institution as listed under the Federalwide Assurances found at: http://www.iupui.edu/%7Eresgrad/spon/fwa.htm, which must have human subjects research reviewed, approved, and monitored by an IUPUI/Clarian IRB. This would also include any entity that is a part of the Indiana University School of Medicine (i.e. Centers for Medical Education) where no other IRB exists.

115. **IUPUI/Clarian Affiliates**: Organizations that maintain a FWA with DHHS in which one or more of the IUPUI/Clarian IRBs is listed as the reviewing IRB or organization that have entered into a formal agreement with IU for the review and approval of human subjects research at their institution. A list of these affiliates maintaining a FWA can be found at: http://www.iupui.edu/%7Eresgrad/spon/fwa.htm.

116. **Legally Authorized Representative (LAR)**: Defined in the federal regulations as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research. In Indiana, a health care representative (as defined by state law) is the equivalent of the federally defined LAR. As a result of this clarification, for studies conducted at the VA, the Indiana state law definition of LAR supersedes the VA definition of LAR. For studies that involve prospective and/or current subject(s) that reside in states other than Indiana, the applicable law(s) of each applicable state will be reviewed to ensure that the applicable requirements for an LAR to consent on behaf of a prospective subject are met.

117. **Life-Threatening**: For purposes of "emergency use," this includes the scope of both life-threatening and severely debilitating. Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end poin t of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible. Severely Debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

118. **Limited Data Set**–This set of data excludes facially identifiable information, but still includes some identifiable information. As a result, the data is still "identifiable" and may be used for limited purposes, including research, public health or healthcare operations as long as there is a data use agreement with the recipient of the limited data set. A limited data set must exclude 16 specified identifiers that are listed in the Rule including: name, street address, telephone and fax numbers, email address, social security number, certificate/license number, vehicle identifiers and serial numbers, URL's and IP addresses, and full face photo's and any other comparable images. The limited data set could include the following identifiable information: admission, discharge, and service dates, date of death, age, (including age 90 and older); and the five digit zip code.

119. **Logon:** A unique, specific, confidential credential that identifies the person as a legitimate and authorized user of the computer and/or electronic system.

120. **Major Protocol Deviation:** A deviation to the IRB-approved protocol that may impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study. Examples: Enrollment of a subject who did not meet all inclusion/ exclusion criteria; performing a study procedure not approved by the IRB; drug/study medication dispensing or dosing

error; failure to perform a required lab test or conducting a study visit outside the required timeframe, if, in the opinion of the investigator, may affect subject safety and/or data integrity.

121. **Management Plan:** Examples of management plans may include one or more of the following:

    a. **Disclosure.** Disclosure is required in most cases including: (i) public disclosure of the financial interests of the Faculty or Staff Member in all relevant publications, presentations (whether or not academic presentations), and (ii) disclosure to the appropriate co-investigators, members of the laboratory or research group, and students or trainees, and (iii) disclosure on Human Subject consent forms;

    b. Study enrollment is blinded and determined by someone other than the Investigator;

    c. Limiting local enrollment not to exceed 20% of the projected total enrollment of in multi-center trials;

    d. Limiting the role of the Investigator with a Financial Interest - requiring that the role of the investigator with the financial interest be limited in some way (e.g., the Faculty or Staff Member may not be allowed to i) serve as principal investigator, (ii) analyze data, (iii) determine whether potential subjects are eligible for enrollment, iv) solicit consent, or v) determine whether an adverse event report is required);

    e. **Oversight.** Appointment of a disinterested individual or group (data safety monitoring board) to monitor the relevant research activity. An oversight committee might be charged, at a minimum, with reviewing abstracts and manuscripts before they are submitted for publication to ensure that the research is conducted and reported according to scientific and ethical standards and that conflict of interest management measures are observed. In other cases, an oversight committee might meet quarterly and review protocols, subject accrual, complications, and other issues as appropriate;

    f. **Proprietary interest in the tested product**: Property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement.

    g. **Restriction on Equity.** i) placement of stock in escrow until a trigger date specified by the Committee, or ii) requirement that options, warrants, and similar instruments not be exercised without the prior permission of the Committee;

    h. **Divestiture.** Allow arrangements to go forward contingent upon the sale or disposal of specified financial interests to eliminate or reduce the financial conflict of interest by a date certain;

    i. Severance of relationships that heighten or create actual or potential conflicts - for example, relinquishing a seat on a board of directors or terminating a consulting arrangement with an outside entity in order to reduce the Financial Interest.

122. **Manufacturer: A**ny person engaged in the business of manufacturing, assembling, or importing of electronic products.

123. **Master Inventory List**: The original itemized catalog of the location of all data and documents being retained and/or stored.

124. **Mature Minor**: Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g. consenting to medical). Not that a mature minor is not necessarily an emancipated minor.

Section II – Applicable SOP Definitions

125. **Medical Device:** An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component or accessory which is recognized in the official National Formulary or the United States Pharmacopoeia, or any supplement to them, intended for the use in the diagnosis of disease or other conditions, or the cure, mitigation, treatment or prevention of disease in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

126. **Minimal Risk:** The probability or magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (as defined by 45 CFR 46.102(i)).

127. **Minimal Risk (for Prisoners):** The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examinations of healthy persons (who are not prisoners). Note: This definition differs from the definition in 45 CFR 46, Subpart A used for reviews by an expedited procedure and the waiver and alteration of consent and consent document, and 45 CFR 46, Subpart D for approval of research involving children as participants.

128. **Minimum Necessary Standard**: A Covered Entity must make reasonable efforts to use, disclose, or request the least amount of information needed for the intended purpose. For example, if the entire medical record is desired, it must be justified as the minimum necessary. Although the Minimum Necessary Standard does not apply to use or disclosure of Protected Health Information under an Authorization, the Investigator is bound by the purposes described in the Authorization. In addition, the Minimum Necessary Standard does not apply to a patient's treatment.

129. **Minor**: Defined by Indiana State Law as a person less than eighteen (18) years of age unless the child meets the Indiana State Law definition of an emancipated minor.

130. **Minor Noncompliance**: Noncompliance that is neither serious nor continuing which does not affect the scientific soundness of the research plan or the rights, safety, or welfare of human subjects. Examples might include: obtaining consent using an invalid/outdated consent document that contains all of the information required by the IRB or failure to submit continuing review documentation prior to expiration of IRB approval.

131. **Minor Protocol Deviation:** A deviation that does not impact subject safety, compromise the integrity of study data and/or affect subject's willingness to participate in the study. Examples: Failure of subject to return study medication, failure to follow the approved study procedure that, in the opinion of the investigator, does not affect subject safety or data integrity (e.g. study procedure conducted out of sequence, omitting an approved portion of the protocol, missing lab results).

132. **National Cancer Institute Central Institutional Review Board Initiative:** The NCI CIRB Initiative is sponsored by the NCI in consultation with the Department of Health and Human Services Office of Human Research Protection (OHRP). The CIRB is an IRB designated by the institution as the IRB of record for certain adult and pediatric multi-center national cancer treatment trials.

133. **Neonate:** A newborn.

Section II – Applicable SOP Definitions

134. **Noncompliance**: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal or state regulations, requirements of VHA Handbook 1200.5, or institutional policies governing human subjects research or the requirements or determinations of the IRB. Noncompliance actions may range from minor to serious, be unintentional or willful, and may occur once or more than once. The degree of noncompliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the noncompliance. Examples include, but are not limited to, failure to obtain IRB approval, inadequate supervision, failure to follow recommendations made by the IRB, failure to report unanticipated problems or protocol changes, etc.

135. **Noninvasive:** When applied to a diagnostic device or procedure, means one that does not by design or intention: 1) penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra or 2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for noninvestigational purposes is also considered noninvasive.

136. **Nonviable Neonate:** A neonate after delivery that, although living, is not viable.

137. **Notice of Privacy Practices:** An individual has a right to adequate notice of the uses and disclosures of protected health information that may be made by the covered entity and of the individual's rights and the covered entity's legal duties with respect to protected health information. The covered entity must provide a notice that is written in plain language.

138. **Observed or Apparent Noncompliance**: Noncompliance that does not require further information to confirm its occurrence.

139. **Off-site:** For purposes of securing research data, this refers to a location not in the immediate vicinity. This could be in a different office or building. While this could mean an "off campus" location, "off-site" does not always mean "off campus."

140. **One-Time**: A single use (or single course of treatment, e.g., multiple doses of antibiotic) of a test article with one subject at one institution (hospital-specific). Note: "Hospital-specific" shall in no case allow the same physician to move a patient from one hospital or physician to another for purposes of meeting the one-time emergency use provision.

141. **Oversight**: The process by which a qualified person or group periodically reviews the results and conduct of a study to date, as it relates to subject safety.

142. **Parent:** A child's biological or adoptive parent.

143. **Permission:** The agreement of parent(s) or guardian(s) to the participation of their child or ward in research.

144. **Persons authorized to consent for incapable parties**: For prospective and/or current subjects that do not reside in the State of Indiana, the Investigator(s) shall consult with University Counsel and Research Compliance Administration to ensure the applicable law(s) of each state are met for an LAR to consent on behalf of a prospective subject. Otherwise, per Indiana Code 16-36-1-5, if an individual incapable of consenting has not appointed a health care representative or the health care representative is not reasonably available or declines to act, consent to health care may be given by

1) A judicially appointed guardian of the person or a representative appointed; or 2) By a spouse, a parent, an adult child, or an adult sibling, if a) There is no guardian or other representative described in 4.14.1 above; b) The guardian or other representative is not reasonably available or declines to act; or c) The existence of the guardian or other representative is unknown to the health care provider; or 3) The individual's religious superior, if the individual is a member of a religious order and a) There is no guardian or other representative described in 4.14.1 above; b) The guardian or other representative is not reasonably available or declines to act; or c) The existence of the guardian or other representative is unknown to the health care provider.

145. **Protected Health Information (PHI):** Health information, including demographic information collected from an individual, and is created or received by a health care provider, health plan, employer, or health care clearinghouse; and relates to the past, present, or future physical or mental health or condition of an individual, or the provision of health care to an individual.

146. **Practitioner:** A physician licensed under IC-25-22.5, a veterinarian licensed under IC 15-5-1.1, a dentist licensed under IC 25-14, a podiatrist licensed under IC 25-29, or any other person licensed by law to prescribe and administer legend drugs in this state.

147. **Pregnancy:** Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

148. **Premarket Approval (PMA)**: Any premarket approval application for a class III medical device, including all information submitted with or incorporated by reference therein. "PMA" includes a new drug application for a device under section 520(1) of the Federal Food, Drug, and Cosmetic Act.

149. **Pre-Screening:** The evaluation of generalized characteristics prior to screening to initially determine eligibility (e.g. review of charts).

150. **Preventive Action**: Action taken to prevent occurrence of an event in the future.

151. **Principal Investigator (PI):** The responsible leader of a team of investigators (and research team), who has the ultimate responsibility for the conduct of the research. Eligibility requirements can be found in the IRB Instruction Packet.

152. **Prisoner:** Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial. Examples of the application of the regulatory definition of "prisoner" include:

    a. Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.

b. Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to nonpenal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.

c. Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.

d. Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population. Please consult the Research Compliance Administration office when questions arise about research involving these populations. (reference: Office for Human Research Protections (OHRP) Human Research Questions & Answers)

153. **Privacy:** A person's desire to control the access of others to themselves. Privacy protects access to the person, whereas confidentiality protects access to data.

154. **Privacy Board:** The group of individuals charged with the review and approval of activities related to privacy and confidentiality. The privacy board must have members with varying backgrounds and appropriate professional competency as necessary to review the effect of the research protocol on the individual's privacy rights and related interests. The IUPUI/Clarian IRBs have been designated as the Privacy Board for all research conducted at IUPUI/Clarian facilities, Roudebush VA Medical Center, Larue Carter and Wishard Memorial Hospital.

155. **Private Information**: Includes information about behavior that occurs in a context in which an individual can reasonable expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonable expect will not be made public (e.g. medical record. Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

156. **Proband:** The affected individual through whom a family with a genetic disorder is ascertained.

157. **Proprietary interest in the tested product**: Property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement.

158. **Prospective Study:** A study in which the collection of tissue or other data related to the individual from whom the biological specimen was collected will occur "in the future". In other words the biological specimen is not "on the shelf" when approval for the research under review is requested. This may refer to tissue that will be obtained specifically for research purposes after the research protocol has been approved by the IRB wherein the subject is asked to undergo a procedure to obtain a specimen for research purposes or specimens to be collected from discarded clinical samples for research purposes that will be obtained after the research is approved by the IRB.

159. **Protocol Deviation:** An alteration/modification to the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation. The IRB-approved protocol includes the detailed protocol, summary safeguard statement, informed consent document(s), recruitment materials, questionnaires, and any other information relating to the research study.

Section II – Applicable SOP Definitions

160. **Radiologic:** A radiologic is defined as any manufactured or assembled article that emits radiation. This may be an implantable device, or a machine (such as bone density machine) that is used as part of an investigation. For the purposes of this SOP, it implies that the article is being used for investigational purposes. The Center for Devices and Radiological Health (CDRH) includes the following definitions:

    a. **Electronic product radiation**: Any ionizing or non-ionizing electromagnetic or particulate radiation; or any sonic, infrasonic, or ultrasonic wave, which is emitted from an electronic product4.9.2 as the result of the operation of an electronic circuit in such product.

    b. **Electronic product**: Any manufactured or assembled product which, when in operation, contains or acts as part of an electronic circuit; and emits (or in the absence of effective shielding or other controls would emit) electronic product radiation, or any manufactured or assembled article which is intended for use as a component, part, or accessory of a product described above and which when in operation emits (or in the absence of effective shielding or other controls would emit) such radiation;

161. **Randomization or Random Assignment:** The process of assigning research subjects to a specific study group (e.g. treatment, control) using an element of chance to determine the assignments in order to reduce bias.

162. **Research Compliance Administration (RCA):** A department within Research and Sponsored Programs on the IUPUI campus responsible for providing administrative support to the IUPUI/Clarian Institutional Review Boards (IRBs).

163. **Recipient-Investigators:** Persons approved to receive specimens from a repository to use for research purposes.

164. **Recruitment**: The process by which individuals are identified, screened and contacted or identified, screened and determined to be not eligible for a specific study.

165. **Regulatory Agencies:** Government organizations, anywhere in the world, that set standards, establish policies, advocate laws and provide oversight of specified activities within a country; e.g., the United States Food and Drug Administration (FDA).

166. **Related or Possibly Related to Participation in Research**: There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

167. **Report:** An occurrence or allegation of noncompliance or unanticipated problem involving risks to subjects or others. Reports may or may not require further information to confirm or deny.

168. **Repository**: a common site for storage of collections of human biologic specimens available for study. This may be one geographic location or may be a virtual aggregation of biologic specimens from many locations. Repositories are also referred to as tissue banks, collections, resources, inventories, or by other terms. Repository activities involve three components: (i) the **collectors** of tissue samples; (ii) the **repository** storage and data management center; and (iii) the **recipient** investigators. Repositories may or may not have identifiable information linked to the specimen.

169. **Representative**: Defined by Indiana State Law, Article 36, Medical Consent, Chapter 1, Health Care Consent, as an individual appointed to consent to health care of another

Section II – Applicable SOP Definitions

170. **Research**: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge (as defined in 45 CFR 46.102d). Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities (45 CFR 46.l02(d)). FDA includes in its definition of a research activity, any experiment that involves a test article and one or more human subjects and that either meets requirements for prior submission to the FDA or the results of which are intended for a research or marketing permit.

171. **Research Certificates of Confidentiality:** In situations where the Investigator requires protection of research of a sensitive nature, the principal investigator can apply to the Department of Health and Human Services to protect this information under a Certificate of Confidentiality. This certificate allows a researcher to protect the privacy of research subjects by withholding from all persons not connected with the research team the names and other identifying information relating to research subjects. The protection will be granted only when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives. Examples include research relating to sexual attitudes, preferences, or practices, the use of alcohol, drugs, or other addictive products, pertaining to illegal conduct or to an individual's psychological well being or mental health, genetic information, information that, if released, could be damaging to an individual's financial standing, employability, or reputation, and information that would normally be recorded in a patient's medical record that, if released, could lead to social stigmatization or discrimination. Researchers may receive a Certificate of Confidentiality regardless of funding source. Researchers who receive a certificate may not be compelled by Federal, State, or local legal processes or subpoenas to disclose information that they possess as a consequence of the research.

172. **Research Compliance Administration (RCA):** A department within Research and Sponsored Programs on the IUPUI campus responsible for providing administrative support to the IUPUI/Clarian Institutional Review Boards (IRBs).

173. **Research Documents**: All records, in any form, (including, but not limited to, written, electronic, magnetic, audio-visual, and optical records and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a study and the actions taken.

174. **Research Oversight Plan:** The detailed map for oversight for a research study, for example, 1.) what will be examined to assure subject well-being; 2.) the rationale of the plan; 3.) who will provide oversight; 4.) when will oversight be done; 5.) who will be informed of oversight results; 6.) what will be done with the findings; 7.) overall risk assessment and rationale; 8.) data to be reviewed by and acted upon by the research area; 9.) composition of oversight committee and method of reporting; and 10.) criteria for stopping the study, unbinding, removing subjects, etc. If the oversight plan is contained within the protocol, this can be referenced.

175. **Research Team:** Any team member (e.g. other faculty, student, resident, lab staff, study coordinator or other) who helps design and conduct the research project or clinical investigation4.2.

176. **Residual Clinical/Diagnostic Specimens:** Specimens obtained for routine patient care that would have been discarded if not used for research.

177. **Retrospective Study:** Studies that utilize existing biological samples that have already been collected when the IRB request for approval is made or for which there is no plan to recontact donors in order to obtain additional new information/data. This may refer to biological samples collected for clinical indications and then stored (i.e. pathology specimens, left over sera, etc.) or a

secondary use of biological samples collected previously for another research protocol (i.e. "leftover" sera from a research study or material in a tissue bank).

178. **Reviews Preparatory to Research**: Reviews of PHI conducted by and within a covered entity to allow analysis of the feasibility of conducting a study or the potential number of patients with a disease "X" for inclusion in a grant proposal. These do not usually require IRB approval, as they are not intended to provide generalizable knowledge nor do they identify individuals for the purpose of recruitment4.13.

179. **Risk**: The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study.

180. **Risk Assessment:** The thoughtful cataloging and consideration of factors that could contribute to an unwanted or negative effect in a research study.

181. **Royalties:** In general, the Indiana University Intellectual Property Policy requires all intellectual property developed while a faculty member is at Indiana University be filed through the technology transfer office.

182. **Sample:** In the context of this policy, a sample refers to any human biological material. This includes, but is not limited to, molecular material such as DNA, cells, tissues (blood, bone, muscle, etc.), organs (liver, bladder, heart, etc.), gametes, embryos, fetal tissue, waste (hair, nail clippings, urine, feces, etc.) and other materials of human origin.

183. **Scheduled Audit**: An audit conducted as part of the research compliance audit plan and schedule; an audit not due to a specific request as defined under "for-cause audit."

184. **Screen Failure:** Process by which a consented subject is found to be ineligible for a research study as a result of the screening process.

185. **Screening:** Process by which a subject is consented to undergo procedures or testing to determine eligibility for a research project.

186. **Secretary:** The Secretary of the Department of Health and Human Services (DHHS) and any other officer or employee of the DHHS to whom authority has been delegated.

187. **Security Plan:** A document that describes the security measures and processes within the local environment that are used to safeguard the confidentiality, integrity and availability of research data. A plan typically identifies data inputs, explains the locations of collections of data and the type of data collected. This is typically accompanied by a data flow diagram. In addition, a plan explains the security controls used to protect the data.

188. **Serious Adverse Event**: Any adverse event that results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurred) results in inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

189. **Serious Noncompliance**: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal or state regulations, requirements of VHA Handbook 1200.5, or institutional policies governing human subjects research or the requirements or determinations of the IRB that increases the risks to subjects,

decreases potential benefits to subjects, adversely affects the rights and welfare of subjects, or compromises the integrity or validity of the research. Examples of serious noncompliance include, but are not limited to, conducting human subjects research without appropriate IRB approval, enrollment of research subjects while study approval has lapsed, etc.

190. **Significant equity interest in the sponsor of a covered study:** Ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices (generally, interests in a nonpublicly trade corporation), or any equity interest in a publicly traded corporation that exceeds $50,000 during the time the clinical investigator is carrying out the study and for 1 year following completion of the study.

191. **Significant Financial Interest**:: A "financial interest" is a "significant financial interest" if at the present time or over the next 12 months, and when aggregated for the individual and his/her immediate family member meets one of the following tests:

    a. the ownership interest (equity or stock options) values $10,000 or more when referenced to publicly traded prices or other reasonable measuress of fair market value;

    b. the ownership interest values five percent (5%) or more in any one enterprise or entity; or;

    c. the ownership interest relates to an investigator's medical/clinical research, in which case an interest in ANY amount must be considered significant.

    In other words, if an ownership interest is either worth $10,000 or more or constitutes at least 5% of the ownership in the entity, it is a disclosable interest; except for researchers engaged in medical/clinical research, in which case ANY amount must be disclosed when it is received from or represents ownership in an entity related to the investigator's field of research.

192. **Significant payments of other sorts:** Payments made by the sponsor of a covered study to the investigator or the institution to support activities of the investigator that have a monetary value of more than $25,000, exclusive of the costs of conducting the clinical study or other clinical studies, (e.g. a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria) during the time the clinical investigator is carrying out the study and for 1 year following the completion of the study.

193. **SOPs (Standard Operating Procedures):** (at IUPUI/Clarian) Documents that define in detail the underlying policies and the procedures for activities involved in the conduct of research involving human subjects.

194. **Source Documents:** Original records pertaining to a clinical trial, including hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries, questionnaires, or evaluation checklists, audio and/or video tapes, interview transcripts, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, at the laboratories, and at medico-technical departments.

195. **Sponsor:** Usually a device company or other entity that is paying for the study, and/or supporting, and/or sponsoring (filing) the IDE. **Sponsor:** An individual, company, institution or organization that takes responsibility for the initiation, management and/or financing of a clinical trial. The Sponsor does not conduct the investigation (i.e. test article administration or dispensing, use).

Usually a pharmaceutical company or other entity that is paying for the study, and/or supporting, and/or sponsoring (filing) the IND.

196. **Sponsor/Investigator:** An individual who both initiates and actually conducts alone or with others, a clinical investigation (i.e. under whose immediate direction the test article is administered or dispensed/used).

197. **Sponsored email:** An email account established for a non-IU employee for a specific purpose, with limited duration, and with the supervision (sponsorship) of an authorized University employee.

198. **Student:** Any individual enrolled for educational credit, including both formal lecture and seminar classes, clinical role courses, independent study courses, and thesis or dissertation projects.

199. **Study Site:** The location where any study-related interactions or interventions occur, including the consent process.

200. **Subsequent Use**: A second use of a test article with the same or another subject. Subsequent use of a test article at an institution is subject to IRB review and approval.

201. **Suspension**: Temporary cessation of some or all activities in a currently approved research study.

202. **Termination**: For purposes of this SOP, this term refers to a determination made by the IRB to permanently withdraw approval for some or all activities of a currently approved research study.

203. **Test Article:** Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under §351 or 354-360F of the Public Health Service Act.

204. **Transitional Device**: A device that the FDA considered to be a new drug or antibiotic before May 28, 1976.

205. **Unanticipated Adverse Device Effect**: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

206. **Unanticipated Problem:** In general, includes any incident, experience, or outcome that meets all of the following criteria:

    a. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

    b. related or possibly related to participation in the research (in this SOP, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

    c. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

207. **Unapproved Medical Device**: A device that is used for a purpose or condition for which the device requires, but does not have, an approved application. An unapproved device may be used in human

subjects only if it is approved for clinical testing under an approved application for an investigational device exemption (IDE).

208. **Unexpected Adverse Event:** Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is **not** consistent with either:

    a. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, summary safeguard statement, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

    b. the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

209. **Viable:** As it pertains to the neonate, it means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

210. **Vulnerable Subjects:** Persons not capable (e.g. mentally, emotionally, or physically impaired) of appropriately judging the risks/benefits of their participation in a research study. Also, individuals with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, refugees, children, persons with developmental disabilities or mental retardation or mental illness, pregnant women, and those incapable of giving consent or whose capacity for giving informed consent is limited. Other vulnerable persons may include individuals whose willingness to volunteer in a research project may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response in case of refusal to participate. Examples include students, subordinate hospital personnel, employees of a company, members of the armed forces, and persons in detention (prisoners.)

211. **Waiver of Authorization:** HIPAA permits waivers of authorization when an Institutional Review Board (IRB) reviews the request according to the required criteria. This review and approval of waiver of authorization requests must be documented. For details, see the Confidentiality and Privacy SOP.

212. **Ward:** A child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law.

Section III – Applicable Regulations and Guidance

1. Department of Health and Human Services (HHS)

a. 45 CFR 46 – Protection of Human Subjects

b. OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, Jan 15 2007

c. 45 CFR 160 & 164 – Standards for Privacy of Individually Identifiable Health Information; Final Rule, Aug 14 2002

d. 45 CFR 162 – Administrative Data Standards and Related Requirements

e. OPRR Guidance – Issues to Consider in the Research Use of Stored Data or Tissues, Nov 7 1997

f. HHS Clinical Research and the HIPAA Privacy Rule, Feb 2004

g. HHS Research Repositories, Databases, and the HIPAA Privacy Rule, Jan 2004

h. OHRP FAQs, Research with Children

i. OHRP Policy Guidance – Informed Consent

j. OHRP Policy Guidance – Informed Consent FAQs

k. OHRP Policy Guidance – Guidance on Research Involving Coded Private Information or Biological Specimens, Aug 10 2004

l. OHRP Policy Guidance – Guidance on the Involvement of Prisoners in Research

m. CMS Security Standard

2. Food and Drug Administration (FDA)

a. 21 CFR 11 – Electronic Records, Electronic Signatures

b. 21 CFR 50 – Protection of Human Subjects

c. 21 CFR 54 – Financial Disclosure by Clinical Investigators

d. 21 CFR 56 – Institutional Review Boards

e. 21 CFR 312 – Investigational New Drug Application

f. 21 CFR 600 – Biological Products

g. 21 CFR 812 – Investigational Device Exemptions

h. 21 CFR 814 – Premarket Approval of Medical Devices

i. 21 CFR 814, Subpart H – Humanitarian Use Devices

j. Comparison of FDA and HHS Human Subject Protection Regulations

k. FDA Information Sheet Guidance – Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors

l. FDA Information Sheet Guidance – Guidance for IRBs, Clinical Investigators, and Sponsors, FDA Inspections of Clinical Investigators, Jan 2006

Section III – Applicable Regulations and Guidance

m. FDA Information Sheets, Guidance for Institutional Review Boards and Clinical Investigators – "Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices, 1998 Update

n. FDA Information Sheets, Guidance for Institutional Review Boards and Clinical Investigators – Medical Devices, 1998 Update

o. FDA Guidance for Industry and FDA Staff – Humanitarian Device Exemption (HDE) Regulation, Jul 18 2006

p. FDA Guidance for Industry – Medical Device Reporting, Alternative Summary Reporting (ASR) Program, Oct 19 2000

q. FDA Center for Devices and Radiological Health (CDRH)

3. National Institutions of Health (NIH)

a. NIH OER Conflict of Interest

b. NIH OER Data Sharing Policy and Implementation Guidance, Mar 5 2003

c. NIH OER Human Subjects Website: FAQs – Data and Safety Monitoring Policy Links

d. NIH OER Certificates of Confidentiality

e. NIH NHLBI Guidelines for Human Tissue Repository, Apr 14 2000

4. Indiana Code (IC)

a. Indiana Code (IC) 4-1-6 – Requests for access to confidential records; improper disclosure; actions

b. Indiana Code (IC) 4-1-10 – Release of Social Security Number

c. Indiana Code (IC) 4-1-11 – Notice of Security Breach

d. Indiana Code (IC) 5-14-3-4 – Records excepted from disclosure requirements; names and addresses; time limitations; destruction of records

e. Indiana Code (IC) 24-4-14 – Persons Holding a Customer's Personal Information

f. 210 IAC 1-6-7 – Research purposes; request for access to information

5. Department of Education – Protection of Human Subjects in Research

6. Federal Bureau of Prisons, Apply to Conduct Research

7. Department of Defense

a. 32 CFR 219 – Protection of Human Subjects

b. National Industrial Security Program Operating Manual (NISPOM)

8. Department of Veterans Affairs

a. 38 CFR 16 – Protection of Human Subjects

b. VHA Handbook 1200.1 – The Research & Development (R&D) Committee Handbook, Mar 2 2007

Section III – Applicable Regulations and Guidance

c. VHA Handbook 1200.5 – Requirements for the Protection of Human Subjects in Research, Jul 15 2003

9. International Conference on Harmonization (ICH)

a. International Conference on Harmonization (ICH) Website

b. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, Apr 1996

10. National Cancer Institute (NCI)

a. Policy of the National Cancer Institute for Data and Safety Monitoring of Clinical Trials, Jun 22 1999

b. NCI Central IRB Initiative

11. The Belmont Report

12. NBAC Report on Research Involving Human Biological Materials: Ethical Issues and Policy Guidance Executive Summary

13. **Humanitarian Use Devices – A Brief Guide for Clinicians, Investigators, and IRB Members,** Dale E. Hammerschmidt, MD, University of Minnesota, Oct 2001

Section IV – Institutional Policies and Guidance

1. Checklist to Determine if you are a Covered Entity or are Involving a Covered Entity as Part of Your Research, Aug 03
2. HIPAA Information Related to Research
3. Indiana University Academic Handbook, Aug 2005
4. Indiana University Policy on Financial Conflicts of Interest in Research, Mar 3, 2006
5. IRB Instruction Packet
6. Exempt Research Checklist
7. Expedited Research Checklist
8. Federalwide Assurances (FWAs)
9. Guidelines for Determining and Amendment Type
10. Protection of Human Subjects in Research – Certifications, Course, and Test
11. IU General Clinical Research Center (GCRC)
12. Indiana University Information Technology (IT) Policies
13. IU School of Medicine, IT and Technology Management Security Policies, Procedures, and Standards
14. IU Information Technology Policy Office, Best Practices for Handling Electronic Institutional and Personal Information
15. IU Information Technology Security Office (ITSO), Best Practices for Securing IT Resources
16. Human Safety in Clinical Research, Applied Clinical Trials, Michael J. Schmidt, Jul 2001
17. Indiana Laws Affecting Research
18. Checklist for Determining Whether an Activity Requires Review by the IRB
19. Prompt Reporting Form
20. Office of Clinical Research

Section V – Appendices

IUPUI Standard Operating Procedures

Section V – Appendices

Appendix A – 21 CFR 11 Self Assessment Tool for Research Protocols

Date:

Principal Investigator:

Protocol:

Will the study be considered FDA regulated?

☐ **NO (**If **NO, STOP** here. If not sure, go on**.)**

☐ YES. If **YES**, who will hold the IND or IDE?

☐ **External Sponsor, Name:**

☐ **Internal Investigator, Name:**

FDA 21 CFR Part 11 applies to **records in electronic form** that are retrieved, created, modified, maintained, archived or transmitted under requirements set for **FDA regulated** studies. It also applies to electronic records submitted to the agency as a part of other application processes, e.g. Investigational New Drug applications. Part 11 does not apply to paper records when the source data (the original or first place in which information is recorded) is in paper form, provided that the paper record is retained for as long as the regulations governing the research require it to be kept. Thus, paper originals that are pertinent to a specific project should be kept. A paper printout of information obtained from an electronic source (e.g. a print out of lab results from a computer) is **not** the source document. Rather, the "source" is the computer system from which it was obtained – to which Part 11 likely applies.

Each research study may use electronic data in different ways; therefore, in order to assist in determining regulatory requirements for each research study, it is important to determine which electronic systems will be utilized to access, transmit or store **source** data.

FOR THE PROTOCOL CITED ABOVE, DETERMINE THE FOLLOWING:

A. Will you use patient care (clinical*) data in the conduct of this research project?
** information generated as a part of routine patient care that may be useful or needed for study-specific purposes*

Section V – Appendices

Appendix A – 21 CFR 11 Self Assessment Tool for Research Protocols

☐ YES ☐ NO

If **YES,** which ones:

1. CLOSED SYSTEMS - check all that apply

> *Definition: Research team does not enter data directly into the system and does not have authority to directly alter or change data, e.g. lab results.*
>
> Reasons why researchers may access these systems include: to access lab results, x-ray finding, other test results, or observations for determining eligibility, adverse events, confirm dosing, case report form completion, etc.

☐ a) Careweb (Clarian)

☐ b) Regenstrief Medical Record System (RMRS) (Wishard)

☐ c) CPRS (VA)

☐ d) Wishard Pharmacy (Comcotech – outpatient; HMM – inpatient)

☐ e) Other, please specify:

2. OPEN SYSTEMS - check all that apply

> *Definition: Various members of the research team may have access to the system/ database and may directly enter data, adjust, or change items or delete data.*

☐ a) Careweb (Clarian) *Provide examples of records:*

☐ b) Regenstrief Medical Record System (RMRS/Wishard) *Provide examples of records:*

☐ c) CPRS (VA)

☐ d) Departmental/Division/Research Area database
Please specify where housed and who is responsible for determining access:

☐ e) Investigator database
Please specify where housed and who is responsible for determining access:

☐ f) Other, Please specify name, where housed and who is responsible for determining access:

Section V – Appendices

Appendix A – 21 CFR 11 Self Assessment Tool for Research Protocols

3. HYBRID SYSTEMS check all that apply

Definition: Members of the research team may be involved in generating the original data that is subsequently added to the one of the patient care systems mentioned above, but are not able to provide direct data entry. *For example, dictation of an X-ray result that is subsequently entered into Careweb by someone else, interpretation of a bone marrow biopsy result that is subsequently entered into Careweb by someone else, dictation of physical exam or clinic note that is subsequently entered into CPRS or RMRS by someone else.*

☐ a) Clarian (Careweb) *Provide examples of records:*

☐ b) Regenstrief Medical Record System (RMRS/Wishard) *Provide examples of records:*

☐ c) CPRS (VA)

☐ d) Other, Please specify name, where housed and who is responsible for determining access:

B. Will you use <u>Study specific (research*)</u> data?
** information generated specifically for research related purposes*

☐ YES ☐ NO

If **YES**, check which databases/electronic records/sources below are (a) utilized specifically for this research protocol or (b) generated by study interventions for which the <u>originals</u> are not available in paper format. This would be data that is not generated solely for routine patient care purposes and therefore is data for which the research team is responsible.

1) Investigational pharmacy ☐ Yes ☐ No

If **YES**, indicate which one(s):

☐ Comcotech or HMM (Wishard outpatient/inpatient pharmacy systems)
☐ CPRS (VA)

Note: Clarian Investigational Pharmacy uses exclusively paper records and therefore is not subject to FDA Part 11 regulations

2) General Clinical Research Center (GCRC) ☐ Yes ☐ No

Section V – Appendices

Appendix A – 21 CFR 11 Self Assessment Tool for Research Protocols

If **YES**, check all data in electronic form that apply:
- ☐ Laboratory results
- ☐ Blood pressure readings
- ☐ Other:

3) Sponsor-provided system ☐ Yes ☐ No

If **YES**, check all that apply:

☐ a) Hardware and software provided by the sponsor and data is stored on the hardware until sponsor comes to physically retrieve it, e.g. laptop or PDA

☐ b) Hardware and/or software provided by the sponsor and data is transmitted electronically (via internet) to the sponsor, e.g. laptop

☐ c) Sponsor wants to load their software onto IU/VA/Clarian/Wishard hardware or electronic systems for temporary data storage and/or electronic transmission to sponsor

- Does the protocol define the system to be used? ☐ Yes ☐ No
  Describe:

- Is your local computer support staff aware of this? ☐ Yes ☐ No

Suggest consulting IUPUI/Clarian SOP for Security of Research Data.

4) Any other database or computer files that are <u>specific</u> to the researcher, his/her department or therapeutic area. ☐ Yes ☐ No

If **YES,** describe data that is collected and systems utilized.

1) For source data:
2) Data collection instruments (not originated by sponsor outside IUPUI):
3) Data analysis and record:

C. For each of the systems in B.4 (above) a <u>Security Plan</u> must be developed.

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Appendix B – Assessing Safety/Risk for Research Involving Human Subjects Guidelines for Investigators and the IRB

Assessing Risk in Social Science/Behavioral Research:

Although behavioral/social science research does not usually involve risks to a person's health or physical well being, there are other risks which must be considered by the researcher and IRB.

Breach of Confidentiality: This is often the greatest risk to participants in behavioral and social science research. If confidentiality is not maintained and information from the research becomes known by individuals outside of the research, reputations may be damaged, employment or insurance may be jeopardized, and there may be risk of legal actions (i.e. information about child abuse or illegal activities).

Assessing the kind and level of risk should be determined by context. For example, research regarding political activism in some countries may put subjects in serious jeopardy, while it would not in other countries. Procedures for ensuring confidentiality can help eliminate or reduce the risk of breach of confidentiality.

Risks Resulting from Study Procedures: Psychological stress caused by research questions or procedures is another potential risk in behavioral and social science research. Questions may raise painful memories or unresolved issues, leading to anxiety, fear, confusion, or depression. Questions about at-risk behaviors may cause embarrassment or feelings of guilt. Although most of these risks are minimal and temporary, investigators and IRBs must consider their potential for harm. Psychological support and referrals can be built into studies involving potential psychological risk.

Assessing Risk in Biomedical Research:
(These guidelines were adopted from the GCRC's Research Subject Advocate Group)

Assessing risk to human subjects in biomedical research encompasses risk related to the study design, the potential loss of confidentiality, the subject population, and potential physical, emotional, and psychosocial harms.

Study Design: In evaluating the potential risks related to the study intervention, one must look at the potential for and severity of adverse events. Consideration should be given to the expected frequency and severity of the adverse events, as well as the amount of experience with the study intervention. For example, phase I studies, which are trying to identify the frequency of the adverse events because they are not known would pose a higher risk to subjects.

Loss of Confidentiality: Although loss of confidentiality is undesirable, loss of confidentiality for subjects in genetics studies (i.e. Huntington's disease), studies of stigmatized conditions (i.e. HIV), or studies where loss of confidentiality could lead to social harm pose a higher risk to subjects. Likewise, a study involving known illegal drug users could pose a higher risk since loss of confidentiality could lead to great social harm.

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Subject Population: Participation of vulnerable subjects[4.7] (minors, prisoners, mentally handicapped, etc.) also poses a greater risk. However, normal volunteer populations should also be considered carefully since any intervention poses greater risk than would be experienced by subjects not participating in the study.

Physical, Emotional, and Psychosocial Harms: A genetics study which might lead to a diagnosis or identification of a predisposition for a serious disease would pose increased risk for study participants.

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Appendix C – COI Policy for IRB Members and Consultants

Policy Basis: Federal regulations prohibit a member of the Institutional Review Board (IRB) from participating in the initial or continuing review of any research project in which the member has a "conflicting interest," except to provide information at the IRB's request. [45 CFR 46.107(e)]

Policy: IRB members must disclose any conflicts of interest associated with a research project and must leave the room prior to the discussion of the project and the related vote, except if the member is providing information at the IRB's request. This conflict will be noted on the meeting agenda or the member must disclose the conflict prior to discussion of the research project. The meeting minutes will document the recusal (*i.e.*, the temporary absence of the IRB member during the deliberation and vote on the project with respect to which the member has a conflict).

In the case of expedited IRB review (outside of a convened meeting, by a designated reviewer), the reviewer should disclose any conflicting interest in a project in advance to the IRB Office and should not review the project.

Policy Guidance

1. To whom does this policy apply?

It applies to all members of the IUPUI/Clarian IRBs and to *ad hoc* reviewers (consultants), who are not IRB members but sometimes are asked to review a research project because of their expertise (collectively, "members").

2. What is a "conflicting interest"?

Generally, a conflicting interest includes (1) participation in the project; (2) a financial interest as defined below; and/or (3) any other examples referenced below. A conflict may arise because of an interest of the member or his/her family; the aggregate interest of the IRB member and family is considered.

Conflicting interest

1. **Participation in the project:** For purposes of this policy, generally means the member is listed on the protocol/project, or will be included (or reasonably may be expected under academic standards to be included) as a co-author on a publication of the project's results. This would include individuals or immediate family involved in the design, conduct, or reporting of the research.

   Participation in the project *excludes* serving as a member of the IRB or the data monitoring board overseeing the project.

2. The following **financial interests** will be considered conflicting interests unless covered under the listed exclusions:

   2.1. An ownership interest (equity or stock options) of $10,000 or greater value when referenced to publicly traded prices or other measure of fair market value or whose value represents 5% or more interest in any one enterprise or entity (equity in a privately held entity for which the

value is not known will be treated as above the 5% threshold), when aggregated for the IRB member (or ad hoc reviewer) and his or her immediate family;

2.2. Salary, royalties, or other payments of $10,000 or more in the past year, when aggregated for the IRB member (or ad hoc reviewer) and his or her immediate family.

2.3. Compensation to the Academic Appointee or Staff Member and his or her Family Members of any amount that could be higher for a favorable outcome than for an unfavorable outcome, such as compensation that is explicitly greater for a favorable result or compensation to the investigator in the form of an equity interest in the sponsor of a covered study or in the form of compensation tied to sales of the product, such as a royalty interest.

2.4. Proprietary or other financial interest by the Academic Appointee or Staff Member and his or her Family Members in the product to be used in clinical trials including, but not limited to, a patent, trademark, copyright or licensing agreement.

2.5. Fiduciary, director, board, or executive position of the Academic Appointee or Staff Member and his or her Family Members in any enterprise or entity regardless of whether the position is compensated

2.6. Exclusions:

2.6.1. Receipt of royalties from licensed University technology when no further related research, teaching or service activities will be pursued within the University by the individual.

2.6.2. Salary or other remuneration from Indiana University.

2.6.3. Income from seminars, lectures, or other educational activities sponsored by not-for-profit entities;

2.6.4. Income from service on advisory committees or review panels for governmental or not-for-profit entities; or

2.6.5. Any financial interest arising solely by means of investment in a mutual, pension, or other institutional investment fund over the management and investments of which the member of the University community does not exercise control.

2.6.6. Receipt of royalties or honoraria for published scholarly works, commissioned papers, and occasional lectures.

2.6.7. Serving as a consultant to a domestic government agency

2.6.8. Income received from a private practice plan recognized by the IU School of Medicine.

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Appendix C – COI Policy for IRB Members and Consultants

3. Other examples of conflicting interests include but are not limited to:

a. Having certain non-financial interests that may raise a real or perceived conflict. These will depend on the circumstances. They may include, for example, having direct supervision over the investigator conducting the project, or participating in a separate project on Technology that may directly compete with the Technology in the project under review.

b. For clarification: (i) a department chair ordinarily does not have a conflict simply by virtue of that position; a conflict could arise, though, if the chair had a closer, direct supervisory relationship over a department researcher; (ii) if a junior person in an IRB member's research group submits a protocol, the IRB member has a conflict and cannot review the protocol.

c. Any real or perceived conflict, or a concern that there may be a real or perceived conflict, that is not addressed above should be raised with the IRB Chair. If the IRB Chair determines there is a conflicting interest, then the member shall recuse himself or herself. The IRB Chair reserves the right to request recusal as appropriate in any particular circumstances.

4. How and when should an IRB member disclose a potential conflicting interest?

a. When IRB members receive materials before a meeting, they should review the list of projects for initial or continuing review with this issue of conflicts in mind and should disclose any potential issue to the Chair in advance of the meeting when possible. At the beginning of each IRB meeting, members also will be reminded of the conflicts policy and should disclose any potential conflict at that time.

b. A designated IRB reviewer performing expedited review of projects similarly should review the list of projects and disclose any potential issue in advance to the RCA Office (see **Policy** section above).

c. The IRB Chair will remind the IRB members of the importance of this conflicts policy at least annually and more often as necessary.

d. The Director of the IRBs will request that all IRB Chairs disclose potential conflicting interests annually in writing.

e. Ad hoc reviewers will receive a copy of this policy with materials for the project they are reviewing.

5. What other issues should be considered?

a. **Senior positions of responsibility:** It is expected that individuals with greater responsibilities for reviewing human subjects research may have potentially more influence over the review and approval of a project and thus should be particularly sensitive to any perceived or real conflicting interest. Accordingly, IRB Chairs and research administrators or institutional officials with research oversight authority who are involved in reviewing a project or projects should disclose

any potential conflicting interest to the appropriate supervisor; such disclosure may require additional institutional review.

b. **IUPUI/Clarian projects:** An IRB member may not consult for a Business to assist it in shepherding a project through the IRB process when the project will be performed within IUPUI/Clarian.

6. Definitions

a. **Business** means any corporation, partnership, sole proprietorship, firm, franchise, association, organization, holding company, joint stock company, receivership, business or real estate trust, or any other legal entity organized for profit or charitable purposes, but excluding the University, any affiliated Hospital, any Private Medical Practice, or any other entity controlled by, controlling, or under common control with the University or an affiliated Hospital.

b. **Clinical Research** means any research or procedure involving human subjects in vivo or the use of human samples for the development and evaluation of patient therapies such as diagnostic tests, drug therapies, or medical devices. It includes early clinical studies, evaluative research, epidemiological studies and clinical trials. It does not include a Faculty Member's participation in the design of a clinical study for which he/she is subsequently neither a participant nor an author.

c. **Executive Position** refers to any position which includes responsibilities for a material segment of the operation or management of a Business.

d. **Participate** means to be part of the described activity in any capacity, including but not limited to serving as the principal investigator, co-investigator, research collaborator or provider of direct patient care. The term is not intended to apply to individuals who provide primarily technical support or who are purely advisory, with no direct access to the data (e.g., control over its collection or analysis) or, in the case of clinical research, to the trial participants, unless they are in a position to influence the study's results or have privileged information as to the outcome.

e. **Private Medical Practice** means the professional services rendered by a physician, including departmental practice plans, and the procedures integral to those services.

f. **Technology** means any compound, drug, device, diagnostic, medical or surgical procedure intended for use in health care or health care delivery.

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Appendix D – Data Documentation Suggestions

1. Record the date of the subject's entry into the study, protocol /site or center number, and subject number (when appropriate).

2. Record the demographic and contact information about the research subject.

3. If applicable, note in the subject's enrollment record or medical chart that the protocol was explained to the patient, that his/her questions were answered and that written informed consent was obtained. The consent form should be dated and signed by subject (or subject's representative), and a witness (the person who conducted the informed consent discussion).

4. Provide evidence that the subject met the study's inclusion criteria and fulfilled none of the exclusion criteria.

5. If applicable, record any current medications and medications discontinued within the last month (or longer, as specified by the protocol).

6. Record subject's diagnosis or status prior to treatment, including documentation of medical, social or psychological history, as appropriate, particularly if relevant for the disease or condition being treated.

7. Maintain study drug dispensing logs and administration records.

8. Record the dates and the results of evaluations and procedures required by the study(i.e. physicals, therapy, interviews, lab results, x-rays, pathology reports, consultations, correspondence, all diagnostic test results, and pre-existing conditions).

9. Note any changes from the protocol and provide an explanation.

10. Record any reported events that required prompt reporting to the IRB that occurred during the treatment period and for a period specified by the sponsor or protocol following the last treatment or intervention.

11. Document telephone contacts with the subjects, regulatory staff and sponsors.

12. Record subject's condition during and/or after a study treatment, intervention or study visit.

13. Document final disposition of the subject and subject status at time of study termination.

14. Maintain a visit log if more than one study visit is required to keep track of missed appointments, procedures, interventions, etc.

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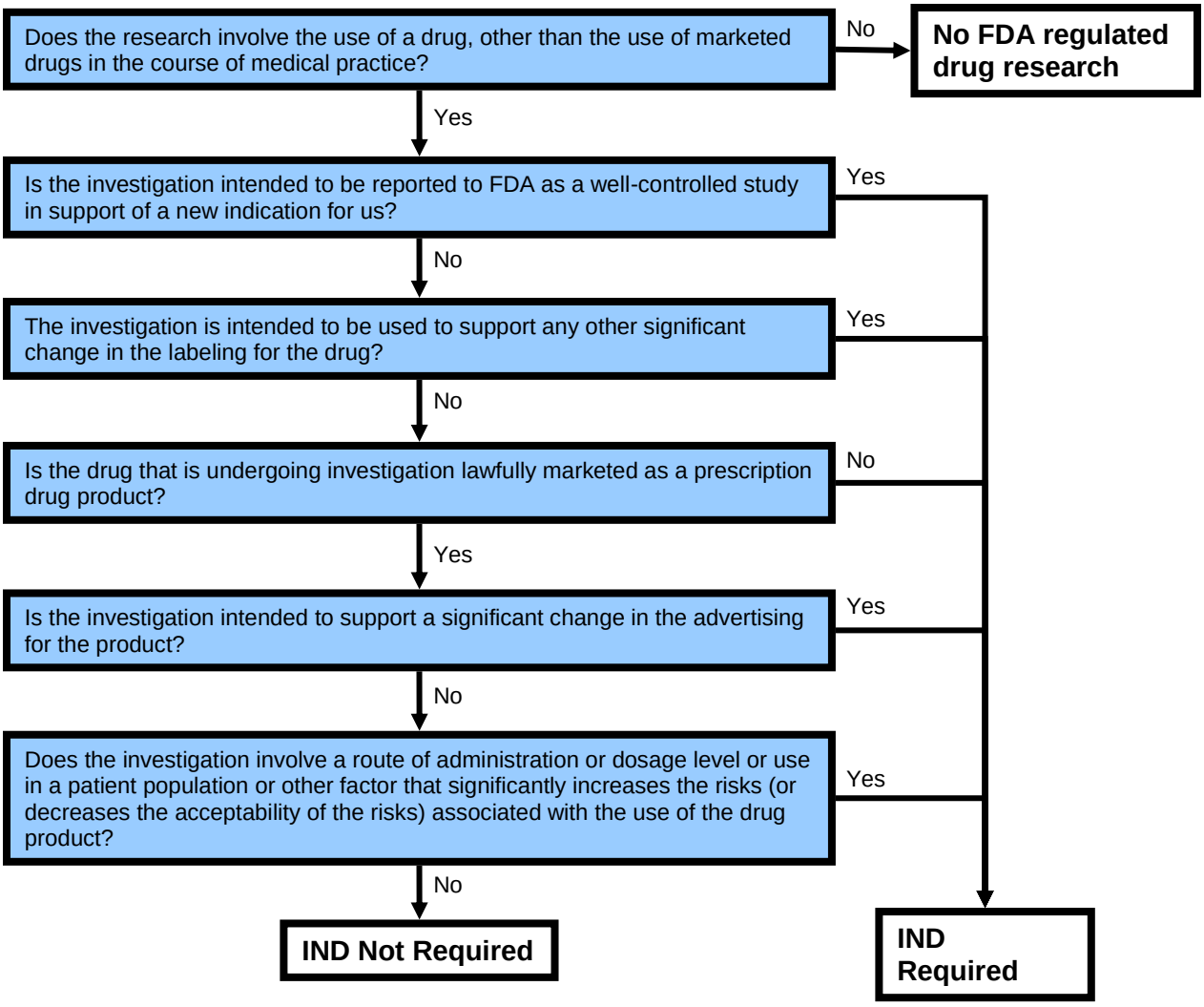
Appendix E – Determining if an IND is Required



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Appendix F – Elements of a Security Plan

This list outlines the elements that should be included in a Security Plan document. Each research project should have a security plan. If all research data are managed at the department level, a single department plan that covers all research projects could be created that would be appropriate.

1. **TECHNOLOGY ENVIRONMENT**
   a. Identify all hardware where research data are stored or accessed
      - Make
      - Model
      - Hard Drive size
      - Memory
      - Operating System
   b. Identify the locations of all servers or workstations storing research data
      - Buildings
      - Room Numbers
      - Access – is the room locked and who has access
   c. Identify software used to store research data (Oracle, SQL Server, Excel, etc.)
   d. Identify any special software used as part of this research project
   e. Identify the technologies used for remote access to the data
      - Vendor tools
      - Authentication Process

2. **DATA MANAGEMENT and STAFF ACCESS**
   a. Identify all research team members who have access to the data
      - Name and Title
      - Department
      - Other Affiliation if not a faculty or staff member of IU
      - Role (e.g. all functions, read only, new data entry, modify existing data)
   b. Identify who decides which people get access to which data
   c. Describe the process for managing data access generated as part of the research project
   d. List any classes of data for which there is restricted access within the team
   e. Describe the process by which authorization for access to all the data, or specific classes of data, is granted
      - IU team members
      - Non-IU team members
   f. Describe the process for terminating access
   g. Describe the audit process for documenting access to the data
   h. Describe the process for authorizing access to data generated by other parties
   i. Describe what data are fed into the database from other systems (either through an automatic interface, or downloaded from one system and uploaded in to the research database)

3. **BACKUP/RECOVERY/RETENTION**
   a. Describe the Backup and Recovery process for electronic data
      - Backup technologies

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Appendix F – Elements of a Security Plan

- Backup frequency
- Recovery testing process and frequency
- Identify where backup data is stored (e.g. onsite, offsite)

b. Describe the backup and recovery process for paper-based data
- Backup technologies
- Backup frequency
- Recovery testing process and frequency
- Identify where backup data is stored (e.g. onsite, offsite)

c. Describe the long-term archival for data once a research project has concluded
- Location of archived materials
- Retention period
- Location of inventory record of archived materials
- Location of contracts from third-party storing archived materials

4. **DATA PROTECTION**

a. Describe the process for keeping servers and workstations updated with the most current anti-virus software.
- Software used
- Scanning frequency

b. Describe process for protecting data stored on mobile devices (laptops, tablets, PDAs)

c. Identify where removable media (diskettes, CDs, zip cartridges, removable drives, audio or video tapes) are stored when not in use

d. Identify where printed data are securely stored

e. Describe the protections in place to secure information sent by email

f. Describe the process for logging and tracking data (in any form) that is being moved to a different location

g. Describe the process for secure disposal of data from:
- Hard drive
- Removable media
- Tape
- Print

A sample plan is available upon request from the Information Services and Technology Management (ISTM) unit. If an individual or department needs assistance with the development of a plan, they should contact the ISTM Help Desk at 274-5336 or iusmot@iupui.edu

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Appendix G – Guidelines for Researchers Using Electronic Data in FDA-Regulated Research

A guide for analysis of risk and compliance with FDA 21 CFR Part 11 Regulations (v11-12-04)

INTRODUCTION:

Conducting research involves proper data management, including security of that research data. The integrity of the research can be compromised if the data itself is from an erroneous source, an error occurs during data entry, or if the data that is collected is stored in a manner in which it may be lost, falsely manipulated or compromised. Appropriate security safeguards must be in place to ensure data integrity.

There are two regulations that govern the oversight of electronic research data:

- Food and Drug Administration Regulation, 21CFR Part 11 (*Part 11*) addresses data validity, integrity, and security in human subjects research,

- Health Insurance Portability and Accountability Act (*HIPAA*) addresses security and privacy of protected health information, including that used in human subjects research.

FDA Part 11 was published in final form in March 1997 and went into effect August 20, 1997. Part 11 applies to all FDA program areas and provides criteria for the acceptable use of electronic records and signatures. The FDA has issued numerous guidance documents to assist with interpretation and application of the regulation with the most recent having been published in August 2003. Studies under the jurisdiction of the FDA include all industry sponsored research from pharmaceutical, biological, and device companies, FDA sponsored studies, and all investigator-initiated studies where the Investigator holds the Investigational New Drug (IND) or Investigational Device Exemption (IDE). It is estimated that there are approximately 1500 such studies on the IUPUI campus.

Part 11 and HIPAA have a number of similarities and complimentary requirements; however, the rules do differ in scope and applicability. Briefly, the primary objective of the security component of HIPAA is to ensure that protected health information (patient care data) is securely stored and transmitted. The regulation does not address the accuracy of the information being stored or transmitted. In contrast, the primary objective of FDA Part 11 is to ensure the integrity of research data, and thus the security and authenticity of that data. While there is considerable overlap within some aspects of the two regulations, it is possible that researchers conducting human subjects research may need to implement one rule's requirements but not the other. To assist in determining whether FDA 21 CFR 11 regulations pertain to his/her research project, the researcher is advised to consult the decision diagram below.

APPLICATION:

- FDA Part 11 **applies** to records (including patient care information) in electronic form that are retrieved, created, modified, maintained, archived, or transmitted under requirements set for FDA regulated studies.

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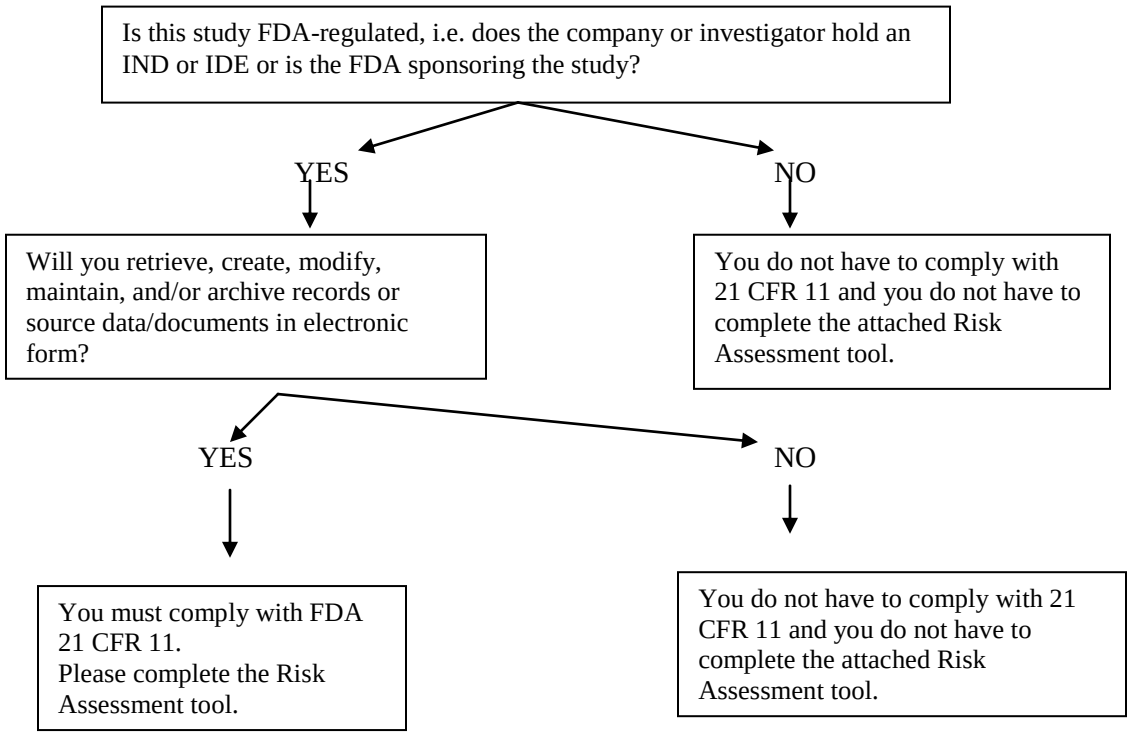
Appendix G – Guidelines for Researchers Using Electronic Data in FDA-Regulated Research

- Part 11 also **applies** to electronic records submitted to the agency as a part of other application processes, e.g. Investigational New Drug applications.
- Part 11 **does not apply** to paper records when the source data (the original or first place in which information is recorded) is in paper form, provided that the paper record is retained for as long as the regulations governing the research require it to be kept. Thus, paper originals that are pertinent to a specific project should be kept.

- **NOTE:** A paper printout of information obtained from an electronic source (e.g. a print out of lab results from a computer) is **not** the source document. Rather, the "source" is the computer system from which it was obtained – to which Part 11 likely applies.

DECISION DIAGRAM - How do you know if you must comply with FDA Part 11?



Examples of records subject to Part 11:

- Original patient care information obtained from or stored in RMRS, CareWeb, VA-CPRS, personal and departmental databases, e.g. lab results

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Appendix G – Guidelines for Researchers Using Electronic Data in FDA-Regulated Research

- Original research related information entered directly into the electronic database of the PI and/or Department. For example, the PI and Research Coordinator type original study notes regarding clinic visits directly into an electronic record or database maintained on the coordinator's hard drive or departmental server.
- Original data imported from RMRS into an electronic database maintained by the PI and or department that also allows for direct data entry by the PI and/or research coordinator. For example: the PI uses this database to store lab data from RMRS and to directly enter and store clinic/study notes. Both sets of records, and thus both electronic systems, are subject to Part 11. RMRS is the "source" for the lab data; while the PI database is the "source" for clinic/study notes.
- Data sent to sponsors via the web. For example, sponsor provides a website for direct data entry and/or provides computer hardware and/or software for direct data capture and transmission to the company.
- The following records sent to the FDA electronically:
    - Investigational drug applications (IND) or New drug applications (NDA)Biologic licensing applications (BLA)
    - Individual post marketing safety reports (ICSR)
    - For a complete list, see: http://www.fda.gov/ohrms/dockets/dockets/92s0251/92s0251.htm

Examples of records NOT subject to Part 11:

- Handwritten clinic notes or handwritten lab analysis results in which the original source (first place recorded) is a paper document and that paper record is retained for as long as regulations and institutional rules require.

IMPORTANT POINTS

- It is important to identify the original **source** of the information used for the study.
- The "source" is the original or first place in which the information is recorded.
- Part 11 does not apply to paper records when the "source" record is in paper form, provided that the paper record is retained for as long as the regulations governing the research require it to be kept.
- If any part of the collection or storage of data used for the study is in electronic form, those electronic records may be subject to Part 11 and sponsors have begun querying researchers as to their FDA Part 11 compliance.
- **In order for you to properly address the concerns of sponsors and the FDA, you must conduct an electronic data risk analysis for each protocol** that you undertake.

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Appendix G – Guidelines for Researchers Using Electronic Data in FDA-Regulated Research

    - In certain research areas, the risk analysis may be identical for all studies; however, in other research areas this may be different for **each** protocol.

- The Indiana University School of Medicine has documentation on file with answers to important questions asked as part of an FDA Part 11 compliance risk assessment program for CareWeb (Clarian), Regenstrief Medical Record System (Wishard), CPRS (VA), Investigational Pharmacy at Wishard Hospital, and General Clinical Research Center (GCRC). A letter that describes what has been done to determine Part 11 risk is available to give sponsors- and can be found on the CTP web page: http://medicine.iupui.edu/ctp/.
    - If these are the only sources of electronic data associated with your study, this compliance information may be sufficient to supply to sponsors or the FDA if requested.
- If you utilize electronic records or databases other than the systems mentioned above, e.g. personal and/or departmental databases, you or your information technology specialist will be required to document FDA Part 11 compliance for those other systems.
- A risk assessment tool is attached to assist you with this process.
    - This tool does not tell you how to respond or how to bring your system into compliance. Therefore, if you do not know how to respond to the questions, this may be an indication that your use of electronic systems is not compliant and you are advised to consult with your local computer support person for assistance.
- Many of the more commonly used "off the shelf" programs (e.g. WORD, EXCEL and ACCESS) typically are **not** Part 11 compliant. If you are using one of these systems in the conduct of a FDA regulated study, you may need to consult with your computer support person for assistance in determining whether, based upon the requirements of Part 11 and your intended use of the electronic system, other arrangements need to be made.
- For additional questions regarding compliance, please contact the School of Medicine Information Technology Office or the School of Medicine Office of Compliance. For non-school of Medicine faculty, please contact your Dean's office for guidance.

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Appendix H – Inspection Readiness Guidance

The purpose of this guidance document is to assist investigators in preparing themselves for an inspection. Investigators, their research teams, departments, or operations supporting research with human subjects may be visited by inspectors from federal regulation agencies*, sponsoring companies**, or the human subjects auditor from the office of Research Compliance Administration***. Most times researchers will be given advanced notice of an upcoming inspection. However, some inspections can occur unannounced. Even though there are no specific regulations for inspections, this document can help investigators to be prepared for such a visit.

See FDA Inspections of Clinical Investigators for additional information on FDA inspections.
See Inspection of the Office of Civil Rights for additional information on HIPAA inspections.

The following suggestions may be used as tools to help you prepare for an **FDA inspection**:

1. An "inspection readiness" binder can be helpful in finding needed documents expeditiously. At a minimum, this binder should include a list of all investigators and their roles, CVs, and documentation of human subjects training and conflict of interest. Ensure appropriate persons are aware of its existence and location. See Appendix AA, Suggested Files for the Regulatory Binder, of the IUPUI/Clarian SOP on Data Management for additional information.

2. If possible, there should be a private room or area identified for the inspector.

3. There should be a person identified as the "inspection host." It is also a good idea to identify additional back-ups in case this person is unavailable.

4. A current organizational chart of the operation with names and titles and including a reporting structure should be available.

5. A brief statement of the purpose/mission of the department and the research interests should be available.

6. Be aware of location of appropriate documents. This could include job descriptions, personnel files, training files, and personnel qualifications.

7. Educate all members of the research team and other appropriate departmental personnel on what to expect during an inspection.

8. Contact the office of Research Compliance Administration for assistance regarding the inspection process.

The following suggestions may be used as tools to help you prepare for an OCR inspection:

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Appendix H – Inspection Readiness Guidance

1. Maintain copies of signed authorizations, IRB waivers of authorization and any additional communication regarding the authorization, waiver of authorization or revocation of authorization.

2. Maintain records of all uses and disclosures of IIHI related to the research study.

3. Be prepared to produce policies and procedures regarding subjects' right to access Individually Identifiable Health Information (IIHI).

4. Maintain policies and procedures regarding the administrative requirements of HIPAA, including implementing data safeguards, communicating to the subjects their right to complain to the Secretary of DHHS if there are inappropriate uses or disclosures of their research, IIHI, standards for sanctioning those who breach the Privacy Rule and for mitigating against those breaches.

5. Maintain copies of Business Associate and Data Use Agreements.

6. Provide verification that all co-investigators and research personnel have been trained in the policies and procedures required under HIPAA.

7. Produce the covered entity's Notice of Privacy Practice with verification of receipt by all subjects.

Regulatory Agency Inspections are conducted by members of agencies such as the Food and Drug Administration (FDA), the European Medicines Agency (EMA), or foreign government. The U.S. Code of Federal Regulations or FDA policies or guidelines guide FDA inspections. EMA inspections are guided by ICH regulations. The Office of Civil Rights enforces the HIPAA Privacy, Security and Transaction requirements. The reasons for regulatory agency inspections are: 1.) to check data integrity and patient safety prior to a decision as to whether to approved a New Drug Application; 2.) to follow-up on an allegation of scientific misconduct reported to the FDA, as in a "for cause" inspection; and 3.) as part of routine periodic assessments of an institution and its practices.

Sponsor company monitoring visits for clinical trials are conducted by the trained staff (clinical research associated – CRAs) or monitors of companies or monitors hired from contract research organizations. Monitors seek to assure that a study is being conducted correctly and according to the IRB-approved protocol. Their goal is to make the site "agency inspection ready" to minimize or prevent findings during a regulatory agency visit.

Sponsor company or organization audits are much like monitoring visits in that the intent, information examined, and the staff interviewed is the same. However, audits are infrequent and determined by the level of risk to subjects and the importance of the study site ("high enrollers" or sites which possess critical data sets or measurements may be more likely to receive an audit). Also, unlike monitors who are part of the medical organization conducting the study, auditors are independent of those conducting the research in the sponsor organization.

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Appendix H – Inspection Readiness Guidance

IUPUI/Clarian oversight is provided in much the same way as detailed above from the office of Research Compliance Administration or research advisors (located in individual departments) who perform monitoring-like activities, along with general education and advisory duties. Reports from auditors or advisors are intended for internal use only. However, sanctions, education for PIs and their staff, or termination of the right to conduct human research can be potential outcomes of serious or continuing noncompliance.

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Appendix I – Investigational Drug Services (IDS) Resources

Investigational Drug Services provided by the
Hospital Pharmacy Departments of Clarian Health Partners,
Wishard and Veterans Administration Hospitals

1. **What they are:**
   Special areas of the pharmacy departments that are dedicated to providing an array of services to physicians, nurses, and subjects involved in investigational drug studies. The various services are provided for a fee. Contact your respective IDS for a fee schedule. *If you must utilize an IDS or would like to use the IDS for an upcoming study, be sure to contact the IDS before the study budget is approved. Failing to do this may result in unexpected study costs that could have been included in the study budget if considered early in the negotiations with the Sponsor.*

2. **What they can do:**
   - Provide assurance that all federal and state laws are followed as they pertain to the control, handling, and dispensing and destruction of investigational drug(s).
   - Provide assurance that the storage conditions of the investigational drug are optimal as well as documented appropriately.
   - Provide assurance that drug control is maintained, with no unauthorized use allowed and that the documentation of dispensing will verify study drug treatment.
   - Provide special preparation as specified in the protocol, written materials and written procedures for all protocols.
   - Provide support to the investigator during audits by internal institutional staff, or monitoring/auditing the study Sponsor and regulatory agencies.
   - Oversee and verify all study drug doses prior to dispensation to the subject.

3. **What the IDS needs from investigators and study coordinators:**
   - Lead time in advance of proposed study startup to prepare for study and get procedures written and in place.
   - A current copy of the study protocol, all protocol amendments, investigator drug brochures and any other study documents, which would affect dispensing of the drug.
   - Adequate warning when study monitors/auditors/inspectors visit so appointments can be scheduled and appropriate study documents made ready.

4. **Contact information for affiliated Investigational Drug Services:**
   - CLARIAN HOSPITALS (Methodist-IU-Riley) Investigational Drug Service
     University Hospital UH 1430
     Office: 274-1900 Fax: 278-1697
   - WISHARD HOSPITAL Investigational Drug Service
     Wishard Hospital-Meyers Pharmacy
     Office: 630-6121 Fax: 630-8772
   - VA MEDICAL CENTER Investigational Drug Service
     Office: 554-0000 x 2949

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Appendix J – IRB Reviewer Materials Determination Chart

Materials provided for reviewers

REVIEWER MATERIALS DETERMINATION CHART

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
New study	**Reviewer Checklist**	**X**	**X**	**X**	**New study**	**Reviewer Checklist**	**X**	**X**	**X**
	CIB/Package insert	**X**				**CIB/Package insert**	**X**	**X**	
	Protocol	**X**	**X**			**Protocol**	**X**	**X**	
	SSS (summary of protocol)	**X**	**X**	**X**		**SSS (summary of protocol)**	**X**	**X**	**X**
	ICS (includes assent if applicable)	**X**	**X**	**X**		**ICS (includes assent if applicable)**	**X**	**X**	**X**
	Authorization	**X**	**X**	**X**		**Authorization**	**X**	**X**	**X**
	Recruitment checklist	**X**	**X**	**X**		**Recruitment checklist**	**X**	**X**	**X**
	Recruitment materials	**X**	**X**	**X**		**Recruitment materials**	**X**	**X**	**X**
	Supporting documents as necessary	**X**	**X**	**X**		**Supporting documents as necessary**	**X**	**X**	**X**
	Complete grant proposal if NIH-funded	**X**				**Complete grant proposal if NIH-funded**	**X**		
	DHHS-approved sample informed consent document and protocol if applicable	**X**				**DHHS-approved sample informed consent document and protocol if applicable**	**X**		
	Mentor letter for new investigators in Dept. of Medicine	**X**	**X**			**Mentor letter for new investigators in Dept. of Medicine**	**X**	**X**	
	DRA	**X**	**X**	**X**		**DRA**	**X**	**X**	**X**
	C of I info (if applicable)	**X**				**C of I info (if app.)**	**X**		

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Tabled Study*	**Reviewer Checklist**	**X**	**X**	**X**	**Tabled Study****	**Reviewer Checklist**	**X**	**X**	**X**
	CIB/Package insert	**X**				**CIB/Package insert**	**X**	**X**	
	Protocol	**X**	**X**			**Protocol**	**X**	**X**	
	SSS (summary of protocol)	**X**	**X**	**X**		**SSS (summary of protocol)**	**X**	**X**	**X**
	ICS (includes assent if applicable)	**X**	**X**	**X**		**ICS (includes assent if applicable)**	**X**	**X**	**X**
	Authorization	**X**	**X**	**X**		**Authorization**	**X**	**X**	**X**
	Recruitment checklist	**X**	**X**	**X**		**Recruitment checklist**	**X**	**X**	**X**
	Recruitment materials	**X**	**X**	**X**		**Recruitment materials**	**X**	**X**	**X**
	Supporting documents as necessary	**X**	**X**	**X**		**Supporting documents as necessary**	**X**	**X**	**X**
	Complete grant proposal if NIH-funded	**X**				**Complete grant proposal if NIH-funded**	**X**		
	DHHS-approved sample informed consent document and protocol if applicable	**X**				**DHHS-approved sample informed consent document and protocol if applicable**	**X**		
	Mentor letter for new investigators in Dept. of Medicine	**X**	**X**			**Mentor letter for new investigators in Dept. of Medicine**	**X**	**X**	
	DRA	**X**	**X**	**X**		**DRA**	**X**	**X**	**X**
	C of I info (if app.)	**X**				**C of I info (if app)**	**X**		
	Minutes excerpt from	**X**	**X**	**X**		**Minutes excerpt**	**X**	**X**	**X**

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Appendix J – IRB Reviewer Materials Determination Chart

	previous meeting					**from previous meeting**			
	Other documents[12]	**X**		**X**		**Other documents**[12]	**X**		**X**

*Original study documents in addition to updated documents **Updated documents only

[1]These documents are distributed if submitted as part of the response to the tabled study, based upon the nature of the changes

[2]These documents may include, but are not limited to, an investigator's memo submitted as part of the revisions

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Exempt study	**Exempt checklist**	**X**			**Exempt study**	**Exempt checklist**	**X**		
	Research instruments	**X**				**Research instruments**	**X**		
	Complete grant proposal if NIH-funded	**X**				**Complete grant proposal if NIH-funded**	**X**		
	C of I info (if app.)	**X**				**C of I info (if app.)**	**X**		

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist						IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Consultants *	Meeting attendees		Document	Primary reviewer	Secondary reviewer**	Meeting attendees
Expedited study	**Reviewer Checklist**	**X**	**X**	**X**	**X**	**Expedited study**	**Reviewer Checklist**	**X**	**X**	
	Expedited research checklist	**X**	**X**	**X**			**Expedited research checklist**	**X**	**X**	
	Protocol	**X**	**X**	**X**			**Protocol**	**X**	**X**	
	SSS (summary of protocol)	**X**	**X**	**X**			**SSS (summary of protocol)**	**X**	**X**	
	ICS (includes assent if applicable)	**X**	**X**	**X**			**ICS (includes assent if applicable)**	**X**	**X**	
	Authorization	**X**	**X**	**X**			**Authorization**	**X**	**X**	
	Recruitment checklist	**X**	**X**	**X**			**Recruitment checklist**	**X**	**X**	
	Recruitment materials	**X**	**X**	**X**			**Recruitment materials**	**X**	**X**	
	Supporting documents as necessary	**X**	**X**				**Supporting documents as necessary**	**X**	**X**	
	Complete grant proposal if NIH-funded	**X**					**Complete grant proposal if NIH-funded**	**X**		
	Mentor letter for new investigators in Dept. of Medicine	**X**					**Mentor letter for new investigators in Dept. of Medicine**	**X**		
	DRA	**X**	**X**	**X**			**DRA**	**X**	**X**	
	C of I info (if app)	**X**					**C of I info (if app)**	**X**		

*Includes RCA staff and Associate General Counsel/Chief Privacy Officer
**Required only if waiver requested

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Major amendment	**Amendment form**	**X**		**X**	**Major amendment**	**Amendment form**	**X**		**X**
	SSS (summary of protocol)[1]	**X**		**X**		**SSS (summary of protocol)[1]**	**X**		**X**
	ICS (includes assent if applicable)[1]	**X**		**X**		**ICS (includes assent if applicable)[1]**	**X**		**X**
	Authorization[1]	**X**		**X**		**Authorization[1]**	**X**		**X**
	Recruitment checklist[1]	**X**		**X**		**Recruitment checklist[1]**	**X**		**X**
	Recruitment materials[1]	**X**		**X**		**Recruitment materials[1]**	**X**		**X**
	Sponsor's amendment[1]	**X**		**X**		**Sponsor's amendment[1]**	**X**		**X**
	Notice to sponsor[1]	**X**		**X**		**Notice to sponsor[1]**	**X**		**X**
	Other documents[1]	**X**		**X**		**Other documents[1]**	**X**		**X**
	Protocol[1]	**X**		**X**		**Protocol[1]**	**X**		**X**
	C of I info (if app)	**X**				**C of I info (if app)**	**X**		

[1]These documents are distributed if submitted as part of the amendment, based upon the nature of the change(s).

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Major amendment (TABLED)	**Amendment form[1]**	**X**		**X**	**Major amendment (TABLED)**	**Amendment form[1]**	**X**		**X**
	SSS (summary of protocol)[1]	**X**		**X**		**SSS (summary of protocol)[1]**	**X**		**X**
	ICS (includes assent if applicable)[1]	**X**		**X**		**ICS (includes assent if applicable)[1]**	**X**		**X**
	Authorization[1]	**X**		**X**		**Authorization[1]**	**X**		**X**
	Recruitment checklist[1]	**X**		**X**		**Recruitment checklist[1]**	**X**		**X**
	Recruitment materials[1]	**X**		**X**		**Recruitment materials[1]**	**X**		**X**
	Sponsor's amendment[1]	**X**		**X**		**Sponsor's amendment[1]**	**X**		**X**
	Notice to sponsor[1]	**X**		**X**		**Notice to sponsor[1]**	**X**		**X**
	Other documents[1][2]	**X**		**X**		**Other documents[1][2]**	**X**		**X**
	Protocol[1]	**X**		**X**		**Protocol[1]**	**X**		**X**
	C of I info (if app)	**X**				**C of I info (if app)**	**X**		
	Minutes excerpt from previous mtg.	**X**		**X**		**Minutes excerpt from previous mtg.**	**X**		**X**

[1]These documents are distributed if submitted as part of the response to the tabled amendment, based upon the nature of the change(s).
NOTE: it is not necessary to share documents submitted with original amendment with reviewer or meeting attendees.
[2] These documents may include, but are not limited to, an investigator's memo submitted as part of the response.

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Minor amendment	**Amendment form**	**X**		**X[2]**	**Minor amendment**	**Amendment form**	**X**		
	SSS (summary of protocol)[1]	**X**				**SSS (summary of protocol)[1]**	**X**		
	ICS (includes assent if applicable)[1]	**X**				**ICS (includes assent if applicable)[1]**	**X**		
	Authorization[1]	**X**				**Authorization[1]**	**X**		
	Recruitment checklist[1]	**X**				**Recruitment checklist[1]**	**X**		
	Recruitment materials[1]	**X**				**Recruitment materials[1]**	**X**		
	Sponsor's amendment[1]	**X**				**Sponsor's amendment[1]**	**X**		
	Notice to sponsor[1]	**X**				**Notice to sponsor[1]**	**X**		
	Other documents[1]	**X**				**Other documents[1]**	**X**		
	Protocol[1]	**X**				**Protocol[1]**	**X**		
	C of I info (if app)	**X**				**C of I info (if app)**	**X**		

[1] These documents are distributed if submitted as part of the amendment, based upon the nature of the change(s).
[2] Meeting attendees receive copy of approved form only.

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Full Board Continuing Review	**Reviewer Checklist**	**X**			**Full Board Continuing Review**	**Reviewer Checklist**	**X**		
	Continuing review form*	**X**		**X**		**Continuing review form***	**X**		**X**
	SSS (summary of protocol)	**X**		**X**		**SSS (summary of protocol)**	**X**		**X**
	ICS (includes assent if applicable)	**X**		**X**		**ICS (includes assent if applicable)**	**X**		**X**
	Authorization	**X**		**X**		**Authorization**	**X**		**X**
	Recruitment checklist	**X**		**X**		**Recruitment checklist**	**X**		**X**
	Recruitment materials	**X**		**X**		**Recruitment materials**	**X**		**X**
	Attachments submitted per the form instructions	**X**		**X**		**Attachments submitted per the form instructions**	**X**		**X**
	Protocol[#]	**X**				**Protocol[#]**	**X**		
	All records from previous year, including amendments	**X**				**All records from previous year, including amendments**	**X**		

*Includes relevant information to determine whether the proposed research continues to fulfill the approval criteria, as well as a status report on the progress of the research

[#]Provided if protocol document has not been resubmitted in the previous year.

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Full Board Continuing Review (TABLED)	**Copy of Original Reviewer's Checklist (from previous meeting)**	**X**			**Full Board Continuing Review (TABLED)**	**Copy of Original Reviewer's Checklist (from previous meeting)**	**X**		
	Continuing review form*[1]	**X**		**X**		**Continuing review form*[1]**	**X**		**X**
	SSS (summary of protocol) [1]	**X**		**X**		**SSS (summary of protocol) [1]**	**X**		**X**
	ICS (includes assent if applicable) [1]	**X**		**X**		**ICS (includes assent if applicable) [1]**	**X**		**X**
	Authorization[1]	**X**		**X**		**Authorization**	**X**		**X**
	Recruitment checklist[1]	**X**		**X**		**Recruitment checklist[1]**	**X**		**X**
	Recruitment materials[1]	**X**		**X**		**Recruitment materials[1]**	**X**		**X**
	Attachments submitted per the form instructions[1]	**X**		**X**		**Attachments submitted per the form instruction s[1]**	**X**		**X**
	Protocol[1]	**X**		**X**		**Protocol[1]**	**X**		**X**
	All records from previous year, including amendments					**All records from previous year, including amendments**			
	Other documents[1][2]	**X**		**X**		**Other documents[1][2]**	**X**		**X**
	Minutes excerpt from previous	**X**		**X**		**Minutes excerpt from previous mtg.**	**X**		**X**

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Appendix J – IRB Reviewer Materials Determination Chart

	mtg.								

[1]These documents are distributed if submitted as part of the response to the tabled continuing review, based upon the nature of the change(s).
NOTE: it is not necessary to share documents submitted with original continuing with reviewer or meeting attendees.
[2] These documents may include, but are not limited to, an investigator's memo submitted as part of the response.
*Includes relevant information to determine whether the proposed research continues to fulfill the approval criteria, as well as a status report on the progress of the research

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Expedited Continuing Review	**Continuing review form***	**X**			**Expedited Continuing Review**	**Continuing review form***	**X**		
	SSS (summary of protocol)	**X**				**SSS (summary of protocol)**	**X**		
	ICS (includes assent if applicable)	**X**				**ICS (includes assent if applicable)**	**X**		
	Authorization	**X**				**Authorization**	**X**		
	Recruitment checklist	**X**				**Recruitment checklist**	**X**		
	Recruitment materials	**X**				**Recruitment materials**	**X**		
	Attachments submitted per the form instructions	**X**				**Attachments submitted per the form instructions**	**X**		
	All records from previous year, including amendments	**X**				**All records from previous year, including amendments**	**X**		
	C of I info (if app)	**X**				**C of I info (if app)**	**X**		
	Protocol	**X**				**Protocol**	**X**		

*Includes relevant information to determine whether the proposed research continues to fulfill the approval criteria, as well as a status report on the progress of the research

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer	Secondary Reviewer	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Terminated Continuing Review	**Continuing review form**	**X**			**Terminated Continuing Review**	**Continuing review form**	**X**		
	Attachments submitted per the form instructions	**X**				**Attachments submitted per the form instructions**	**X**		
	All records from previous year	**X**				**All records from previous year**	**X**		

Methodist					IUPUI				
	Document	Primary reviewer[2]	Secondary Reviewer[2]	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees*
General Information	**General information item**			**X**	**General Information***	**General information item**	**X**		**X**
	Protocol[1]			**X**		**Protocol[1]**	**X**		**X**
	SSS (summary of protocol)[1]			**X**		**SSS (summary of protocol)[1]**	**X**		**X**
	ICS (includes assent if applicable)[1]			**X**		**ICS (includes assent if applicable)[1]**	**X**		**X**
	Authorization[1]			**X**		**Authorization[1]**	**X**		**X**
	Recruitment checklist[1]			**X**		**Recruitment checklist[1]**	**X**		**X**
	Recruitment materials[1]			**X**		**Recruitment materials[1]**	**X**		**X**
	Other documents[1]			**X**		**Other documents[1]**	**X**		**X**

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Appendix J – IRB Reviewer Materials Determination Chart

	CIB/Package insert[1]			**X**		**CIB/Package insert[1]**	**X**		**X**
	C of I info (if app)			**X**		**C of I info (if app)**	**X**		**X**

*In some cases (as determined by Team Leaders or Directors), all members shall review the item, based on the nature of the general information item.
[1]These documents are distributed if submitted as part of the general information item, based upon the nature of the general information item. [2] Not applicable.

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Appendix J – IRB Reviewer Materials Determination Chart

Methodist					IUPUI				
	Document	Primary reviewer[2]	Secondary Reviewer[2]	Meeting attendees		Document	Primary reviewer	Secondary reviewer	Meeting attendees
Unanticipated Problems and Noncompliance	**Applicable form**			**X**	**Unanticipated Problems and Noncompliance**	**Applicable form**	**X**		
	Materials Related to the Event			**X**		**Materials Related to the Event**	**X**		**X**
	SSS (summary of protocol)			**X**		**SSS (summary of protocol)**	**X**		
	ICS (includes assent if applicable)			**X**		**ICS (includes assent if applicable)**	**X**		
	Authorization			**X**		**Authorization[1]**	**X**		
	Other documents[1]			**X**		**Other documents[1]**	**X**		

[1] Other relevant study documents are distributed if deemed necessary by RCA staff or IRB Chair (or designee), based upon the nature of the unanticipated problem and noncompliance.
[2] Not applicable

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Appendix K – Managing Research Data – 8 Simple Rules

1. The Principal Investigator is responsible for ensuring the security and confidentiality of all data associated with their project. While some of the security duties may be delegated, the ultimate responsibility is with the PI

2. All research team members should know and follow the school's security policies and procedures. This includes the steps to protect data and the process for reporting a security incident

3. All research data must be protected regardless of its format or the place it is stored (hard drive, diskette, tape, CD, PDA, paper). Any computer system storing data must utilize anti-virus software and that software must be kept up-to-date

4. Only those people explicitly authorized to access your research data should be able to get to it. A data access management process needs to be formalized and followed. Those authorized to access your research data should use strong passwords that are difficult to crack. Passwords should not be written down or shared with others

5. Backing up data in at least two places (onsite and offsite) should be done on a regular basis. Don't forget that periodic testing of the data restoration process will guarantee your backup data is truly useful in case you lose your original data

6. Never assume that email is secure. Unless you have taken specific steps to secure each email message, you should not communicate confidential, sensitive, or protected information via email

7. Data disposal is as important as data management. When the data are no longer needed, they must be destroyed in a way the prevents recovery by the bad guys

8. Don't panic. There are plenty of people in the school that can help you do these things. If no one is available in your department, or you just don't know whom to call, the Information Services and Technology Management (ISTM) team will help. Contact them at: 274-5336 or iusmot@iupui.edu

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Appendix L – Methodist Research Review and Consent Review Committees

I. Overview

The Research Review Committee (RRC) and Consent Review Committees (CRC) were formed by the Methodist Research Institute to perform a "pre-review" of each full-review research protocol submitted to the Institutional Review Board (IRB) at Methodist Hospital. These pre-review committees function independently of the IRB at Methodist Hospital and are organized, facilitated and funded by the Methodist Research Institute (MRI). The charge of these two committees is to aid investigators in complying with the current federal, state, and local requirements for informed consent and for insuring scientific merit of the proposed protocol.

Both committees serve in an advisory capacity only and do not hold veto authority over any submitted protocol. The combined information gained by both committees assists the investigator by providing the IRB with a more detailed and precise protocol submission for full review, thereby protecting the health and welfare of human subjects.

The mission of the Methodist Research Institute (MRI) is to support the conduct of clinical research that will enhance the clinical mission of Clarian Health Partners. MRI will facilitate the conduct of research by the Clarian professional staff in the exploration of ideas and research questions that have the greatest relevance and benefits to those served by Clarian.

A 9-member Board of Directors governs the Methodist Research Institute. The Board meets quarterly to review the Institute's operations, goals, programs, and to make decisions regarding the overall direction of the Institute. The Medical Director/Chief Executive Officer and the Administrative Director oversee the operation of the Institute.

The Methodist Research Institute is a 501C-3 corporation, wholly owned subsidiary of Clarian Health Partners.

Medical Director:

The Medical Director is responsible for providing executive, decision-making, leadership, and strategic planning involving research priorities/objectives and the efficient and productive use of personnel, material, and financial resources to accomplish those objectives. The Medical Director establishes the long-term mission, culture, and values of the Research Institute and works with the Administrative Director in seeing the goals accomplished. The Medical Director fosters collaborative relationships with all researchers within Clarian, provides medical and scientific direction along with the management of relationships and communications with internal and external customers. The Medical Director is responsible to the Board of Directors of the Methodist Research Institute, provides direct supervision to the Administrative Director, and scientific direction to researchers. The Medical Director of the Methodist Research Institute also sits as co-chairman of the Institutional Review board at Methodist Hospital. This position requires an M.D. degree and license to practice medicine within the State of Indiana.

Administrative Director:

The Administrative Director of the Methodist Research Institute is responsible for providing administrative decision-making, leadership, and strategic planning decisions involving the efficient and productive use of personnel, material, and financial resources. The Administrative Director provides direct supervision to the support staff, clinical research nurses, and provides non-scientific direction to the research staff. This position also ensures compliance with all applicable quality and accreditation

standards within the assigned areas of accountability and ensures optimal utilization of resources and quality while maintaining established budgetary standards. This position requires appropriate education in the area of administration, state and national regulatory agency guidelines, state and federal law relative to assigned area and broad knowledge of the medical arena.

II. The Research Review Committee

A. Purpose: The charge of the Research Review Committee is the determination of the scientific merit and comprehensiveness of a protocol and other submitted documents to be reviewed by the IRB, and to report their findings to the IRB. The Research Review Committee does not hold veto power. It is an informational service for the Institutional Review Board that has proven to benefit the investigators and the IRB by providing a more efficient approval process. Oversight of the RRC is the responsibility of the Administrative Director and the Medical Director of the Methodist Research Institute.

B. Membership: The Research Review Committee is appointed by and/or approved by the Chair of the Committee or the Medical Director of the Methodist Research Institute. The Committee is composed of physicians, research nurses/coordinators, investigational drug pharmacists, a biostatistician, a research associate, the IRB Manager and the Institute's Medical Writer. The current Chair of the Committee is an oncology physician. In the past the Committee has been Chaired by an endocrinologist, a research scientist and by a biostatistician. The Committee varies from 7 to 9 members and is chosen to bring a variety of medical, research, and administrative expertise to the Committee. All members have experience in the area of human research. Periods of appointment to the Committee are not of a set duration, but accommodate time restrictions and generosity of the appointees. The Committee is basically of consistent membership, but some adjustments to the membership are needed on an occasional basis. When an opening occurs, it is filled as soon as possible. All participants volunteer their time, with the exception of the Committee's Chair, who receives a small stipend. The stipend is furnished by the Methodist Research Institute.

C. Responsibilities:

1. IRB Manager:
   a. Receives 20 copies of each new study for full review
   b. Distributes 17 copies to the Institute's Medical Writer
   c. Incorporates RRC minutes and investigator responses into IRB packet
2. Medical Writer
   a. Determines and assigns a primary and secondary reviewer to each study
   b. Reformats the informed consent statements according to the Clarian/IUPUI Research Compliance Administration specifications
   c. Prepares and delivers review packets to Committee members approximately one week before the Research Review Committee meeting. Protocols reviewed at this meeting are scheduled for review at the IRB the following month

      NOTE: Each packet contains a reviewer assignment sheet, study documents for each study (including a copy of the investigator's brochure when provided and when necessary), and the formatted informed consents for each study
   d. Records questions, concerns, and recommendations from the meeting on specified documents and following review by the Committee Chair, distributes these documents via email to investigators

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Appendix L – Methodist Research Review and Consent Review Committees

e. Processes investigators' responses, which must be received within approximately 7 to 10 days, and distributes these to the IRB manager

3. Primary reviewer
   a. Reviews assigned studies
   b. Presents oral overview of assigned studies
   c. Makes recommendations regarding assigned studies
4. Secondary reviewer
   a. Reviews assigned studies
   b. Presents additional findings (supplementary to primary reviewer) at meetings
   c. Makes recommendations regarding assigned studies
5. Chair
   a. Facilitates meeting discussion
   b. Approves written comments to investigators prior to distribution
6. Members present
   a. Review materials (all Committee members are expected to become familiar with all of the studies submitted for that particular meeting)
   b. Discuss materials at meetings

D. Procedures/Interactions:

1. Pre-Meeting: Once copies of each study are received by the deadline in the IRB office, the appropriate number of copies is distributed for processing and assignment of a primary and secondary reviewer. Informed consent statements are reformatted and the studies are distributed into packets for reviewers. Reviewers prepare for the meeting.
2. Meeting: Members gather once per month one week after the IRB deadline to discuss each study, form questions, and to make recommendations regarding the study. Discussions regarding protocols, the evaluation of scientific merit, possible subject risks, statistical strengths, etc. are held at this time. Also included are reviews of the Documentation of Review and Approval form, the Summary Safeguard Statement, and the Authorization for Release of Health Information for Research form. Erroneous documentation or omissions are noted. Questions, concerns, and recommendations are formulated at this time and recorded; however, no formal minutes are taken at this meeting.
3. Post-Meeting: Any questions or recommendations are typed and distributed to the investigators. Following investigator response, these comments or corrections are incorporated into the study, including processing and assembling the edits, corrections, additions, deletions, and answers to questions posed by the Committee. The revised study is then forwarded to the IRB office for incorporation into the IRB packet and subsequent distribution to IRB members.

NOTE: Occasionally, a reviewer may contact an investigator to obtain additional information regarding a protocol to be reviewed, and the biostatistician is available to assist an investigator with the statistical elements during the pre-review process and prior to the final review by the IRB. At this point, the RRC's responsibilities are complete. Any follow-up to their questions/recommendations is not a part of their role.

III. The Consent Review Committee

A. Purpose: The charge of the Consent Review Committee is to review the informed consent statement for completeness and accuracy to reflect the protocol and adequately inform

subjects of the study. This overview includes information regarding a detailed purpose of the study, the procedures, risks, benefits, information regarding cost, and assurance of confidentiality. The Committee attempts to ensure the consent is clearly and adequately written and to ensure that all elements are present as required by the federal and state regulations and local policy. The Consent Review Committee does not hold veto power. The Consent Review Committee's role is ensuring full disclosure of the elements and requirements of a protocol. It is an advisory service for the IRB and has proven to benefit the investigators and the IRB by providing a more efficient approval process. Oversight of the Consent Review Committee is the responsibility of the Administrative Director and the Medical Director of the Methodist Research Institute.

B. Membership: The Consent Review Committee is appointed by and/or approved by the Chair of the Committee, the Administrative Director, or the Medical Director of the Methodist Research Institute. The Committee is composed of research nurses, an attorney, an ethicist, the IRB Manager, and the Institute's Medical Writer. The current Chair of the Committee is the Methodist Research Institute Medical Writer. The Committee varies from 5 to 7 members who are chosen to bring a variety of medical, research, legal ethical and administrative expertise to the Committee. Periods of appointment to the Committee are not of a set duration, but accommodate time restrictions and generosity of the appointees. The Committee is basically a consistent group, but some adjustments to the membership are needed on an occasional basis. When an opening occurs, it is filled as soon as possible. All participants volunteer their time.

C. Responsibilities:

1. IRB Manager:
   a. Receives 20 copies of each new study for full review
   b. Distributes 17 copies to the Institute's Medical Writer
   c. Incorporates CRC minutes and investigator responses into IRB packet
2. Medical Writer
   a. Determines and assigns a primary reviewer to each study
   b. Reformats the informed consent statements according to the Clarian/IUPUI Research Compliance Administration specifications, performs initial edits (additions, deletions, grammar corrections, etc.) and highlights changes
   c. Prepares and delivers review packets to Committee members approximately one week before the Consent Review Committee meeting.
      NOTE: Each packet contains a reviewer assignment sheet, a copy of the Reviewer Checklist, study documents for each study and the formatted consents for each study.
   d. Records the Committee's remarks and forwards (via e-mail) to investigators
   e. Processes investigators' responses, which must be received within approximately 7 to 10 days, and distributes these to the IRB manager
3. Primary reviewer
   a. Reviews assigned studies
   b. Presents oral overview of assigned studies
   c. Makes recommendations regarding assigned studies
4. Members present
   a. Review materials (all Committee members are expected to become familiar with all of the studies submitted for that particular meeting)

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Appendix L – Methodist Research Review and Consent Review Committees

b. Discuss materials at meetings, utilizing checklist to ensure all required elements are present.

D. Procedures/Interactions:

1. Pre-Meeting: Once copies of each study are received by the deadline in the IRB office, the appropriate number of copies is distributed for processing and assignment of a primary reviewer.
   Informed consent statements are reformatted and the studies are distributed into packets for reviewers. Reviewers prepare for the meeting.
2. Meeting: Members gather once per month one week after the IRB deadline to discuss each study. At the monthly meeting, the assigned reviewer summarizes the study. Under the guidance of the reviewer, the Committee proceeds to dissect the informed consent for completeness, appropriateness and to ensure that all elements are present as required by the federal and state regulations and local policy. The Committee uses the checklist to be sure that all required elements are present. Also, a special emphasis is placed on full disclosure of study plan, information pertaining to subject safety, appropriate language, consent readability, and reading level.
3. Post-Meeting: Any questions or recommendations are typed and distributed to the investigators. Following investigator response, these comments or corrections are incorporated into the study, including processing and assembling the edits, corrections, additions, deletions, and answers to questions posed by the Committee. The revised study is then forwarded to the IRB office for incorporation into the IRB packet and subsequent distribution to IRB members.

NOTE: Occasionally, prior to the meeting, a reviewer may contact an investigator to obtain additional information regarding a consent or protocol to be reviewed. At this point, the Consent Review Committee's responsibilities are complete. Any follow-up to their questions/recommendations is not a part of their role.

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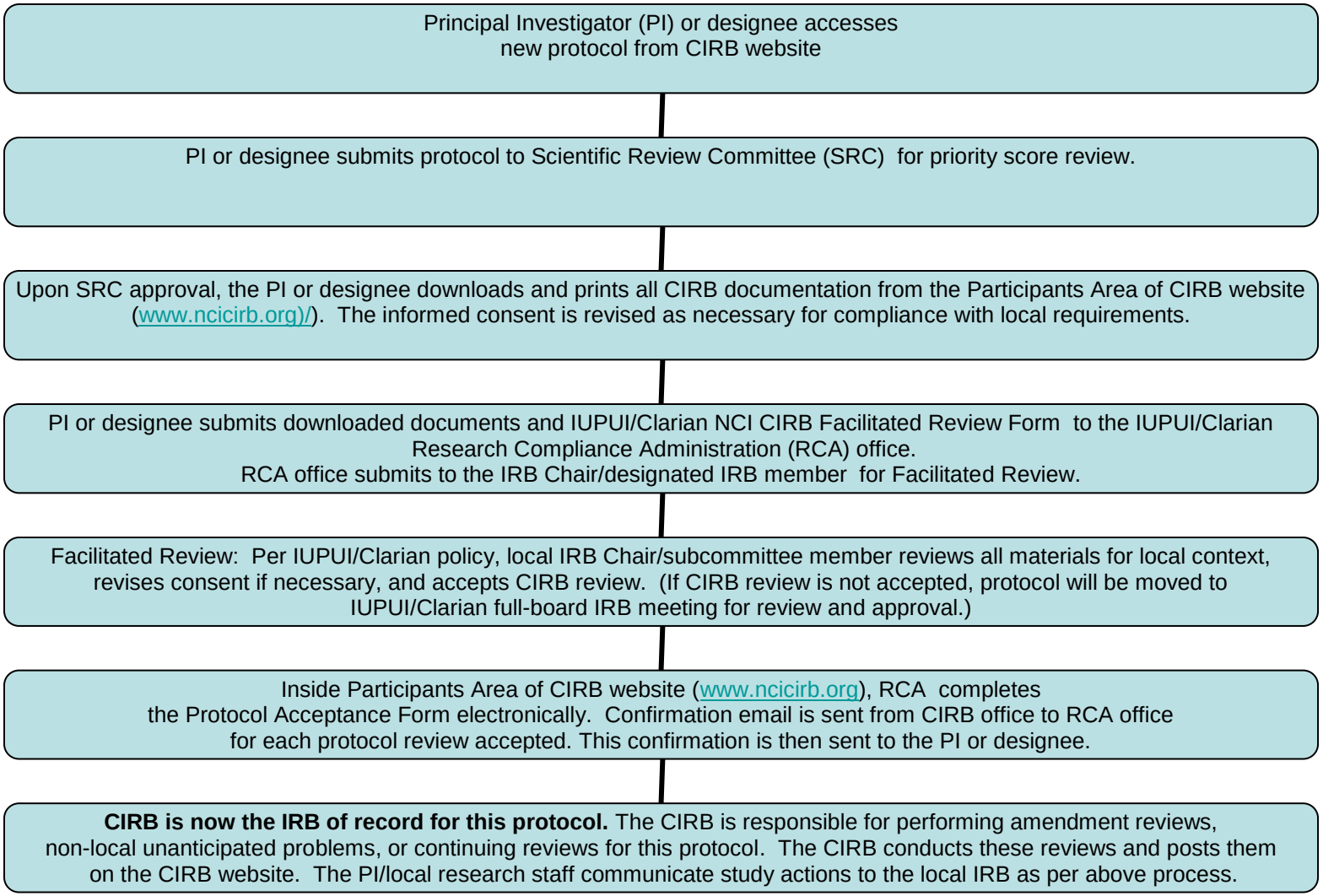
Appendix M – NCI CIRB Review Process



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Appendix N – Recruitment of Students as Subjects in a Research Study

Two issues frequently arise when researchers seek to use students in research projects:

(1) Under what circumstances can class credit be given to student participants? and
(2) Can a researcher use his/her own students as subjects?

Under what circumstances can class credit be given to student participants?

Giving course credit or extra credit to students who participate in research as part of a course requirement is generally acceptable only when alternative means of obtaining credit is made available to students who do not wish to volunteer as research subjects. The IRB will carefully review the alternatives to make sure that students are not being coerced into becoming research subjects. For example, the IRB is likely to view the choice of either volunteering for a 30 minute experiment involving filling out a questionnaire or writing a 5-page paper as coercive, since writing a 5-page paper involves considerably more time, effort, and stress.

The informed consent statement should make clear the consequences of withdrawing from a project prior to completion (e.g., will credit be given despite withdrawal?). As a general matter, the IRB favors giving credit even if the subject withdraws, unless the student withdraws immediately or there is evidence of bad faith on the part of the student.

Can a researcher use his/her own students as subjects?

Introduction

These guidelines are designed to assist researchers who wish to use their own current students as subjects in research protocols. An underlying principle of the regulations governing use of human subjects in research is that the subject's participation is voluntary, based upon full and accurate information. The relationship of teacher and student is inherently one that raises the issue of "voluntariness." No matter how well intentioned the teacher is, students may feel compelled to participate, believing that failure to do so will negatively affect their grades and the attitude of the teacher (and perhaps other students) toward them. For this reason, the IRB generally believes that teachers should not use their own students as subjects in their research if it can be avoided. This general policy is in accord with that of other institutional review boards. The IRB recognizes, however, that in some research situations, use of one's own students is integral to the research. This is particularly true of research into teaching methods, curricula and other areas related to the scholarship of teaching and learning. The following are two models of research design that are suggested for such circumstances which are believed to strike a balance between the two interests.

Collection of Data by Third Party

In situations where the activities to be undertaken by the students are not part of required class activities, and thus students may or may not choose to participate, the instructor/researcher should arrange to have the data collected by an independent third party, so that the instructor does not know who participated,

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Appendix N – Recruitment of Students as Subjects in a Research Study

and does not have access to the identifiable data or identity of participants for any purpose until grades have been assigned and entered.

For example, if the instructor wants to administer pre- and post- tests to determine the efficacy of a particular curriculum, the necessary consent forms could be obtained, and administration of the tests conducted, by a colleague at times when the instructor was not present. [A graduate teaching assistant in the class in which the students/subjects are enrolled does not qualify as a third party for collecting data on behalf of the instructor as described above.] .

Collection of Data by Instructor/Researcher

In situations where the collection of data by a third party is not feasible, the IRB requires that the student's written consent to the use of his or her own data, e.g., test results, papers written, homework, etc., be obtained after grades are entered.

For example, use of a particular teaching method throughout the class might not be capable of being structured so that students could opt out. Typically, the instructor/researcher should provide written information at the beginning of the course concerning the study, which makes clear that the students will have an opportunity, after the course is finished and grades entered, to agree or not to agree to the inclusion of their data in the instructor's study. By fashioning the student's participation in this manner, we do not place the student in the position of having to either choose to participate or find an alternative course. Moreover, at the primary and secondary levels of education, election of alternative classes is not likely to be possible.

Problem Practices

1. ***Use of Extra Credit for Participation.*** Sometimes participation in the teacher's research is structured as an available extra credit assignment. Even when other means of obtaining extra credit are available, it is not sufficient to overcome the power disparity and the perception of students that participation in the instructor's research is advisable, even if not required.

2. ***Group activities*.** Group activities that are required as part of the course instruction pose a particularly difficult situation because the practicality of a student opting out is very limited. If the data is a group project or perhaps a videotape of the group interaction, each student's consent is necessary for the use of that data in the instructor's research. If one student does not consent, the data may be used only if the non-consenting student's data can be effectively excluded. In many cases this will not be possible. Thus, none of the data can be used.

3. ***Use of student grades and other assessments*.** In research where the instructor wants access to identifiable student academic records, signed consent forms are required even if the research activities conducted in the classroom are conducted by a third party and otherwise fall under an exempt category of research. For example, administration of a pre- and post-test by a third party will normally qualify as exempt research under either category 1 or 2 (see Exempt Research Checklist), eliminating the need for a signed informed consent, but suggesting the inclusion of an

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Appendix N – Recruitment of Students as Subjects in a Research Study

information sheet. If, however, part of the research also includes access to the individual, identifiable student's other grades etc., signed consent from each student is necessary.

4. ***Minors*.** Research involving minors (under 18 years of age) as subjects, (even 17 year old college students) in most instances requires a signed parental consent, as well as that of the student.

5. ***Graduate Teaching Assistants*.** Research conducted by graduate students in a class in which the researcher teaches, assists in the class or does any grading are subject to the same restraints described above.

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Appendix O – Research Oversight Plan Template

Principal Investigator:		**IRB Study #:**	
Study Title:			
1. Who will be responsible for the data and safety monitoring? (Examples include: a DSMC or DSMB, medical monitor, investigator, independent physician, IRB) **Clarify if this individual or committee is independent from the sponsor and/or investigator.**			
2. What will be monitored. (Examples include: data quality, subject recruitment, accrual, and retention, outcome and adverse event data, assessment of scientific reports or therapeutic development, results of related studies that impact subject safety, procedures designed to protect the privacy of subjects)			
3. What are the procedures for analysis and interpretation of data, the actions to be taken upon specific events or endpoints, the procedures for communication from the data monitor to the IRB and site, and other reporting mechanisms?			
4. What is the frequency of monitoring? (The appropriate frequency of data and safety monitoring will be dependent on the nature and progress of the research; however, monitoring must be performed on a regular basis (e.g., at least annually).			
5. What information will be reported to the IRB? (Minimally, the IRB requires the following information at the time of continuing review: 1) frequency and date(s) of monitoring; 2) summary of events that require prompt reporting to the IRB; 3) assessment of external factors (i.e. scientific reports, therapeutic developments, results of related studies) that impacted the safety of subjects; 4) summary of subject privacy and research data confidentiality outcomes; and 5) any changes to the risk-benefit ratio.			

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Appendix P – Risk Assessment Survey – for Biomedical and Behavioral/Social Science Research

Risk Assessment Survey for Biomedical Research

**** This survey is provided, not as a formula, but as factors to consider when evaluating the risk to a particular research study.***

Risk Survey For Biomedical Research							
Level of Risk	**Study Design**				**Research Team**	**Subjects Population**	**Proposed Oversight**
Low	Scientific Review Done	Short Duration	Phase IV	Approved Single Drug	Experienced	Healthy Subjects	Monitored by DSMB
Moderate	↓	↓	↓	↓	↓	↓	↓
High	No Scientific Review Done	Long Duration	Phase I	Investigational, Multi-Dose Drug Altered PK (Renal/Liver)	Not Experienced	Vulnerable Subjects/Unhealthy Subjects	Investigator-Initiated/No Oversight

Example of LOW RISK biomedical research:

Investigator-initiated, single blood draw of healthy females to measure specific hormone level → Safety monitoring by investigator sufficient.

Example of MODERATE RISK biomedical research:

Sponsored, phase III, open-label study comparing investigational drug to standard treatment. Study lasts 3 months and involves 4 visits → Safety monitoring plan may include an independent individual, committee, or DSMB to review the data and subject safety.

Example of HIGH RISK biomedical research:

Investigator-initiated study comparing two existing standard treatments. Study lasts 2 years and involves 12 visits, which include x-rays, numerous blood draws, and tumor biopsies. → Safety monitoring may include a Data and Safety Monitoring Board (DSMB) with quarterly safety reports.

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Appendix P – Risk Assessment Survey – for Biomedical and Behavioral/Social Science Research

Risk Assessment Survey for Behavioral/Social Science Research

**** This survey is provided, not as a formula, but as factors to consider when evaluating the risk to a particular research study.***

Risk Survey For Behavioral/Social Science Research					
Level of Risk	**Research Team**	**Subject Population**	**Survey/ Questionnaire**	**Confidentiality**	**PHI**
Low	Experienced	Healthy Subjects	Benign questions	Anonymous, data seen only by investigator	De-identified data
Moderate	↓	↓	↓	↓	↓
High	Not Experienced	Vulnerable Subjects/Unhealthy Subjects	Sensitive, at-risk behavior questions	Identifiable, data released to multiple entities	Identifiable, illegal, stigmatized data

Example of LOW RISK behavioral/social science research:

Observational study evaluating customer interactions with fast-food employees (no intervention) → Safety monitoring by investigator sufficient.

Example of MODERATE RISK behavioral/social science research:

Investigator to administer a "survey" to elementary-aged children about their perceptions of school violence → Safety monitoring might require an independent individual evaluating the safety of the children involved.

Example of HIGH RISK behavioral/social science research:

NIH-sponsored, multi-site study on HIV-infected individuals surveying their sexual activities. → Safety monitoring might require an independent central DSMB evaluating the subject's safety and trends.

IUPU Standard Operating Procedures

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Appendix Q – SAMPLE – Checklist for Submission of a Research Study to Storage

Title of Protocol:

Sponsor: P.I.:

Sponsor Study Number: I.U. Study Number:

IRB Closure Date (if applicable): # of boxes:

CRS: Date form completed:

Yes	No		
❑	❑	1.	Have all loose papers been removed from the front pocket of the CRF binders and filed appropriately? Study-related information should be placed in the study file. Patient information placed in a page protector, or 3-hole punched and placed in the patient CRF binder. All copies of medical records should be placed in clinic chart.
❑	❑	2.	If possible, have individual patient CRFs been combined and the appropriate listed on the outside of the binder?
❑	❑	3.	Has all paperwork been removed from the front pocket of the study binder and filed in the appropriate section?
❑	❑	4.	Are copies of the IRB original, amendments, and annual approvals as well as the study closure notice filed in the IRB section of the study file notebook?
❑	❑	5.	Have all extra, blank pages been removed from the CRFs and study file notebook and discarded? This would include forms for cycles of therapy that the patient did not receive, extra sample shipping forms, unused patient diaries, etc.
❑	❑	6.	Are copies of all versions of the investigative drug brochure present?
❑	❑	7.	If the study binder is too full, has it been transferred to two binders with the second binder labeled with the study name, protocol number, sponsor, and "book 2 of 2"?

Studies should be submitted to the storage room committee within 3 months of closing the study to accrual and all data for treatment has been completed. Outstanding follow-up and queries do not exempt a study from being transferred to the storage room

BOX location ID: _____ (assigned by storage coordinator)
Box Number _____Contents_____

Format for Storage Box Labels

IU IRB# / PI
Sponsor#/Sponsor Name
Program/Abbreviated ID
IRB Closure Date:
Box ID Number:

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Appendix R – SAMPLE – Device Accountability Log

DEVICE RECEIPT					DEVICE USE				DEVICE RETURN/REPAIR/DESTRUCTION						
Date Rec'd	Initials of Receiver	Lot #/ Serial or Model #	Device Type/ Batch #	Comments	Date Used	Initials of Device Dispenser	Patient ID	Comments	RET=Returned DES=Destroyed REP=Repaired	Date	Initials	Auth #	# of Units	Reason	Comments

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Appendix S – SAMPLE – Drug Accountability Log

Institution: _____ **Clinic:** _____ DRAFT

Protocol Number: _____ **Study Material:** _____

Location Drug: _____ **Drug Administered:** _____

PI: _____

Title: _____

Line Nu.	Date Received Or Returned Or Dispensed	Subject Initials	Subject Number	Lot Number	Dose	Quantity Received or Dispensed	Balance Forward	Recorder Initials	Initials of CRA who verifies
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									

Notes / Comments:

Recorder Initials ____Recorder Name_____Recorder Initials ____ Recorder Name_____

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Appendix T – SAMPLE – Emergency Use Consent Document

Description:

1. Specifically address:
   a. The patient's diagnosis requiring emergency treatment;
   b. The conditions justifying emergency use of the experimental agent/device, that is:
      i. The patient has a life-threatening condition that requires immediate treatment, and
      ii. No generally acceptable alternative for treating the patient is available.
   c. The identity of the experimental agent/device, and the fact that it's use for this treatment is "experimental;"
   d. A rationale for the emergency use of the experimental agent/device (i.e. why is it felt that the experimental agent/device may be of benefit in this specific patient?).
2. List each of the specific procedures that will be performed for the purpose of the emergency experimental treatment. Do not include procedures that are performed as part of the subject's routine medical care. Indicate, where applicable:
   a. The volume of blood to be drawn (in common measurement terms);
   b. The dose, route, and dosage schedule of the experimental agent and of any other drugs that will be used in the emergency treatment;
   c. All procedures associated with the use of the experimental device, including the number and frequency of patient exposures to these procedures;
   d. The FDA approval status of any other agents/devices that will be used in the treatment; and/or
   e. Complete descriptions of diagnostic or treatment procedures and the number of time each will be performed.

Risks and Benefits:

1. Address all reasonably foreseeable risks (e.g. physical, psychological, legal, or economic) and discomforts.
2. List expected side effects/adverse events associated with the experimental agent/device and their expected frequency of occurrence.
3. Include a statement that there may be unforeseen risks or even death associated with the use of the experimental agent/device.
4. Specify any safeguards to be taken to avoid or minimize the risks.

Alternative Treatment:

Specify that no generally acceptable alternative for treating the patient is available and that an alternative is no additional treatment.

New Information:

Include a statement that the patient or patient's legally authorized representative will be promptly notified if any new information, good or bad, about this emergency experimental treatment develops during its course and which may cause the patient or patient's authorized representative to change their minds about continuing treatment.

Costs and Payments:

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Appendix T – SAMPLE – Emergency Use Consent Document

1. Address if the patient, or his/her third-party insurance provider, will be responsible for the costs of any of the listed emergency experimental procedures (i.e. procedures not considered routine medical care).
2. If applicable, the patient should be informed that certain third-party insurance providers will not pay for experimental procedures and that, under such circumstances, the patient will be responsible for these costs. The patient should be provided an estimate of these costs.

Compensation for Injury:

1. State that in the event of injury caused from the experimental procedure, the patient will receive necessary medical treatment.
2. Specify whether the patient, the patient's insurance provider, or the sponsor will be responsible for these costs, or if the costs will be covered otherwise.

Confidentiality:

1. State that information about the patient and his/her emergency treatment will be handled in a confidential manner consistent with other hospital records.
2. State the in limited circumstances, however, the patient's records may be inspected by appropriate government agencies or be released according to a court order.
3. State that appropriate Food and Drug Administration (FDA) employees and the IUPUI/Clarian Institutional Review Board or its designees may inspect the patient's records as a result of the use of an experimental agent/device.

Voluntary Participation/Right to Withdraw:

1. State that the patient has the right to not take part in this emergency experimental treatment and should he/she take part, may withdraw from the treatment at any time.
2. State that the patient's care and benefits will be the same whether he/she participates in the emergency experimental treatment or not.
3. State what events may require that the patient be removed from the experimental treatment. If applicable, address any dangers associated with early withdraw or removal from the experimental treatment. List any recommended follow-up procedures.

Contacts for Questions or Problems:

1. Specifically list the investigator's name and contact information for the patient for any questions about the study or to report any treatment-related injuries.
2. Include a 24-hour emergency contact number for the patient.

Consent:

1. Include a statement that the patient is agreeing to the emergency experimental treatment.
2. Include appropriate signature lines.

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Appendix U – SAMPLE – HUD Sample Consent Document

CLINICAL CONSENT FOR USE OF A HUMANITARIAN USE DEVICE (HUD)

Name of Humanitarian Use Device (HUD): [*Add Device Name*]

Humanitarian Device Exemption (HDE) #: [*Add HDE #*]

You have been diagnosed with [*add name of condition*]. The standard treatment for your condition may not be the best treatment for you. Your physician has suggested another procedure that may give you a better chance of recovery. The device used in this treatment has been given the Humanitarian Device Exemption (HDE) designation by the FDA. Your condition fits in this category. The FDA defines an HDE device as *"intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 in the United States…where no comparable device is available."* As required by the FDA, this HDE will have oversight by the local Institutional Review Board (IRB). The IRB has already granted approval for your physician to use this HDE device.

What will be involved with the use of the device?

During your surgical procedure your physician would like to use the HUD [*name of device*], in the repair of your [*state the disease or indication for use*]. [*Provide any additional necessary information regarding the device and how it will be used*].

What are the possible risks, side effects, and discomforts associated with the use of this device?

Based on the results of prior research studies on this device and experience with its approved use, the possibility of adverse events or side effects from the [*name of device*] are the following: [*Provide quantitative information (using percentages and number of people out of 100) on the frequency of possible adverse events. Use the following categories: Likely – occurs in more than 25% of people (more than 25 out of 100 people); Common – occurs in 1-25% of people (1 to 25 out of 100 people); Rare – occurs in less than 1% of people (less than 1 out of 100 people). In addition, it is recommended that the risks are listed within the three categories in order of severity (i.e. death would be listed before hives).*

There may be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious or life-threatening.

What are the possible benefits associated with the use of this device?

It is felt that the use of this [*name of device*] during your [*add name of the procedure*] may benefit you in terms of [*list all benefits of the device*].

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Appendix U – SAMPLE – HUD Sample Consent Document

What alternative treatments or procedures are available?

If you decide not to take part in this treatment protocol, you may choose to have [*add list of alternatives*].

Will my insurance provider or I be charged for the costs of this device or any procedure associated with its clinical use?

You or your insurance provider will be responsible for any costs or charges associated with the use of the [*name of the device*] and the surgical procedures needed to insert the device. All other costs relating to your normal care will be billed in the usual manner.

What if I have questions about or problems with the device?

For questions about or problems with the device, please contact your physician, [*name of physician-investigator*], at [*telephone number, including area code*].

Patient's Consent:

Patient's Signature:_____ Date:_____

Physician Signature:_____ Date:_____

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Appendix V – SAMPLE – Repository Informed Consent Document

IUPUI AND CLARIAN CONSENT STATEMENT FOR

Collection and Storage of Human Biological Materials for Research Purposes

[*NAME OF REPOSITORY*]

PURPOSE:

A "repository" is a storage bank of medical information. You are invited to give tissue/specimens/medical information about yourself for future research purposes to the [*name of repository*] Repository. This facility was developed to study the following diseases/conditions: [*list diseases/conditions, etc.*]. The goals of this research are to [*list purpose of the repository]*.

NUMBER OF PEOPLE TAKING PART IN THE STUDY:

If you agree to participate, you will be one of approximately *[xxxx]* subjects who will be participating in this research. Approximately *[xxx]* subjects will participate at Indiana University.

DURATION OF SUBJECT'S PARTICIPATION:

[Indicate for how long samples will be stored, if known. If not known, indicate such.]

PROCEDURE FOR THE STUDY:

If you agree to be in the study, we will be collecting human biological materials which includes *[examples: both healthy and diseased tissues such as blood, bone, muscle, skin, breast, intestine, lung, liver, bladder, heart, kidney and placenta (tissues that provide food for an unborn baby), gametes (e.g. sperm and ova), as well as hair, nail clippings, urine, feces, and sweat.]*

These materials will be collected *[can normally be listed in one of three ways – choose what applies:*

1. *As an additional sample obtained at the time of obtaining a sample for a separate research project.*
2. *As leftover material from a medical procedure that is not needed for your diagnosis and/or medical treatment.*
3. *As part of a general request for a sample of human biological materials not associated with a particular research project or as part of your normal medical treatment.]*

There will be no medicines to take and no treatments provided as part of this collection effort.

Your tissues or medical data will be used for the following research purposes: [*list all anticipated uses]*. [If applicable: Your tissue specimen or medical data may be shared with (*list investigators or description of investigators*) for (*list allowable reasons for sharing the tissue specimen*) without making your identity known.]

(*If the purpose of the study is for future, unspecified research, explain this fact. Explain to subjects that by the very nature of such research being conducted in the future, it is difficult to define what future*

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Appendix V – SAMPLE – Repository Informed Consent Document

research methodology will entail and it may not be possible to identify all of the ways in which the specimen will be used.)

(Indicate whether or not subjects will be told the results of any screening done on specimens, if applicable.)

(Include information about possible secondary uses of the stored specimens, or the possible creation of an immortalized cell line based on the specimen, if applicable.)

STORAGE

In most cases the samples collected will need to be identified so that it can be linked to your medical information; however, your identity will not be released to any users of the repository.

[*Note to investigators: If the intention is to store this material in another fashion, please describe whether the samples will be stored as unidentified, unlinked or coded samples and the general process for doing so.*]

The biological materials will be stored in security protected collections belonging to and managed by [*xxxxx*]. We will use the following security measures to protect your samples/information *(describe security methods).* The information in the repository will be available only to scientists who have approval to do research studies. [*Indicate whether the materials will only be available for research purposes to faculty and staff of IUPUI/Clarian or whether they will be made available to outside investigators*.][*If specimens are identifiable, indicate which individuals will have access to the identifiers, e.g., only the PI]* [*Explain how access will be given to investigators who need the materials for research purposes, e.g., a steering committee, PI, etc., have to approve]*.

(Depending on the research, consider offering the following options, if possible: permitting only unidentified or unlinked use of their biological samples in research, permitting coded or identified use of their biological samples for one particular study only, with no further contact permitted to ask for permission to do further studies, permitting coded or identified use of their biological samples for one particular study only, with further contact permitted to ask for permission to do further studies, permitting coded or identified use of their biological samples for any study relating to the condition for which the sample was originally collected, with no further contact allowed to seek permission for other types of studies, permitting coded or identified use of their biological sample for any study related to the condition for which the sample was collected with further contact allowed to seek permission for other types of studies).

RISKS OF TAKING PART IN THIS EFFORT:

The physical risks associated with participation in this effort are *[list risks of sample acquisition, if any]*

[If appropriate, include the following: The major risk of your participation is the possible risk of loss of confidentiality of private medical information. In addition, since DNA can be extracted from these tissues, potentially harmful information could be gained (for example, paternity). If we utilize your DNA,

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Appendix V – SAMPLE – Repository Informed Consent Document

you should realize that every person's DNA is unique; therefore, it may be possible some day that someone could find out who you are just from knowing your DNA sequence.]

(If tests results will be shared, list the potential fiscal, psychological, and social risks of disclosure of test results.)

(If genetics studies will be performed, include the risks of participating in genetic studies including the effects of the knowledge that one is the carrier of a disease gene that might affect their life course, employability or insurability, if results will be shared. If subjects want to be told list the precautions that will be taken to minimize the potential harm of receiving bad news and to preserve the confidentiality of the results

Also include the risks stigmatization of a subject or group, discrimination in insurance or employment, generation of conflict within a family, harm to relatives, inappropriate commercialization of findings, or use of samples in projects objectionable to the subject, if applicable)

Since we do not yet know the exact questions that will be studied by scientists in the future, we cannot tell you what specific information they will be looking at or what that might mean to you.

[Describe procedures to minimize risks such as: Any materials that are collected will be collected by experienced technicians to reduce the chance of any physical harms, etc.]

BENEFITS OF TAKING PART IN THE EFFORT:

This is a research effort and is not intended to provide any direct health benefit to you. The benefits of research using tissue or data include learning more about (*list subjects*). This information may be valuable in preventing, treating, or curing (*list diseases or conditions if known*) in the future.

CONFIDENTIALITY:

Every effort will be made to keep your personal information confidential. In order to protect the confidentiality *[list procedures to protect confidentiality, as applicable. For example:*

1. *we will ensure that your personal information file is kept separate from the file containing information learned from your biological material and that the connections between these two files are secured by coding all identifiers,*
2. *the files can only be accessed by a limited number of staff,*
3. *files will be made secure by encryption (use of a secret code unknown to unauthorized personnel) and will be maintained and accessed only by authorized staff*
4. *the Repository Manager has been assigned to manage the storage bank and is the only person able to relate your medical information to your name or identity. Should the storage bank ever be closed in the future, all identifying information about you will be removed so that it will never be possible to trace the information back to you.*
5. *The medical information you contribute to the storage bank will not be released to any insurance company, potential employer, government agent or agency, family member, or friend.*

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Appendix V – SAMPLE – Repository Informed Consent Document

6. *A certificate of confidentiality has been obtained from the federal government. This certificate will allow the researchers to protect your private information in cases where law enforcement officials may request it, such as with a subpoena].*

Your personal information may be disclosed if required by law, to federal regulatory agencies such as the Office of Human Research Protections, the Food and Drug Administration, and to the Institutional Review Boards and their designees. *[If applicable: In addition, your original medical records may be reviewed by the Institutional Review Board or its designees, or regulatory agencies.]*

If the results from any research study of your tissue/medical information are ever published for scientific purposes, your name and identity will remain confidential and will not be mentioned in any reports.

The Repository Manager will release medical information for research purposes to answer specific research questions, but only when each scientist has received approval from the Institutional Review Board (IRB) responsible for overseeing this repository.

ALTERNATIVES TO TAKING PART IN THE EFFORT:

The alternative to participation in this research is to not give tissue or data to the repository. This will not alter your care or your relationship to any of your physicians. [*If applicable if samples are identifiable: You may also withdraw your tissue or data at any time by contacting xxxx at (telephone number) No further use will be made of the samples/information you gave.]*

COSTS/COMPENSATION:

There is no cost to you for participating. There is no compensation provided for participation. Donating biological materials is an act purely to aid future medical research. In the event of physical injury resulting from your participation, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

RECONTACT FOR FUTURE USE [Use this section only if samples are identifiable]

In the future, researchers may design a particular research study that requires use of the biological material you have given as well as additional samples and/or information. If, in the future, we would like to obtain additional samples or information, we will need to contact you to request your permission. Please indicate below whether or not you give permission for us to contact you about obtaining more information.

☐ I give my permission for researchers to contact me about obtaining additional samples and/or information.

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- ☐ I do not give permission for researchers to contact me about obtaining additional samples and/or information.

(For genetic studies, if the research investigator wishes to contact relatives of a proband, the proband must be asked whether this contact is acceptable. If the proband declines to allow contact of relatives, the project may not proceed. If permission is granted for contact, the investigator must design a separate consent form to address the issue of information that may be forthcoming from the research project. The relatives should be given the option to decide whether they are willing to contribute samples. If they are willing to give their specimens, they must be given the option of accepting or declining information derived from the research study.)

CONTACTS FOR QUESTIONS OR PROBLEMS:

For questions about this collection effort or a research-related injury, contact the researcher managing the collection of samples, *[PI]* at *[telephone number]*.

For questions about your rights as a research participant or complaints about a research study, contact the IUPUI/Clarian Research Compliance Administration office at 317/278-3458 or 800/696.2949.

Due to unforeseen circumstances such as flood, fire, earthquake, tornado or electrical failure, your human biological materials may need to be discarded.

VOLUNTARY NATURE OF PARTICIPATION AND WITHDRAWAL:

Taking part in this effort is voluntary. You may choose not to take part at this time. Also, you may agree to have your material stored and later decide that you want to withdraw it from storage. If so, you should call the investigator listed above and tell him or her to discard your sample or remove all personal identifiers. He, or she, will then discard your sample or remove the identifiers, but any data that has been obtained from testing your biological material until that point will remain part of the research.

(Indicate whether the subject can obtain future access to the stored samples for information that may be of clinical relevance to him/he. Similarly, subjects must be told if such information will not be available in the future (e.g. because personal identifiers are to be removed).)

(*If identified material is to be de-identified for use, indicate what consideration has been given to the fact that de-identification may deny the donor or the donor's descendants of assured or implied access to results of research.)*

COMMERCIAL USE OF HUMAN BIOLOGICAL MATERIALS:

As this is a research institution, specimens obtained in medical situations may later be used for research purposes. The investigator intends to include specimens taken from you along with other specimens that may also be used in an attempt to develop products to be sold, and it is not the intention of the

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investigator to enter into an agreement with you to become partners in sharing the profits or losses in the sale of those products.

SUBJECT'S CONSENT:

In consideration of all of the above, I give my consent to participate in this collection effort.
I acknowledge receipt of a copy of this informed consent statement.

SUBJECTS SIGNATURE:_____ Date:_____
(must be dated by the subject)

(IF SUBJECT IS A MINOR:)
SIGNATURE OF PARENT:_____ Date:_____

SIGNATURE OF PARENT:_____ Date:_____

(AGE 7 AND ABOVE:)
SIGNATURE OF CHILD:_____ Date:_____

SIGNATURE OF WITNESS:_____ Date:_____
(person obtaining consent.)

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Appendix W – SAMPLE – Repository Usage Agreement

[NAME OF REPOSITORY]

USAGE AGREEMENT

The recipient acknowledges that the conditions for use of this research material are governed by the IUPUI/Clarian Institutional Review Board [IRB-xx] in accordance with Department of Health and Human Services regulations at 45 CFR 46. The recipient agrees to comply fully with all such conditions and to report promptly to the [NAME OF REPOSITORY] Principal Investigator any proposed changes in the recipient's research project and any unanticipated problems involving risks to subjects or others. The recipient remains subject to applicable State or local laws or regulations and IUPUI/Clarian policies that provide additional protections for human subjects.

The research material provided to the recipient may be utilized only in accordance with the conditions stipulated in this Usage Agreement, as approved by the IUPUI/Clarian IRB, as follows:

- The recipient will receive no information that could identify the subject.
- If the recipient requests identifying information, the personnel of the [NAME OF REPOSITORY] will not provide it.
- The recipient may not contact individuals who are collecting the material to obtain any identifying information.
- All material is identified by a code number that is assigned by the [NAME OF REPOSITORY] for tracking purposes.
- Subject information will be kept confidential … (describe specifics, e.g., "in a locked file that can be accessed only by [name of repository personnel" or "in password-protected computer files in a secure, non-public area and can only be accessed by [name of repository] personnel").
- In addition to the research material itself, at the recipient's request, the [NAME OF REPOSITORY] may provide the recipient with the following information about the subject/material:

  List specific variables that the Repository PI would be willing to share with recipients, e.g., sex, age, race, weight, diagnosis, etc.

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Appendix W – SAMPLE – Repository Usage Agreement

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Any use of this material beyond the terms of this agreement requires prior review and approval by the IUPUI/Clarian IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an application Office of Human Research Protections approved Federalwide Assurance.

_____ _____

[NAME], Principal Investigator Date
[NAME OF REPOSITORY]

_____ _____

Recipient Investigator Date

Recipient Investigator's Project Title:_____

IRB Approval Date:_____

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Appendix X – SAMPLE – Submittal Agreement for Biologic Specimens

(See #8 of OHRP Guidance Document)

[This document is used when investigators at non-IUPUI/Clarian or affiliated institutions are collecting specimens, with Informed Consent from subjects, and sending those specimens to a specimen repository located at an IUPUI/Clarian or affiliated facility. The non-IUPUI/Clarian investigator is the "collector-investigator" and the IUPUI/Clarian investigator is the "recipient-investigator".

SUBMITTAL AGREEMENT FOR BIOLOGIC SPECIMENS

I, the collector-investigator, affirm that I will not provide the IUPUI/Clarian recipient-investigator access to the identities of the donor-subjects or to information through which the identities of the donor-subjects could readily be ascertained.

A copy of my IRB-approved Informed Consent Document for the collection of these specimens is attached.

IUPUI/Clarian Recipient-Investigator's Name:_____

Collector-Investigator's Name:_____

Collector-Investigator's Institution:_____

Institution's Federalwide Assurance Number:_____

Collector-Investigator's Signature:_____

Date:_____

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Appendix Y – SAMPLE – Physicians Orders and Authorization to Dispense Study Drug Signature Log

Principal Investigator: Jane Doe, MD
Site Name: Indiana University
Department: Outpatient Clinical Research Facility
Location: 535 Barnhill Drive, Room 150
Indianapolis, IN 46202

Study Title:
Protocol:

PHYSICIAN ORDERS

- Study drug(s) may be dispensed by those who are authorized by the Principal Investigator. This may include the nurses (LPN, or RN) within this department and the MDs who are listed as sub-investigators on the IRB form Summary Safeguard Statement.
- Study drug(s) will be dispensed according to the dose, route and frequency written in the specific protocol.
- Standing additional orders may be written and placed in the individual subject chart.
- Used and unused study drug(s) will be collected back from the subject(s).
- Subjects will be properly instructed in the use and precautions and potential known risks to the study drug(s).
- Study drug(s) will be properly accounted for and tracked with adequate documentation.
- If titration/dosing changes occur, dosing errors are made, ~or~ protocol dosing changes are purposely made to better treat the subject, then there must be a physician written source document, order, or prescription that states the change in the orders.

Specific Instructions/Orders:

Principal Investigator Signature:_____ **Date:**_____

The following individuals are authorized by the Principal Investigator to dispense drug(s):

Name (PRINTED)	**Signature & Date**	**Initials**
Investigator Signature & Date		

*Note. This log can be used as a generic form for all studies in which case the study title, protocol, specific instructions would be deleted, or can be protocol specific.

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Appendix Z – Security Plan Outline

This list outlines the elements that should be included in a Security Plan document. Ideally, each research project should have a security plan. However, if research data are managed at the department level, a single department plan that covers all research projects can be created.

1. TECHNOLOGY ENVIRONMENT

a. Identify all hardware where research data are stored or accessed
   i. Make
   ii. Model
   iii. Hard Drive size
   iv. Memory
   v. Operating System
b. Identify the locations of all servers or workstations storing research data
   i. Buildings
   ii. Room Numbers
   iii. Access – is the room locked and who has access
c. Identify software used to store research data (Oracle, SQL Server, Excel, etc.)
d. Identify any special software used as part of this research project
e. Identify the technologies used for remote access to the data
   i. Vendor tools
   ii. Authentication Process

2. **DATA MANAGEMENT and STAFF ACCESS**

a. Identify all research team members who have access to the data
   i. Name and Title
   ii. Department
   iii. Other Affiliation if not a faculty or staff member of IU
   iv. Role
      (1) All Functions
      (2) Read Only
      (3) New Data Entry
      (4) Modify Existing Data
b. Identify who decides which people get access to which data
c. Describe the process for managing data access generated as part of the research project
d. List any classes of data for which there is restricted access within the team
e. Describe the process by which authorization for access to all the data, or specific classes of data, is granted
   i. IU team members
   ii. Non-IU team members
f. Describe the process for terminating access
g. Describe the audit process for documenting access to the data
h. Describe the process for authorizing access to data generated by other parties
i. Describe what data are fed into the database from other systems (either through an automatic interface, or downloaded from one system and uploaded in to the research database)

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Appendix Z – Security Plan Outline

3. **BACKUP/RECOVERY/RETENTION**
   a. Describe the Backup and Recovery process for electronic data
      i. Backup technologies
      ii. Backup frequency
      iii. Recovery testing process and frequency
      iv. Identify where backup data is stored
         (1) Onsite
         (2) Offsite
   b. Describe the backup and recovery process for paper-based data
      i. Backup technologies
      ii. Backup frequency
      iii. Recovery testing process and frequency
      iv. Identify where backup data is stored
         (1) Onsite
         (2) Offsite
   c. Describe the long-term archival for data once a research project has concluded
      i. Location of archived materials
      ii. Retention period
      iii. Location of inventory record of archived materials
      iv. Location of contracts from third-party storing archived materials

4. **DATA PROTECTION**
   a. Describe the process for keeping servers and workstations updated with the most current anti-virus software.
      i. Software used
      ii. Scanning frequency
   b. Describe process for protecting data stored on mobile devices (laptops, tablets, PDAs)
   c. Identify where removable media (diskettes, CDs, zip cartridges, removable drives, audio or video tapes) are stored when not in use
   d. Identify where printed data are securely stored
   e. Describe the protections in place to secure information sent by email
   f. Describe the process for logging and tracking data (in any form) that is being moved to a different location
   g. Describe the process for secure disposal of data from:
      i. Hard drive
      ii. Removable media
      iii. Tape
      iv. Print

A sample plan is available upon request from the Information Services and Technology Management (ISTM) unit. If an individual or department needs assistance with the development of a plan, they should contact the ISTM Help Desk at 274-5336 or iusmot@iupui.edu

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Appendix AA – Suggested Files for the Regulatory Binder

Many items on this list are typically needed for all types of research studies. Some items need to be documented for FDA approved studies, and many NIH/VA multi-center studies. However, each study may have its own specific requirement.

For all types of research studies, the following items should be included:

1. Dated, documented IRB approval of the following:
   a. all protocol versions;
   b. all amendments;
   c. all informed consent versions (or documentation of waiver of informed consent or waiver of written informed consent);
   d. authorization form, waiver of authorization, or documentation that neither are required;
   e. all continuing review forms;
   f. any written information to be seen by the subjects, including advertisement(s) for subject recruitment, subject compensation, and/or informational sheets or pamphlets, if any; and
   g. any other documents that are given IRB approval.
   h. Any formal communications to and from the IRB.
2. Any reported events that require prompt reporting to the IRB.
3. Original signed and dated informed consent forms (may be kept in regulatory or study subject binder) documenting they were obtained prior to the subject's participation in the study , if applicable.

For other types research studies, as applicable, the following items should be included:

1. MedWatch, IND Safety Reports, and relevant sponsor communication.
2. Written concurrence of a licensed physician and a brief description justifying the use of a drug or device without obtaining informed consent
3. Subject screening log, identification code list (master study participant listing) and enrollment log.
4. Signature sheet documenting the signature and initials of all persons authorized to make entries and/or corrections of the CRFs/study forms or Delegation of Authority/Activities log.
5. Record of retained body fluids/tissue samples (if any).
6. The financial disclosure form if required by the sponsor.
7. Investigational products accountability log/sheet at the site (if applicable).
8. Case history, including:
   a. Case Report Forms;
   b. Supporting data, including medical records (i.e. progress notes of the physician, subject's hospital chart, nurses' notes), data on subject's condition and history previous to the study, during the study, and results of all diagnostic tests, and a record of exposure to the drug or device, date and time of exposure, and any other therapy;
   c. Protocol with documentation of dates and reasons for any changes; and
   d. Any other records that are required to be maintained by regulation (i.e. FDA) or specific requirement for a category of investigations or a particular investigation.
9. Institutional Review Board composition or letter from the IRB with the Assurance number.
10. Regulatory authority(ies) authorization/approval/notification of protocol approval (where required).

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Appendix AA – Suggested Files for the Regulatory Binder

11. Curriculum Vitae and/or other relevant documents evidencing qualifications of investigator and sub-investigators.
12. Normal values/ranges for medical laboratory/technical procedures and/or tests included in the protocol for all laboratory facilities.
13. Lab certificates for all facilities.
14. Instructions for handling of investigational products and trial related materials (if applicable) as well as Clinical Investigational Brochures, package inserts or device descriptions
15. Shipping records for investigational products and trial related materials (if applicable).
16. Decoding procedures for blinded trials.
17. Report documenting monitoring/oversight visits.
18. Relevant communications other than site visits (i.e., letters, meeting notes, notes of telephone calls, required reports) between sites or other investigators, sponsors and oversight agencies other than the IRB.
19. 1571/1572 and other sponsor or Federal "agreements"
20. Contact information for all persons involved in the study

For studies involving investigational devices:

1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
2. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering and during the course of the investigation, including information about relevant pervious medical history and the results of all diagnostic tests.
3. A record of exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

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Appendix BB – Important Points When Undertaking Drug Studies

1. Have overall plan for the study:
   - Define and document who can write orders for study drugs (investigator and sub-investigators listed on the IRB form Summary Safeguard Statement and the Form 1572 if an IND study).
   - Define and document who can dispense study drugs.
   - Have signature and initial list for all involved in study.
   - Discuss how the study will be carried out and how access will be limited to appropriate staff.
   - Delineate where the study drugs will be stored in a locked secure area.
   - Define what labeling must go on any drug container dispensed.
   - Plan for the long-term retention of all study documents.

2. Have all study paperwork in order:
   - Make sure order(s) for study drug appear(s) on subject's record.
   - Maintain drug accountability for all dispensing that includes date dispensed, name or code of subject, quantity and dose dispensed, quantity remaining, initials of person dispensing.
   - Retain all shipping records, and document initial receipt and quantities on the accountability log.
   - Document accountability of returned doses if returned to Sponsor or destruction if allowed by Sponsor (destruction of study drug on site should be witnessed and documented).
   - If storage of drug requires use of refrigerator or freezer, maintain appropriate daily log of storage temperature.
   - Keep current protocol and amendments in study binder as well as IRB approval letters and IRB correspondence.
   - Maintain copies of all correspondence with study Sponsor.
   - Maintain copies of all internal and external unanticipated problems involving risks to subjects or others and noncompliance reports.