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OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

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**SOP Title: TRANSFER OF PROTOCOLS BETWEEN INSTITUTIONAL REVIEW
BOARDS (IRBS)**

**Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB
Chairs, IRB Administrators, Protocol Navigators**

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SOP 27 - TRANSFER OF PROTOCOLS BETWEEN INSTITUTIONAL REVIEW BOARDS (IRBS)

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SOP 27 - TRANSFER OF PROTOCOLS BETWEEN INSTITUTIONAL REVIEW BOARDS (IRBS)

27.1 PURPOSE

This Standard Operating Procedure (SOP) addresses administrative actions to be considered by Institutional Review Boards (IRBs), engaged institution(s), and investigators when non-exempt human subjects research is transferred from one IRB to another.

27.2 POLICY

Transfer of previously approved protocols from one IRB to another should be accomplished in a way that assures continuous IRB oversight with no lapse in either IRB approval or the protection of human subjects and with minimal disruption to subjects and research activities. Office of Human Subjects Research Protections (OHSRP) is delegated to provide oversight for the protocol transfer process relating to NIH intramural IRBs.

When transferring protocols, prior approval must be sought from the NIH Investigator's IC Officials (Clinical Director (CD) or Scientific Director (SD), as appropriate, and from the Director, OHSRP who will obtain input from the NIH IRB Chair(s).

When transferring between the NIH and a non-NIH institution, a written protocol transfer agreement is required and a reliance agreement may be required. Transfers between NIH IRBs should have a written agreement. For more information for the requirements for reliance, see SOP 20A - Obtaining a Reliance (Authorization) Agreement at the NIH.

27.3 DEFINITIONS

- A. **Human Subjects Research:** In this SOP, this term refers to activities which: (1) meet the 45 CFR 46 definition of research (45 CFR 46.102(d)); (2) involve human subjects, according to 45 CFR 46.102(f), and (3) are **not** exempt from IRB review under the provisions of 45 CFR 46 under 45 CFR 46.101(b). The term "human subjects research" in this SOP, therefore, always means non-exempt human subjects research. (Note that this defined term differs from

terminology used in other SOPs, where “human subjects research” also includes research that is exempt from the requirements of 45 CFR 46.)

- B. **Investigator:** Any individual who is involved in conducting human subjects research studies. Such involvement includes: (1) obtaining information about living individuals by intervening or interacting with them for research purposes; (2) obtaining identifiable private information about living individuals for research purposes; (3) obtaining voluntary informed consent of individuals to be subjects in research, and/or (4) studying, interpreting, or analyzing identifiable private information or data for research purposes (see OHRP: Frequently Asked Questions: Who are “investigators”? in **References** and SOP 19 - Investigator Responsibilities).
- C. **IRB of Record:** The IRB responsible for review of research and determining that the research meets IRB regulatory requirements for approval.
- D. **Memorandum of Understanding:** A written agreement between two or more entities (such as research institutions, government agencies) that outlines the terms and details of an agreement between the parties, including each party’s expected activities and goals.
- E. **Original IRB:** The IRB that transfers oversight responsibility to another IRB
- F. **Receiving IRB:** The new IRB that accepts responsibility of IRB oversight of the protocol from the original IRB
- G. **Sponsor:** A person (or other entity) “who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A[n] [entity] other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct a clinical investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators” (21 CFR 50.3(e); 21 CFR 56.102(j)).
- H. **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 to, or used involving, a subject. The term does not include any person other than an individual, e.g.,

corporation or agency” (see 21 CFR 312.3 and 21 CFR parts 50.3(f) and 56.102(k)).

I. Types of Protocol Transfers Between IRBs:

1. Transfer between NIH IRBs
2. Transfer from an NIH IRB to a non-NIH IRB
3. Transfer from a non-NIH IRB to an NIH IRB

27.4 PROCESS FOR TRANSFER OF PROTOCOLS BETWEEN IRBS

The transfer process will vary based on the type of transfer. Transfers may be temporary or permanent (see **27.4.2.G** below) and may involve one or more protocols. Per **27.2** above, transfers of protocols in or out of the NIH require a written agreement that addresses **27.4.1** and, as applicable, **27.4.2** and/or **27.5**. When transferring within the NIH, a memorandum or other written agreement should be established, outlining the responsibilities of each IRB in the transfer. OHSRP should be consulted to provide approval for transfer of protocols and may be consulted regarding the written agreement.

27.4.1 BASELINE RESPONSIBILITIES AND DOCUMENTATION

The following responsibilities are to be satisfied and appropriately documented in a written agreement when applicable:

- A. Identify those studies for which IRB oversight is being transferred: One of the first actions in the transfer process is determining those studies for which IRB oversight is being transferred to ensure effective planning and continuity.
- B. Establish an effective date for transfer of oversight for the clinical investigation(s):
 1. A transfer date for each protocol for which oversight is being transferred should be determined. Such an action promotes continuity, helps prevent a lapse in IRB coverage, and minimizes confusion regarding which IRB is responsible for review and action if, for example, an unanticipated problem should arise or research needs to be quickly suspended or terminated.

2. The exact transfer date may be specified in advance or the date may be made contingent upon the review and acceptance of the research project by the receiving IRB. When a large number of research projects are being transferred, it may be preferable to phase-in the transfer over a period of weeks or months to facilitate a smooth transition. If oversight is being transferred because of the closure of an IRB, the original IRB should inform all investigators and/institutions, as appropriate, of the pending closure date.
3. If there is difficulty working out effective dates for protocol transfers between IRBs, please contact OHSRP.

C. Ensure the availability and retention of pertinent records:

1. Availability of records:

- a. If the original and receiving IRBs are both within the intramural research program (IRP), records regarding the research projects affected by the transfer must be transferred to the appropriate electronic system for the receiving IRB (PTMS, iRIS™ etc.).
- b. If both the original and receiving IRBs are not within the IRP, before the receiving IRB accepts oversight of the transferred research project, it should obtain copies of all pertinent records.
- c. The original IRB should make pertinent records available to the receiving IRB as follows:
 - i. Scientific Review(s)
 - ii. Research protocol
 - iii. Consent form(s)
 - iv. Investigator's brochure (or other relevant attachments)
 - v. Continuing Review (CR) memorandums or other progress reports submitted by the investigator for review by the IRB
 - vi. Statements of significant new findings provided to subjects

- vii. Copies of all correspondence between the IRB and the investigator
 - viii. Any other relevant submissions to the IRB, including but not limited to amendments and reports of problems.
- d. The receiving IRB should also obtain meeting minutes from the original IRB's reviews of the protocol as this information may be critical to the receiving IRB's assessment of the adequacy of the previous review (e.g., discussion of controverted issues, quorum, etc.).
 - e. Both the original IRB and the receiving IRB should maintain adequate records regarding the research projects affected by the transfer. Such records should include any written agreement between the original and receiving IRBs, the title of the protocols being transferred, the research sites affected, the names of the investigators, the identities of the original IRB and the receiving IRB, and the date(s) on which the receiving IRB accepts responsibility for oversight of the research projects. In addition, the original and receiving IRBs should keep records of all communications to all affected investigators. For more information about retention of IRB records, see SOP 4 - Human Research Protection Program (HRPP) Documentation and Records.
2. Retention of IRB records: An engaged institution must be able to access documentation of IRB activities and records relating to the research project for at least 3 years after completion of the research at the engaged institution (45 CFR 46.115(b)). In addition, the records must be accessible for inspection and copying by OHRP at reasonable times and in a reasonable manner. If the receiving IRB is an NIH IRB, IRB records relating to the protocol shall be retained for at least 3 years after completion of the research as per SOP 4 - Human Research Protection Program (HRPP) Documentation and Records. Factors to consider in selecting an appropriate record retention arrangement may include the reasons for the transfer, as well as the nature of the research projects and the records.

27.4.2 ADDITIONAL RESPONSIBILITIES AND DOCUMENTATION

The following responsibilities should be considered. If applicable, the responsibilities should be implemented and appropriately captured in the written agreement between the parties.

A. Conduct a review of the study(ies) by the receiving IRB, where appropriate, before it accepts responsibility for the study(ies):

1. Continuing Review of research when transferring between NIH IRBs:
 - a. When the research project is transferred from one NIH IRB to another NIH IRB or the research project remains at the same engaged institution, the receiving IRB is not required to review the project prior to the next CR date established by the original IRB, however such a review may be done depending on the circumstances of the transfer and characteristics of the specific research project. The receiving IRB may decide to undertake an initial review (IR) or a CR (either by the convened IRB or under an expedited review procedure, if appropriate).
 - b. Alternatively, the receiving IRB may decide not to conduct any review prior to the next continuing review date established by the original IRB; especially if such a review is not deemed to substantively add to human subject protections. In such a circumstance, some receiving IRBs nonetheless may request that the IRB chairperson, another IRB member, an IRB administrator, or another qualified administrative staff member perform an informal assessment of the research project.
2. Initial or Continuing Review of research by the receiving NIH IRB when being transferred from a non-NIH IRB: When the research project moves to the NIH and responsibility for review is transferred to an NIH IRB, the receiving IRB must conduct an IR or CR of the research project before the NIH becomes engaged in the human subjects research project (45 CFR 46.103(b)) unless there is a reliance agreement in place for the NIH to rely on the original IRB at the original institution in which case a new IR or CR is not necessary. It may be appropriate for a protocol amendment to be submitted to the original IRB to notify them of the change in location of the research.
3. Initial or Continuing Review of research by the receiving non-NIH IRB when being transferred from an NIH IRB: When the NIH research project moves to a new institution and responsibility for review is transferred to another IRB, the non-NIH IRB is expected to conduct an IR or CR of the research project before the new institution becomes engaged in the human subjects research project (45 CFR 46.103(b)). In such a case, a protocol amendment must be submitted to the NIH IRB to notify them of the change in location of the

research. This amendment may constitute a minor change to the research, in which case the NIH IRB may choose to use expedited procedures to review.

4. Suspension or Termination: Receiving IRBs have the authority to suspend or terminate approval of research under certain circumstances, for example, when the research project is not being conducted in accordance with the receiving IRB's requirements or has been associated with unexpected serious harm to subjects (45 CFR 46.113). IRBs should ensure that the rights and welfare of currently enrolled subjects are protected, subjects are not put at risk, and subjects receive appropriate care during any period in which the IRB and clinical investigator are attempting to resolve any issues. The receiving IRB must also promptly report, including the reasons for the suspension or termination, to the investigator, institutional officials and, if at NIH, also to OHSRP who will subsequently report the suspension or termination of IRB approval to OHRP (45 CFR 46.103(b)(5)).

B. Confirm or establish the date for the next continuing review:

1. If the receiving NIH IRB performs a review at the time of research project transfer (whether an IR or a CR), it may choose to maintain the anniversary date established by the original IRB or establish a new date of approval. If it is decided that a new anniversary date will be established, the new date must be within one year of the receiving NIH IRB's approval. For more information about establishing and maintaining anniversary dates, see SOP 9 - Continuing Review by the Convened IRB.
2. If the receiving NIH IRB does not conduct an IR or CR at the time of transfer, the date of research project approval by the original IRB is presumed to remain in effect for the full approval period established at the time of the most recent review by the original IRB.
3. In the unforeseen circumstance that the protocol is transitioning close to its expiration date, in order to avoid a lapse in IRB review, if the receiving IRB is unable to complete the CR prior to the current expiration date of the protocol, the original IRB should provide the review and the effective date of the transfer should be updated accordingly.

C. Determine whether the consent form needs to be revised:

1. Under 45 CFR 46.116(a)(7), the informed consent document is required to contain “[a]n 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”. Therefore, if a change in IRB oversight results in changes in the contact information regarding subject rights and/or whom to contact in the event of research-related injury, the new contact information must be provided promptly to subjects (45 CFR 46.116(a)(7)). For subjects who were previously enrolled, this may be accomplished in a number of ways, for example, with a letter providing the relevant contact information. For new subjects, the informed consent, assent, and/or parental permission form must be revised to reflect the new contact information (45 CFR 46.116(a)(7)).
 2. Other changes to the consent form may also be necessary if the receiving NIH IRB requires modifications to the consent form at the site(s) under its jurisdiction as a condition of approval (e.g., changes in template language, changes in risks, etc.) (45 CFR 46.109(a) and (b)). The required changes may be conveyed to the investigator as stipulations to secure IRB approval for the research at that site or sites (see, e.g., 45 CFR 46.109(a)).
- D. Notify the key parties (e.g., investigator, Data Safety Monitoring Board, Office of Protocol Services (OPS), etc.) of the transfer of responsibility of IRB review as soon as possible, and provide contact information of the receiving IRB.
- E. Address IRB regulatory issues: If an NIH IRB is the receiving IRB, the processes for reviews and actions should be consistent with the NIH HRPP SOPs. Problem reports submitted for potential unanticipated problems, protocol deviations or noncompliance should be reviewed by the appropriate IRB (original vs. receiving IRB) based on the effective date of the transfer. As such, IRB review of potential unanticipated problems, deviations and noncompliance should follow applicable NIH HRPP policies (see SOP 16 -Reporting Requirements for Unanticipated Problems, Adverse Events, and Protocol Deviations, and SOP 16A - Allegations of Non-compliance with Requirements of the NIH Human Research Protection Program (HRPP)).
- F. Central IRBs: For studies for which the original IRB acts as a central IRB, those local institutions/IRBs that have written agreements to rely on the original IRB for review responsibility should be notified that responsibility for the study is now being transferred to a new central IRB (receiving IRB). Local institutions/IRBs should be given the option to enter into new written agreements with the

receiving IRB or opt out of the central review arrangement if they do not believe central review by the receiving IRB is appropriate for their local institution.

G. Temporary Transfers: Sometimes the transfer to a receiving IRB is temporary and the responsibility for IRB review eventually will revert back to the original IRB. This may be the case when a natural disaster temporarily disrupts the functioning of an IRB. In such instances, the transfer procedure back to the original IRB may only involve:

1. Identifying studies for which IRB oversight is being transferred;
2. Ensuring availability and retention of pertinent records;
3. Establishing an effective date for transfer of oversight; and
4. Notifying the key parties.

Appropriate actions depend on the specific circumstances of the transfer.

27.4.3 PROCESS FOR TRANSFER OF PROTOCOLS THAT ARE ALSO FDA REGULATED

Further considerations for FDA-regulated research in addition to the above:

Entities involved in a transfer of IRB review responsibilities for a clinical investigation include not only the original IRB and the receiving IRB but also involve the sponsor who initiates the clinical investigation and the clinical investigator who conducts the investigation. The investigator may also be the study sponsor (sponsor investigator) (see SOPs 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications, 15A - Research Regulated by the Food and Drug Administration (FDA): Information and Policies Specific to Research Involving Investigational New Drugs (Including Biological Products) and 15B - Research Regulated by the Food and Drug Administration (FDA): Information and Policies for Investigational Device Exemption (IDE) Applications for additional information related to conducting FDA regulated research).

The process for transfer of protocols regulated by the FDA is very similar to the steps listed above (see FDA: Guidance for IRBs, Clinical Investigators and Sponsors Considerations When Transferring Clinical Investigation Oversight to Another IRB in **References** below). Additional requirements and concerns regarding FDA regulated clinical investigations include the following:

A. Ensure the availability and retention of pertinent records:

1. Access: Since FDA may require access to the records at any reasonable time, it is important for the parties to agree which entity (e.g., the original IRB, the receiving IRB, the institution that housed the original IRB, a Contract Research Organization (CRO) or other responsible third party) will maintain the records once clinical investigation oversight has been transferred. Whichever party assumes responsibility for the records is responsible for ensuring that they are retained in accordance with 21 CFR 56.115(b).
2. Availability of pertinent records: In addition, the original and receiving IRBs should keep adequate records of all communications to all affected sponsors, clinical investigators, and FDA, and comply with all other recordkeeping requirements
3. Retention of records: There may be circumstances where the original IRB reaches an agreement with the receiving IRB to retain some of the documentation for the transferred trials, yet may not be able to commit to retaining the documents for at least 3 years after the completion of the research (21 CFR 56.115(b)). This situation may arise, for example, where an IRB ceases operations yet retains responsibility for some records for trials that are still ongoing, either by physically maintaining these records or by reaching a storage arrangement with a responsible third party. In this instance, the original IRB should contact the FDA to discuss possible retention arrangements.

B. Notifying key parties: After IRB transfer of oversight for the clinical investigation is complete, the sponsor must update the associated IND or IDE with the name and contact information of the receiving IRB, and should include the effective date of transfer.

C. Suspensions and terminations: The NIH sponsor reporting policy/ies should be considered and addressed as applicable (see SOP 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications). For example, if an NIH IRB terminates or suspends its approval of a trial, the PI will inform the sponsor, and OHSRP will report the suspension or termination of IRB approval to FDA (21 CFR 56.108(b)) (see SOP 11 - Suspensions and Terminations of IRB Approval and Administrative Holds and SOP 24 - OHSRP Reporting to the Office for Human Research Protections

(OHRP) and the Food and Drug Administration (FDA) Regarding Unanticipated Problems, Serious or Continuing Noncompliance, or Terminations or Suspensions).

- D. Contacting FDA: An original or receiving IRB may have questions that are not resolvable through communications with the sponsor or clinical investigator. In such situations, either IRB may contact FDA for additional guidance. Affected sponsors and clinical investigators may also contact FDA in these situations.

27.5 ADDITIONAL CONSIDERATIONS

- A. The protocol transfer should strive to establish mutually agreed upon and realistic timelines for transfer which assures continuous IRB oversight with no lapse in IRB approval or the protection of human subjects and which will result in minimal, if any, disruption of research activities.
- B. At NIH, plans for protocol transfers should include the various NIH stakeholders, such as the study PI, Clinical Director (CD), Scientific Director (SD), OHSRP, sponsor and OGC, as appropriate.
- C. A comprehensive checklist of items to be included in the protocol record may be provided to the original non-NIH IRB that will transfer the protocol to a receiving NIH IRB.
- D. IRB composition: The receiving NIH IRB should have members with sufficient background to promote complete and adequate review of research activities associated with the protocol being transferred (e.g. for research regulated by the FDA, the Board must be able to apply FDA regulations in its review). For more information about NIH requirements for composition of its IRB, see SOP 2 - IRB Membership and Structure and SOP 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications.
- E. Consideration needs to be given to database compatibility between systems used by the original and receiving IRBs.
- F. When the receiving IRB is an NIH IRB:

1. The NIH IRB may consider auditing the study records of the original IRB, and concerns outlined in the audit report should be addressed prior to protocol transfer.
2. Applicable study records (as noted in **27.4.1.C**) covering at least the prior 3 years should be transferred (preferably electronically) to the receiving NIH IRB.
3. The NIH IRB should ensure that there will be an appropriate data and safety monitoring plan in place and such information may be included in the protocol and described in the transfer agreement, if appropriate.
4. Scientific Review: If the NIH IRB is receiving a protocol from a non-NIH IRB and the outside protocol is funded by an NIH grant, there is no need to address scientific review. Otherwise, the IRB will forward information to the CD about what scientific review, if any, occurred, and the CD will decide if it is adequate.

REFERENCES

- A. FDA: Guidance for IRBs, Clinical Investigators and Sponsors Considerations When Transferring Clinical Investigation Oversight to Another IRB:
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM307779.pdf>
- B. 21 CFR 50-Informed Consent and Children:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50>
- C. 21 CFR 56- Institutional Review_Boards:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56>
- D. 21 CFR 312-Investigational New Drugs:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312>
- E. OHRP: Frequently Asked Questions: Who are “investigators”? :

<http://www.hhs.gov/ohrp/policy/faq/investigator-responsibilities/who-are-investigators.html#>