

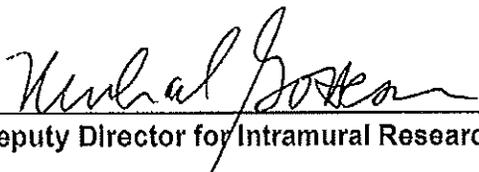
**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &
IMPLEMENTATION**

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: 4

**SOP Title: HUMAN RESEARCH PROTECTION PROGRAM (HRPP) DOCUMENTATION
AND RECORDS**

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

Approval:  2/26/14
Deputy Director for Intramural Research Date

Date of Implementation: 2/26/14

Materials Superseded: SOP content unchanged from version 2; revision to Appendix
A- NIH Minutes Format v.2 10/1/2013

SOP 4: HUMAN RESEARCH PROTECTION PROGRAM (HRPP) DOCUMENTATION AND RECORDS

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SOP 4: HUMAN RESEARCH PROTECTION PROGRAM (HRPP) DOCUMENTATION AND RECORDS

4.1 PURPOSE

This policy describes requirements and procedures for recordkeeping by NIH IRBs and the Office of Human Subjects Research Protections (OHSRP). It is consistent with, but does not supersede, other applicable government record policies.

4.2 POLICY

The NIH keeps adequate records of its IRBs' and the OHSRP's activities. These records may be on paper or in electronic format and are stored in the IRB administrative office or on NIH servers. IRB documents will be accessible for inspection and reproduction by the OHSRP, authorized representatives of the FDA, OHRP, sponsors, and other NIH authorized entities. For FDA requirements regarding documentation and records, see SOP 15 "Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications."

4.3 RECORDS KEPT BY NIH IRBs

4.3.1 RECORDS KEPT BY THE IRB ADMINISTRATIVE OFFICE

Records kept by the IRB administrative office include, but are not limited to:

- A. IRB membership rosters (see 4.3.2, below)
- B. IRB Research Protocol Files – All Protocols (see 4.3.3, below).
- C. IRB Research Protocol Files –Additional Documentation for Expedited Reviews (see 4.3.3.B, below).
- D. Copies of convened IRB meeting minutes (see 4.4, below, IRB Minutes).

- E. Training records for IRB members and IRB administrative staff (see SOP 25 “Training Requirements for the NIH Human Research Protection Program (HRPP)”).
- F. Records of IRB quality assurance and quality improvement (QA/QI) activities including QA/QI reports from internal and external site visitors (see SOP 23 “Quality Management System for the NIH Human Research Protection Program (HRPP)”).
- G. Institute-specific IRB operating procedures, if any, approved by OHSRP.

4.3.2 IRB MEMBERSHIP ROSTER

Consistent with requirements set forth in SOP 2 “IRB Membership and Structure”, NIH IRBs will maintain current membership rosters, report membership changes as they occur to OHSRP and verify roster information annually.

4.3.3 IRB RESEARCH PROTOCOL FILES

- A. All Protocols: The IRB will keep a separate file for each research study that is received for review. Each research protocol will be assigned a unique identification number and entered into an IRB tracking system. Each research study file must include the following minimum information, if applicable:
 - 1. Initial IRB application and all related documents (including informed consent forms), for more information see SOP 8 “Procedures and Required Documentation for Submission and Initial Review of Protocols”.
 - 2. All IRB-approved, dated versions of the protocol.
 - 3. Documentation of scientific review or deferral of this requirement by designated Institute officials.
 - 4. For research involving FDA regulated drugs, the Investigator’s Brochure is kept securely.

5. For research involving FDA regulated devices, required documentation is provided and kept (see SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”).
6. Continuing review application and all related documents (see SOP 9 “Continuing Review by the Convened IRB”).
7. Amendments to the research protocol and all related documents (see SOP 10 “Amendment to IRB-approved Research”).
8. Reports of Unanticipated Problems, Adverse Events and Protocol Deviations (see SOP 16 “Reporting Requirements for Unanticipated Problems, Adverse Events, and Protocol Deviations”).
9. Authorization/reliance agreements with the IRB.
10. Material Transfer Agreements (MTAs), including human Material Transfer Agreements (h-MTAs); Cooperative Research and Development Agreements (CRADAs); or other human subjects agreements if provided by the PI.
11. Advertisements or recruiting materials.
12. IRB-approved PI communications that convey significant new findings or other information to subjects.
13. Documentation of all IRB review actions (Section 4.4 IRB Minutes) including the approval period.
14. Documentation pertaining to Data Safety and Monitoring Board reports.
15. Documentation pertaining to audits, investigations, reports of site visits relating to specific protocols, if provided by the PI.
16. All other IRB correspondence with the investigators, and with any other relevant entities associated with the research (See SOP 7B “Requirements for the Conduct of Research Review at a Convened NIH Institutional Review Board (IRB) Meeting” for

more details). Examples include the IRB approval letter with any attachments or requests to the PI for more information and including copies of stipulations describing what is required of Principal Investigators in order to conduct the study.

B. Additional Documentation for Expedited Reviews: IRB actions through expedited procedures must be consistent with requirements set forth in SOP 7A “Requirements for Expedited Review of Research by NIH Institutional Review Boards (IRBs).” IRB records for actions subject to expedited review must include in addition to 4.3.3.A:

1. The specific approval category, if expedited review is appropriate.
2. The approval period.
3. If applicable, approval of waiver or alteration of the consent process.
4. Any other information documenting the expedited review process.

4.4 IRB MINUTES

4.4.1 FEDERAL REQUIREMENTS FOR THE CONTENT OF IRB MINUTES

45 CFR 46.115(a)(2) provides minimal requirements for the content of IRB minutes:

- A. Minutes of the IRB meetings shall be in sufficient detail to show attendance at the meeting;
- B. Actions taken by the IRB;
- C. Any determinations required by the regulations including protocol-specific findings supporting those determinations, and
- D. The vote on these actions including the number of members voting for, against and abstaining; the basis for requiring changes in or

disapproving research; and a written summary of the discussion of controverted issues and their resolution.

4.4.2 PREPARATION OF IRB MINUTES

The minutes may be prepared by the IRB office staff or by a contractor hired for the purpose.

Proceedings from the IRB meeting will be documented in the meeting minutes and available for review at the next regularly scheduled IRB meeting. Once approved by the IRB, the minutes can no longer be revised or altered. Any subsequent corrections may be done through a documented IRB action and the information appended to the minutes. A copy of the IRB-approved minutes will be provided to the Institutional Official (IO) and other authorized officials upon request.

4.4.3 FORMAT FOR IRB MINUTES

The recommended NIH format for minutes (see Appendix A) may be downloaded from OHSRP's website (see List of Links below).

Note: This format is recommended for use by all NIH IRBs, but an NIH IRB may develop its own format as long as the required core elements contained in Appendix A are included.

4.4.4 CONTENT OF IRB MINUTES

Minutes of IRB meetings must include the following:

- A. Meeting date, location, Chair presiding, time meeting convened with a quorum, time adjourned.
- B. Attendance:
 - 1. Names of the primary and alternate members who are present and absent at the beginning of the meeting identifying their status (as scientists, non-scientists, unaffiliated, etc. consistent with requirements set forth in SOP 2 "IRB Membership and Structure"). When alternates attend, the minutes will state the name of the primary member for whom they are substituting and

the reason for their attendance (e.g., the primary member is absent, or is recused).

2. The minutes should document the name and status of members who attended any part of the IRB meeting.
3. Names of primary and alternate members who are participating through videoconference or teleconference. Documentation that they received all pertinent material prior to the meeting and were able to participate actively in all discussions.
4. Name(s) of IRB administrative staff, OHSRP staff, and any consultants and/or guests present.
5. Name(s) of investigators present.

C. Review and vote on the minutes from the previous meeting

D. Announcements and informational items.

E. Documentation of the quorum and voting: The presence of a quorum throughout the meeting must be reflected in the minutes, including the presence of one member whose primary concern is in a non-scientific area. The minutes will indicate, by name, those members who are absent or recused for each vote during the meeting. There will be a notation in the minutes when a member's recusal occurs because of a conflict of interest. Also see Appendix A, page 2, Recommended Format for All NIH IRB Minutes, re Conflict(s) of Interest.

F. In order to document the continued presence of a quorum, each research study reviewed must have a record of the number of votes as follows:

Total #: For (#), Against (#), Abstained (#)
Recused (#; name), Absent (#; name)

G. Review of interim reports, e.g. unanticipated problems; protocol violations/deviations; serious or continuing non-compliance (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)"); suspensions/terminations, etc.(see SOP 11 "Suspensions and Terminations of IRB Approval and Administrative Holds)" and corresponding IRB determinations.

- H. For the review of previously deferred protocols, new protocols, amendments and continuing reviews, the following must be recorded:
1. PI name, protocol number, and complete protocol title.
 2. Determinations of whether or not the IRB Protocol Review Standards are met (see SOP 7 "Requirements for the Ethical and Regulatory Review of Research by NIH Institutional Review Boards (IRBs)").
 3. Discussion and deliberations of controverted issues and how they are resolved.
 4. Evaluation by the IRB of the required elements of 45 CFR 46.111.
 5. Actions taken by the IRB, including separate deliberations and votes on each action including the basis or justification for these actions.
 6. Designating who will review and approve the PI's response to stipulations (e.g., the full committee, a subcommittee, or by the Chair).
 7. Approval period for initial and continuing approved protocols, including identification of research that warrants review more often than annually and the basis for that determination.
- I. Documentation of Specific Findings: Findings of the IRB, and the protocol-specific information justifying these findings, must be recorded in the minutes. These may include, but are not limited to, the following:
1. Alteration or waiver of requirements for informed consent: When approving a consent procedure that does not include or that alters some or all of the required elements of informed consent,

or when waiving the requirement to obtain informed consent, protocol-specific documentation that the research meets the required criteria (45 CFR 46.116(d)).

2. Waiver of requirements for written documentation of informed consent: When the requirements for written documentation of consent are waived, protocol-specific documentation that the research meets the required criteria (45 CFR 46.117(c)).
 3. Research involving vulnerable subjects: When approving research that involves populations covered by 45 CFR 46 Subparts B (pregnant women), C (prisoners), or D (children), the minutes will document the IRB's justifications and findings that regulatory requirements are met or its agreement with information and justifications as provided by the investigator (e.g., whether the signature of one parent is sufficient to enroll a child in research). When the research may involve other groups that are likely vulnerable to coercion or undue influence such as mentally disabled persons or economically or educationally disadvantaged persons, the IRB should document additional safeguards have been included in the study to protect the rights and welfare of these subjects.
 4. Research involving adults who are or may be unable to consent: Document that NIH requirements are satisfied (see SOP 14E "Research Involving Adults Who Are or May be Unable to Consent").
- J. The rationale for significant risk/non-significant risk device determinations (See SOP 15B "Research Regulated by the Food and Drug Administration (FDA): Information and Policies for Investigational Device Exemptions (IDE) Applications").
- K. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research.
- L. Key information provided by consultants.

- M. Documentation that the IRB went into executive session (when applicable) – see SOP 7B “Requirements for the Conduct of Research Review at a Convened NIH Institutional Review Board (IRB) Meeting”.

4.5 RECORDS MAINTAINED BY OHSRP

4.5.1 RECORDS MAINTAINED BY THE OHSRP

Records maintained by the OHSRP include, but are not limited to:

- A. The NIH Federalwide Assurance.
- B. The NIH Human Research Protection Program (HRPP) Standard Operating Procedures.
- C. Copies of authorization/reliance agreements.
- D. Current membership rosters for all NIH IRBs.
- E. Copies of approved exemptions (see SOP 5 “Research Activities with Human Data/Specimens” and SOP 6 “Determinations Including Exemptions Made by the Office of Human Subjects Research Protections (OHSRP) under 45 CFR 46”).
- F. Records of all HRPP personnel who have taken required training (see SOP 25 “Training Requirements for the NIH Human Research Protection Program (HRPP)”).
- G. Agendas and attachments, minutes and other official records of the Human Subjects Research Advisory Committee (HSRAC).
- H. Records of the HRPP’s investigations of complaints and non-compliance (see SOP 22 “Research Subject Information and Services and Research-related Complaints from Research Subjects” and SOP 16A “Allegations of Non-compliance with Requirements of the NIH Human Research Protection Program (HRPP)”).
- I. Formal written communications with OHRP, FDA and other regulatory bodies as appropriate.

4.5.2 DOCUMENTATION OF EXEMPTIONS

Only OHSRP is authorized to grant exemptions. OHSRP's documentation of verified exemptions includes the regulatory citation and documentation that supports the determination (see SOP 6 "Determinations Including Exemptions Made by the Office of Human Subjects Research Protections (OHSRP) under 45 CFR 46").

4.6 RESEARCH PROTOCOL RECORDS MAINTAINED BY THE CC

- A. Office of Protocol Services. The Clinical Center Office of Protocol Services maintains files of NIH IRB-approved protocols. Each file normally contains a copy of the protocol, notations and records of approval actions including approval by the Director of the Clinical Center as necessary, names of Principal Investigators, and related correspondences and memoranda.
- B. Medical Record Department: The Clinical Center Medical Record Department maintains signed protocol-related informed consent document(s).

4.7 PROTECTION OF AND ACCESS TO IRB RECORDS

NIH IRBs must protect the confidentiality of research information:

- A. All IRB paper records are kept secure in locked filing cabinets or locked storage rooms. Doors to offices where IRB records are kept must be closed and locked when the rooms are unattended.
- B. Electronic IRB records are maintained according to applicable laws, regulations and NIH policies and procedures for computer and electronic record security.
- C. Subject to applicable law and Federal policy, access to IRB records is limited to the Institute Clinical Director, the IRB Chair, IRB members, the IRB staff, authorized NIH and OHSRP officials, and officials of Federal regulatory agencies (OHRP, FDA, etc...). Appropriate accreditation bodies may be provided access to IRB records as needed.

- D. Research investigators may be provided reasonable access to IRB files related to their protocol(s). The IRB Chair or Institutional Official will determine if research investigators should be allowed to view IRB records (and to what extent). This determination will be based on documentation of a legitimate need and made in accordance with applicable laws and regulations.

- E. Records may not be removed from the IRB office; however, the IRB staff will provide copies of records or access for inspection if copying is not permitted by authorized personnel (see a description of authorized personnel in paragraph 4.7.C).

4.8 RECORD RETENTION

IRB records will be retained for at least three (3) years after completion of the research. IRB records not associated with research or protocols cancelled without participant enrollment will be retained at least 3 years after closure. After that time, IRB offices and OHSR will comply with NIH Manual Chapter 1743 --- Keeping and Destroying Records (see List of Links below).

LIST OF LINKS

- A. DHHS regulations at 45 CFR 46:
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>
- B. FDA regulations at 21 CFR 56:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56>
- C. NIH Manual Chapter 1743 --- Keeping and Destroying Records (see <http://oma.od.nih.gov/manualchapters/management/1743/>)
- D. OHSRP website <https://federation.nih.gov/ohsr/nih>

LIST OF APPENDICES

Appendix A Recommended format for NIH IRB Minutes.

Appendix B NIH Protocol Review Standards

APPENDIX A RECOMMENDED FORMAT FOR NIH IRB MINUTES

RECOMMENDED FORMAT FOR ALL NIH IRB MINUTES

The order in which agenda items are reviewed is at the discretion of IRB Chairs. Instructional language is italicized and should be removed from the template before use. Bracketed language should be replaced with the applicable terminology. Any changes to this template must be approved by the Office of Human Subjects Research Protections (OHSRP)

Minutes of the [Institute] IRB Meeting Held on [date]

Members Present: _____ (Chair) _____ (Vice Chair)
 (List name and role: _____
 indicate who is _____
 a non-scientist, _____
 non-NIH affiliated, _____
 who is an alternate _____
 covering for a _____
 member and who _____
 is attending by phone)

Members Absent: _____

(NOTE: As per SOP 4, this list should include, “Names of the primary and alternate members who are present and absent at the beginning of the meeting... The minutes should document the name and status of members who attended any part of the IRB meeting.” Entrances and departures of IRB members should be noted at the point at which they occur below.)

Guests: _____
 (Include Affiliation _____
 and indicate if _____
 a consultant)

The meeting convened at --:-- [a.m./p.m.] with a quorum of [#] members present. The quorum for this IRB is [#] members. (Note: the Chair counts towards the quorum, unless recused)

CONFLICT(S) OF INTEREST (list any members with known conflicts of interest and the action where the conflict exists)

MINUTES OF THE MEETING HELD ON (DATE)

(The minutes must be voted on and any changes documented.)

ANNOUNCEMENTS

INITIAL REVIEWS

Principal Investigator:

Protocol Title:

Protocol Number:

Protocol Précis: (optional)

Discussion:

Include the general discussion, including informal discussions with consultants and determinations of the Board. Also include the length of the period of approval; and whether the IRB made determinations as required by FDA regulations (i.e. device exemption, Significant Risk (SR) or Non-significant Risk (NSR) risk determinations, etc...) See SOP 2 "IRB Membership and Structure" regarding consultants and whether more information is needed from independent sources.

- A. Specific discussions: (include the following headings)
- B. Scientific design: (discuss and note that Institute pre-scientific review has been done)
- C. Subject selection including equitability (45 CFR 46.111(a)(3)):
(discuss populations to be studied & recruitment plan)

ADDITIONAL SAFEGUARDS FOR VULNERABLE SUBJECTS (45 CFR 46.111(B))

Risks are reasonable in relationship to anticipated benefits, if any (45 CFR 46.111(a)(2): (Assign a level of risk at the time of the IRB decision and vote, in item (d) below consistent with the NIH IRB Protocol Review Standards form (See Appendix B). If children or prisoners are to be enrolled, cite the regulatory reference, 45 CFR 46.404, 46.405, 46.406, 46.407. See the Resources for IRB Determinations for special circumstances such as enrollment of prisoners.)

Minimization of risks to subjects (45 CFR 46.111(a)(1)):

Monitoring data to ensure the safety of subjects (45 CFR 46.111(a)(6)):

Privacy and confidentiality (45 CFR 46.111(a)(7)):

Informed Consent process is adequate and is appropriately documented (46 CFR 46.111(a)(4), 46.116 and 46.117): (document that all required elements are present, or waiver of consent or documentation is permitted, in accordance with 45 CFR 46.116 and 46.117, for example

- A. Alteration or waiver of requirements for informed consent (when applicable):
 - 1. The research involves no more than minimal risk to the subjects.
 - 2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
 - 3. The research could not practicably be carried out without the waiver or alteration, and
 - 4. Whenever appropriate, the subjects must be provided with additional pertinent information after participation.

- B. Waiver of requirements for written documentation of informed consent: (when applicable))

(Note that alteration or waiver of requirements for informed consent or waiver of written documentation of informed consent may not be permitted for research including certain vulnerable populations).

Period of Approval: (state the length of the approval period)

Additional considerations: (when appropriate)

(List any other considerations related to the type of research to be conducted (e.g., IND, ionizing radiation; collaborative research, other...; state if these considerations do not apply. For more information about special considerations, see the "[Resource for IRB Determinations](#)". For example, document the rationale for significant risk/non-significant risk device determinations (See SOP 15B "Research Regulated by the FDA: Information and Policies for IDE Applications".)

- A. Stipulations/Conditions: (stipulations are the conditions for approval, number the stipulations)
- B. Recommendations (recommendations are suggested but not required for approval, number the recommendations)
- C. IRB Decision and Vote (Executive Session):

The IRB moved and seconded the motion that this [ACTION] be [Approved, Deferred, etc...] [with stipulation responses] to the [Chair, Board, etc...] (Terminology for IRB actions include: "Approved", "Approved with Stipulations/Conditions", "Deferred" or "Tabled, or "Disapproved", for more information, see SOP 7B, Section 7B.8. If the protocol is approved with stipulations/conditions and/or recommendations, the minutes must state whether the IRB votes that the stipulations and/or recommendations are to be reviewed by the Chair (designee), by a subcommittee of the IRB, or by the full IRB)

- D. Risk Assessment:

(Assign a level of risk consistent with the NIH IRB Protocol Review Standards Form (see Appendix B). If children or prisoners are to be enrolled, cite the regulatory reference 45 CFR 46.404, 46.405, 46.406 and 46.407 or the Resource for IRB Determinations for special circumstances such as enrollment of prisoners (see Appendix C).)

- E. Benefit Assessment:

Vote: Total #: For [#], Against [#], Abstained [#] Absent [#; name]
Recused [#; name] (list members who have a conflict of interest)

- F. (Include a written summary of the discussion of controverted issues and their resolution.
- G. Movement of members must also be noted, for example if a member came late it should be noted when they arrived, their name and role so that the quorum at time of vote makes sense.
- H. The minutes will indicate, by name, those members who are absent or recused for each vote during the meeting, for more information, see SOP 4 “Human Research Protection Program (HRPP) Documentation and Records”.
- I. 2., 3. etc...(Follow the same format as above for additional problems)
- J. Guidance provided above applies below as applicable for each action type.

EXPEDITED INITIAL REVIEWS, EXPEDITED CONTINUING REVIEWS OR EXPEDITED AMENDMENTS, OR EXPEDITED STUDY CLOSURE

Expedited [Initial, Continuing Review, etc...]

Principal Investigator:

Protocol Title:

Protocol Number:

Protocol Précis: (optional)

Date approved by IRB Chair or designee: (Optional if captured on the Expedited Reviewer Form in the IRB Member Packet)

Description of expedited action: (Expedited actions must be listed separately in the minutes. The Chair should provide a brief explanation of any expedited actions. A vote is not required but the IRB has the prerogative to discuss, rescind or amend expedited actions.)

2., 3. etc...(Follow the same format as above for additional problems)

CONTINUING REVIEWS OR CONTINUING REVIEWS WITH AMENDMENT (as applicable)

The entire protocol file should be available for reference at the meeting. When a Continuing Review is accompanied by an Amendment, each action must be voted upon separately.

Continuing Review (or) Continuing Review with Amendment

Principal Investigator:

Protocol Title:

Protocol Number:

Expiration Date:

Protocol Précis: (optional)

Discussion: (including a discussion of PI continuing review reports required by SOP 16 and SOP 9)

- A. Specific discussions: (include the following headings)
- B. Research progress and rationale for continuation of the study: (discuss whether the research is progressing as expected and whether the study may continue)
- C. Changes in previously approved research: (specify if material changes have occurred or not; if they have changed, indicate the appropriate regulatory citation as applicable, see Initial Review above for regulatory citations)
- D. Significant new findings: (discuss if any information has appeared in the literature or evolved from this or similar research that might affect the IRB's evaluation of the risk/benefit assessment for this protocol or the subjects' willingness to continue participation in the research)
- E. Protocol recruitment: (discuss whether the protocol is meeting its recruitment goals)

Summary of Adverse Events, Protocol Violations, Serious or Continuing Non-compliance and Unanticipated Problems: (discuss events that have occurred on the study in this review period and whether the protocol or consents must be amended)

Scientific design: (when appropriate)

Informed consent process is adequate and is appropriately documented (45 CFR 46.111(a)(4), 46.116 and 46.117): (when appropriate)

Additional safeguards for vulnerable subjects (45 CFR 46.111(a)(1)): (when appropriate)

Monitoring of data to ensure safety of subjects (45 CFR 46.111(a)(6)): (when appropriate)

Privacy & confidentiality (45 CFR 46.111(a)(7)): (when appropriate)

Risks are reasonable in relationship to anticipated benefits/benefits, if any(45 CFR 46.111(a)(2): (discuss if any information has appeared in the literature or evolved from this or similar research that might affect the IRB's evaluation of the risk/benefit assessment for this protocol.)

Period of Approval:

Additional considerations: (when appropriate)

A. Stipulations/Conditions:

B. Recommendations:

C. IRB Decision and Vote (Executive Session):

1. The IRB moved and seconded the motion that this [ACTION] be [Approved, Deferred, etc...] with stipulation responses to the [Chair, Board, etc...]
2. Risk Assessment:
3. Benefit Assessment:

4. Continuing Review Vote:

- a. Total #: For [#], Against [#], Abstained [#] Absent [#; name]
- b. Recused [#; name] (list members who have a conflict of interest)
- c. Amendment Vote: (when applicable)
 - i. Total #: For [#], Against [#], Abstained [#] Absent [#; name]
 - ii. Recused [#; name]

D. 2., 3. etc...(Follow the same format as above for additional problems)

AMENDMENTS (The entire protocol file should be available at the meeting)

Amendment

Principal Investigator:

Protocol Title:

Protocol Number:

Protocol précis: (optional)

Expiration Date:

Description of the amendment:

Discussion:

- A. Specific discussions: (include the following headings)
- B. Changes to previously approved research:
- C. Scientific design: (when appropriate)

- D. Subject selection including equitability (45 CFR 46.111(a)(3)): (when appropriate)
- E. Additional safeguards for vulnerable subjects (45 CFR 46.111(a)(1)): (when appropriate)
- F. Minimization of risks to subjects (45 CFR 46.111(a)(1)): (when appropriate)
- G. Monitoring of data to ensure safety of subjects (45 CFR 46.111(a)(6)): (when appropriate)
- H. Privacy & confidentiality (45 CFR 46.111(a)(7)): (when appropriate)
- I. Informed consent process is adequate and is appropriately documented (45 CFR 46.111(a)(4), 46.116 and 46.117): (when appropriate)
- J. Risks are reasonable in relationship to anticipated benefits/benefits, if any(45 CFR 46.111(a)(2):
- K. Additional considerations: (when appropriate)
- L. Stipulations/Conditions:
- M. Recommendations:
- N. IRB Decision and Vote (Executive Session):
The IRB moved and seconded the motion that this [ACTION] be [Approved, Deferred, etc...] with stipulation responses to the [Chair, Board, etc...]
- O. Risk Assessment:
- P. Benefit Assessment:
- Q. Vote: Total #: For [#], Against [#], Abstained [#] Absent [#; name] Recused [#; name] (list members who have a conflict of interest)
- R. 2., 3. etc...(Follow the same format as above for additional problems)

REPORT OF UNANTICIPATED PROBLEMS (UPs), - PROTOCOL DEVIATIONS (PDs) AND SERIOUS OR CONTINUING NON-COMPLIANCE

(See SOPs 16 and SOP 16A for more information)

UPs, PDs and Serious or Continuing Non-compliance

Principal Investigator:

Protocol Title:

Protocol Number:

Date of the problem:

Description of the problem(s):

Discussion:

(Document the IRB's discussion, include PI actions taken as a result of the event; IRB stipulations/conditions for further actions, if any, (e.g., suspension of subject accrual, etc...) and any necessary recommendations for further reporting to NIH officials, the Director CC, FDA, etc...)

Determination:

(Document the IRB's determination regarding the nature of the event including UP, serious or continuing non-compliance, suspension or termination of approval)

Stipulations/Conditions (stipulations are the conditions for approval, number the stipulations)

Recommendations (recommendations are suggested but not required for approval, number the recommendations)

2., 3. etc...(Follow the same format as above for additional problems)

EMERGENCY INDS (EINDs) or EXPANDED ACCESS INDS (when applicable)

Emergency IND or [Expanded Access] IND

(If Expanded Access IND specify the type: Single-patient IND, Intermediate-size Population IND, or Treatment IND)

Principal Investigator:

Protocol Title:

Protocol Number:

Discussion: (For Emergency INDs, document the IRB's discussion and specify the period of approval, while the IRB does not vote to approve this action it is required to review the EIND at least yearly if still open consistent with 21 CFR 56.109(f).

Expanded Access INDs are reviewed and approved consistent with 21 CFR Parts 50 and 56 and may not be implemented prior to meeting these requirements in addition to those specified in 21 CFR 312 Subpart I.)

Period of Approval:

Stipulations/Conditions:

Recommendations:

2., 3. etc...(Follow the same format as above for EINDs or Treatment INDs)

INFORMATION ITEMS (when applicable)

Informational Item

Principal Investigator:

Protocol Title:

Protocol Number:

Discussion: (Document the IRB's discussion. Include PI actions taken as a result of the event; IRB recommendations for further actions, if any, (e.g., suspension of subject accrual, etc.), and any necessary recommendations for further reporting to NIH officials, OHSRP, Director CC, or FDA, etc...)

Stipulations/Conditions:

Recommendations:

2., 3. etc...(Follow the same format as above for additional problems)

ADJOURNMENT The meeting adjourned at --:-- (a.m./p.m.).

APPENDIX B: NIH PROTOCOL REVIEW STANDARDS

Sample Requirements for IRB Protocol Review and Discussion

SECTION I – REGULATORY CRITERIA FOR IRB APPROVAL FOR NEW PROTOCOLS

(To be used by the Principal Investigator at the initial protocol presentation to the IRB)

Sample regulatory review requirements to be addressed for initial protocols by the PI at the convened IRB meeting	Suggested questions for IRB discussion
1. The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk.	a) Is the hypothesis clear? Is it clearly stated? b) Is the study design appropriate to prove the hypothesis? c) Will the research contribute to generalizable knowledge and is it worth exposing subjects to risk?
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result. Risks to subjects include physical, psychological, social, legal and socioeconomic risks.	(a) What does the PI consider the level of risk/discomfort/inconvenience to be? (See Attachment 1, risk assessment guide attached to this form). (b) Does the IRB agree with the PI's risk assessment? (c) Is there prospect of direct benefit to subjects? (See Attachment 1, benefit assessment guide attached to this form.) (d) Are risks reasonable in relation to anticipated benefits, if any to subjects?
3. Risks to subjects are minimized.	Do data and safety monitoring plans make adequate provision for monitoring the data collected to ensure the safety of subjects.
4. Subject selection is equitable taking into account the purpose and setting of the research	a) Who is to be enrolled? Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously-ill persons? Adults who may be unable to give

	<p>consent? Healthy volunteers?</p> <p>b) Are these subjects appropriate for the protocol?</p>
5. Additional safeguards are included for subjects likely to be vulnerable to coercion or undue influence.	a) Are appropriate regulatory or other protections in place for vulnerable subjects, e.g., pregnant women, fetuses, socially- or economically-disadvantaged, prisoners, adults who may be unable to give consent?
6. Informed consent is obtained from research subjects or their legally authorized representative(s) as required by 45 CFR 46.116 and appropriately documented in accordance with, and to the extent required by 45 CFR 46.117 and for FDA-regulated research, 21.CFR 50.	<p>a) Does the informed consent document include the eight required elements?</p> <p>b) Is the consent document understandable to subjects?</p> <p>c) Who will obtain informed consent (PI, nurse, other?) & in what setting?</p> <p>d) If appropriate, is there a children's assent?</p> <p>e) (e) Is the IRB requested to waive or alter any informed consent requirement?</p>
7. Subject privacy & data confidentiality are maximized.	<p>a) Will personally-identifiable research data be protected to the greatest extent possible from unauthorized access or use?</p> <p>b) Are any special privacy & confidentiality issues appropriately addressed in the research plan, e.g., distribution of identifiable genetic information?</p>
ADDITIONAL CONSIDERATIONS	
1. Ionizing radiation.	If ionizing radiation is used in this protocol is it medically indicated or for research use only?
2. Collaborative research.	Is this domestic or international collaborative research? If so, are FWAs or written agreements required (such as a Reliance Agreement or CRADA)?
3. FDA-regulated research	Does the research involve the use of a product that is subject to FDA regulation?

	If so, is an IND or IDE involved in this protocol? Is an IND/IDE required? (For help in determining the need for an IND/IDE see SOP 15).
4. Duration of approval	Does the protocol require review more frequently than annually?

SECTION II –POINTS TO CONSIDER BY THE IRB AT CONTINUING REVIEW AND FOR AMENDMENTS

1. Regulatory criteria.	After any changes, will the protocol still meet all of the regulatory and policy criteria necessary for an IRB to approve research (46.111)?
2. Continuing review/amendment requirements	Have the relevant continuing review/amendment requirements as set forth in SOPs 9 and 10 been met?
3. Changes in previously approved research	Does the protocol require verification from sources other than the investigator(s) that no material changes have occurred since the previous review? (Material change means any change that would affect the determination of whether the research meets the regulatory criteria for IRB approval.)
4. Research risks	Has any information appeared in the literature or evolved from this or similar research that might change the IRB's initial evaluation of the risk/benefit analysis of human subjects involved in this protocol?
5. Significant new findings	Are there any significant new findings that might affect the subjects' willingness to continue participation in research?
6. Protocol recruitment	Is the protocol meeting its recruitment goals?
7. Research progress and rationale for	Is the research progressing as

continuing the study	proposed/expected? Should the study continue?
8. Unanticipated problems (see Section III, below)	Have there been any unanticipated problems involving risks to subjects since the last review? If so, is amendment of the protocol required? Have any new risks been identified in the summary of adverse events, protocol deviations, UPs or UADEs?

4.1 SECTION III: POINTS TO CONSIDER BY THE IRB WHEN REVIEWING UNANTICIPATED PROBLEMS OR PROTOCOL DEVIATIONS WHETHER REPORTED PROMPTLY AS PROBLEMS OR IN AGGREGATE AT TIME OF CONTINUING REVIEW

<p>Definition of an Unanticipated Problem (UP) An unanticipated problem is any incident, experience or outcome that:</p> <p>a) Is unexpected in terms of nature, severity or frequency given (i) the research procedures that are described in the protocol-related documents, such as the IRB- approved research protocol and informed consent document; and (ii) the characteristics of the subject population being studied, AND</p> <p>b) is related or possibly related to participation the research (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</p>	<p>a) Is the incident, experience or outcome unexpected given the research procedures that are described in the IRB-approved research protocol, consent, or other study documents, and the characteristics of the subject population being studied?</p> <p>b) Is the incident, experience or outcome related or possibly related to participation in research?</p> <p>c) Does the incident, experience or outcome suggest that the research places subjects or others at greater risk of harm?</p> <p>If yes:</p> <p>d) Is there a pattern of UPs/protocol deviations (PDs)?</p> <p>e) Is any action required on the part of the IRB or the PI as a result of UPs/PDs (e.g., change in protocol procedures/change in consent document)?</p>
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harm) than was previously known or recognized.	f) Should the UP be reported to OHSRP? If no: Is any further action required on the part of the IRB or PI?
Definition of a Protocol Deviation (PD) Any change, divergence, or departure from the IRB-approved research protocol. PDs may be serious or non-serious. For examples of PDs see SOP 16 “Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations”	a) Is this PD also a UP? b) Does this PD represent serious or continuing non-compliance? (see SOP 16A) c) Will the PD result in change to the risk/benefit analysis or to the protocol or informed consent? (d) Should the PD be reported to OHSRP?

ATTACHMENT 1: RISK/BENEFIT ASSESSMENT GUIDE

The IRB should ensure that 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 of its responsibility.

Regulatory definition of minimal risk: Minimal risk means that the probability and 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 (45 CFR 46.102(h)(i)). (Note that minimal risk is defined differently for prisoners, see 45 CFR 46.303(d).)

RISK LEVEL FOR ADULTS

Check appropriate risk category:

1. _____ Research not involving greater than minimal risk.*
2. _____ Research involving greater than minimal risk to subjects.*

3. _____ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
4. _____ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects.

***Note:** These risk analyses apply to competent adults (see SOP 14E “Research Involving Adults Who Are or May Be Unable to Consent” for adults who have surrogate decision-makers).

BENEFIT TO SUBJECTS

Note that the risk/benefit analysis for pregnant women, fetuses, or neonates may differ from the categories below, see 45 CFR 46.204 and .205.

A research benefit can be a health-related, psychosocial or other value to an individual research subjects. Money or other compensation for participation in research is not considered to be a benefit, but rather compensation for research-related inconveniences.

Check appropriate benefit category:

1. _____ No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition;
2. _____ No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge to further society's understanding of the disorder or condition under study;
3. _____ The research involves the prospect of direct benefit to individual subjects.

RISK/BENEFIT LEVEL FOR CHILDREN

(See SOP 14D “Research Involving Children”)

Check appropriate risk category:

1. _____ Research not involving greater than minimal risk to subjects (45 CFR 46.404)

2. _____ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405)
3. _____ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406)
4. _____ Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (CFR 46.407)