

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

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: 20A

SOP Title: OBTAINING A RELIANCE (AUTHORIZATION) AGREEMENT AT THE NIH

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

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SOP 20A OBTAINING A RELIANCE (AUTHORIZATION) AGREEMENT AT THE NIH

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SOP 20A OBTAINING A RELIANCE (AUTHORIZATION) AGREEMENT AT THE NIH

20A.1 PURPOSE

NIH is committed to reducing the burden to researchers that is involved when protocols involve review by multiple Institutional Review Boards (IRBs), by doing Reliance (Authorization) Agreements so that only one IRB is needed for a specific research protocol

20A.2 POLICY

NIH complies with 45 CFR 46.114 and, when applicable, 21 CFR 56.114. This Standard Operating Procedure (SOP) contains the NIH policy requirements for obtaining Reliance Agreements.

20A.3 DEFINITIONS

A. **Authorization Agreement (also known as a “Reliance Agreement”)**: An agreement between NIH and one or more institutions involved in the same cooperative research (see definition below) that assigns regulatory responsibilities to a specific IRB. The terms “authorization agreement” and “reliance agreement” are used interchangeably in this SOP. At the NIH, the preferred term is “reliance agreement.” **The following terms and phrases are frequently used in the context of authorization/reliance agreements:**

- 1. Central IRB:** The IRB responsible for reviewing a research protocol for multiple performance sites engaged in the same project. The Central IRB assumes responsibility as the IRB of Record for performance sites relying on the Central IRB for review of the research project, (see also the definition of Centralized IRB Review Process below). This “Central IRB” may also be called the “IRB of Record.”
- 2. Centralized IRB Review Process:** A centralized IRB review process involves an agreement in which institutions engaged in multisite cooperative research rely in whole, or in part, on the review of a single IRB that may or may not be affiliated with the research site(s).

3. **Single Study Agreement:** An authorization/reliance agreement that pertains to only one protocol.
4. **Joint IRB Review Agreement:** An agreement in which two or more institutions *divide* specified responsibilities for IRB review so that each IRB is responsible for only part of the IRB review and oversight. For example, a Joint IRB Review Agreement might be desirable if investigators at one institution design the protocol and receive identifiable data, but the protocol is implemented at a different institution where the subjects are located. One IRB may approve the protocol but another IRB may approve the consent to ensure that it adequately addresses local concerns. Different research interventions may occur at more than one institution, and each institution may wish to have IRB review and oversight of protocol activities that occur at its own institution. If each site's IRB is reviewing only a portion of the same protocol, then a reliance agreement is needed to clarify that each institution is relying on the other site's IRB review and oversight of those specific protocol activities.
5. **Program-wide Agreement:** This term refers to an authorization/reliance agreement that applies to all future collaborative studies, as defined in the agreement and conducted by the signatory institutions, unless exceptions are made.
6. **Cooperative Research:** Research in which more than one institution is engaged in human subjects research. 45 CFR 46.114 states, "Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy."
7. **Coordinating Center (Entity) for Multisite Studies:** A coordinating center is the entity that is responsible for overall planning, document collection, monitoring and communication among all sites participating in a multisite research project. A coordinating center may also be responsible for data management and analysis and may be designated either by a sponsor or by mutual agreement of the participating sites. The sponsor may delegate some of its responsibilities to the coordinating center as discussed in SOP 20C – Responsibilities When the NIH Intramural Research Program Serves as a Coordinating Center for a Multisite Trial.

8. **Federalwide Assurance (FWA):** A Federalwide Assurance is a written commitment by an institution to comply with the **protection of human subjects regulations** of 45 CFR 46. The FWA is filed with the DHHS Office for Human Research Protections (OHRP).
9. **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 the 45 CFR 46.102(f), and (3) are not exempt from 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. However, in 45 CFR 46, “human subjects research” includes also research exempt from the requirements of 45 CFR 46.
10. **IRB of Record:** The IRB responsible for review of research and determining that the research meets IRB regulatory requirements for approval.
11. **NIH Investigator:** With regard to reliance agreements, this may be the NIH study Principal Investigator (PI) or, if the study is being performed at a non-NIH site with a non-NIH PI, this is the most senior NIH investigator who will be involved in the study. The name of the NIH investigator will be listed on the reliance agreement when NIH relies on an outside IRB and when an outside site relies on an NIH IRB.
12. **Performance Site (enrollment site):** A performance site, or an enrollment site, is a place where human subjects participate in research activities (e.g. often a clinic or hospital). The performance site’s location may be different from the location where the IRB review occurs. Subjects are usually enrolled or followed at performance sites.
13. **Reliance Agreement:** See definition of Authorization Agreement.

B. Site Terminology:

1. **Multisite protocol (multisite research):** Multisite research/protocols refer to projects that will be conducted at more than one **Performance Site**. Usually a multisite study involves conduct of a protocol carried out at more than one medical institution or site. Sites may also include schools, nursing homes, community rehabilitation facilities, private practices,

individual homes, etc. As part of the protocol application, the investigator shall disclose the entity that will serve as the coordinating center for the project.

20A.4 RELIANCE (AUTHORIZATION) AGREEMENTS

- A. A Reliance Agreement may be appropriate when more than one institution is engaged in cooperative research, if each is engaged in human subjects research,¹ (see OHRP 2008 Guidance, Engagement of Institutions in Human Subjects Research, SOP 20 – NIH HRPP Requirements for Collaborative Research, and FDA Information Sheets: Non-local IRB Review and Cooperative Research, see **References** below).
- B. Reliance Agreements may be utilized for:
1. Single-study agreements where the cooperative research involves only one research protocol, or
 2. Program-wide agreements that cover more than one protocol (see **20A.6.D** and **E**);
 3. Joint IRB review agreements for situations in which IRBs divide the responsibility for review and oversight of a protocol;
 4. Multisite protocols when a study is carried out at more than one medical institution or site in which institutions engaged in multisite research rely in whole or in part on the review of a centralized IRB (see **20A.10**);
 5. When an institution relies on another IRB, the relying institution continues to have responsibility under 45 CFR 46 and, if applicable, FDA regulations pertaining to the conduct of the research and the safety of research subjects.

¹ Researchers at one institution may collaborate in a human subjects research protocol at another institution without personally engaging in human subjects research. For example, an outside researcher may act solely as a scientific advisor or analyze specimens that do not contain identifiable information. In this case, a reliance agreement is not required. Contact OHSRP for guidance.

20A.5 NIH OFFICIALS RESPONSIBLE FOR RELIANCE (AUTHORIZATION) AGREEMENTS

The NIH Deputy Director for Intramural Research (DDIR), the Director, OHSRP and the Deputy Director, OHSRP are the only NIH officials authorized to make final decisions about entering into a Reliance Agreement. OHSRP negotiates and executes those agreements. Decisions are made on a case-by-case basis.

20A.6 PROCESS FOR OBTAINING AND MAINTAINING RELIANCE (AUTHORIZATION) AGREEMENTS

The process for obtaining a Reliance Agreement is as follows:

- A. An NIH PI/AI or member of the NIH research team must complete an electronic Application for Reliance Agreement (see **Appendix A** below); this form can be found on the OHSRP website (see **References** below).
- B. OHSRP evaluates the Application for Reliance Agreement (see **Appendix A** below), and notifies the NIH investigator about whether an agreement is appropriate. If a reliance agreement is appropriate, the NIH and non-NIH investigator roles are defined in the IRB-approved protocol. This does not pertain to multisite protocols in which many sites are performing the same study and for which PIs and AIs have parallel roles. However, when the study is not multisite, and the investigator at the relying institution is involved in a limited or specific aspect of the protocol, the role/responsibilities should be described in the protocol. OHSRP will work with the outside institution and the NIH PI/AI (as well as the NIH IRB, if the outside institution will rely on NIH) to facilitate the agreement using templates previously approved by NIH Office of General Counsel (OGC), see **Appendices B-D**.
- C. OHSRP keeps records of all finalized reliance agreements and supporting documentation, including a copy of the protocol. If the agreement involves relying on an NIH IRB, OHSRP will send a copy of the final agreement to the appropriate IRB which must keep a copy of the agreement as set forth in **20A.11.G** below.
- D. The DDIR participates in decisions about all program-wide reliance agreements, often in consultation with OHSRP staff, the NIH OGC and the PI engaged in the research project. The DDIR signs program-wide agreements.

- E. OHSRP must inform the appropriate Clinical Director (CD) of any program-wide reliance agreements on outside IRBs.
- F. When multiple reliance agreements will be needed for a very large multisite study which seeks to rely on a central IRB based at NIH, OHSRP may delegate some of its responsibilities for obtaining and maintaining these agreements to the involved NIH Institute/Center (IC).

20A.7 OHSRP CRITERIA AND POINTS TO BE CONSIDERED WHEN EVALUATING REQUESTS FOR RELIANCE (AUTHORIZATION) AGREEMENTS

- A. NIH will only enter into reliance agreements when: 1) the other institution has an FWA; and 2) if the non-NIH IRB is to serve as the IRB of record, it must be registered with OHRP.
- B. If the substantive content of the reliance agreement departs from the NIH template (see **20A.15**), OHSRP and OGC must approve the agreement.
- C. An agreement may not state that an NIH IRB will agree to follow laws, regulations or policies of another federal agency, state, country or institution, unless **OHSRP and OGC** approve such language.
- D. **If an NIH IRB serves as the IRB of Record for studies supported or funded by the Department of Defense (DoD), or if an investigator is considering initiating a collaboration with the DoD involving a potential reliance agreement, consult with OHSRP. Additional review by the involved DoD component may be required per the terms of a reliance or other agreement.**
- E. **The protocol that is the subject of the agreement must clearly state the research activities of the researchers from the “relying institution”². (This does not pertain to multisite protocols in which many sites are performing the same study and for which PIs and AIs have parallel roles).** The OHSRP, in consultation with OGC as needed, may waive this requirements, depending on the circumstances.

² For example, if the Food and Drug Administration (FDA) is relying on an NIH IRB, the NIH protocol must clearly state the roles and responsibilities of the FDA researcher in that protocol. If NIH is relying on an IRB at Johns Hopkins Medical Center, the protocol approved at Johns Hopkins must clearly state that roles and responsibilities of the NIH researchers.

- F. If the subject population involves a different culture, vulnerable subjects, or raises concerns related to local context, OHSRP may require local IRB review of those issues, (see SOP 20B - NIH IRB Responsibilities When Reviewing Local Context Considerations for Offsite Research).
- G. An individual who is not an NIH employee may be covered by the NIH FWA and, as such, no dual IRB review or reliance agreement is required by NIH policy (see SOP 20D - Collaborations Involving Non-NIH Employees Working on NIH Protocols, for information regarding which non-NIH employees are covered by the NIH FWA). In other cases, the individual may need IRB review at his/her own institution, or the other institution may request it rely on the NIH IRB (through a reliance agreement) for the NIH human subjects research activities of that individual.
- H. In cases where a reliance agreement is being requested and the protocol is not a multisite one, OHSRP may consider factors, such as (but not limited to) location of the PI and where the subjects will be seen, in determining which site will be the IRB of Record.
- I. OHSRP evaluates whether there is any other issue involved in the agreement that requires additional action before the agreement is signed.

20A.8 ADDITIONAL REQUIREMENTS FOR A RELIANCE (AUTHORIZATION) AGREEMENT WHEN NIH RELIES ON AN OUTSIDE IRB

When NIH relies on an outside IRB, the following additional requirements apply:

- A. Approval: The NIH investigator's IC Official (Lab/Branch Chief) or the NIH investigator's supervisor, if the investigator is a Lab/Branch Chief, must approve the request. This approval may be documented in an e-mail to OHSRP.
- B. Scientific Review: If the outside protocol is funded by an NIH grant or contract, there is no need to address scientific review. Otherwise, OHSRP will forward information to the CD about what scientific review, if any, occurred, and the CD will decide if it is adequate.
- C. Conflict of Interest: The NIH investigator must comply with NIH conflict of interest policies, including SOP 21 - Conflict of Interest Requirements for Researchers and Research Staff, (please refer to SOP 21 for additional information).

- D. Consent forms: If subjects will be seen at the NIH Clinical Center (CC), NIH consent template language (see NIH Form 2514, as an example) may not be changed by a non-NIH IRB without Office of Protocol Services (OPS) and NIH OGC review and approval, (see SOP 12 - Requirements for Informed Consent, for additional information).

20A.9 ADDITIONAL REQUIREMENTS FOR A RELIANCE (AUTHORIZATION) AGREEMENT WHEN AN OUTSIDE INSTITUTION RELIES ON AN NIH IRB

Consent forms: If NIH is the IRB of Record, the NIH IRB must review the consent forms to be used at the study sites including any local required template language, (see SOP 12 - Requirements for Informed Consent, for additional information).

20A.10 ADDITIONAL REQUIREMENTS WHEN AN NIH RESEARCHER REQUESTS THAT NIH SERVE AS THE CENTRAL IRB

If the reliance agreement is for an NIH IRB to be the central IRB for a multisite protocol, the NIH IC supporting the protocol is responsible for providing additional IRB resources, if needed, to manage IRB responsibilities for the multisite protocol. The NIH PI for the protocol should submit a memo to the CD, OHSRP, the DDIR and the IRB Chair explaining the plans for this project.

- A. The memo should explain the NIH resources available for this work, including budget and personnel, the responsibilities of NIH personnel, the role of outside entities, including contractors, and a plan to ensure adequate communication and regulatory compliance for IRB responsibilities. If reliance agreements will be needed for a large number of sites, the PI should state whether the IC will provide necessary resources to obtain the agreements in collaboration with OHSRP staff.
- B. The memo should address the points to consider set forth in **20A.7** above.
- C. The memo should include any SOPs and forms that will be used to manage the central IRB activities for the protocol.
- D. If the central IRB arrangement is for a Food and Drug Administration (FDA)-regulated clinical trial, the memo must contain written procedures addressing the

following topics, pursuant to FDA Guidance, "Using a Centralized IRB Review Process in Multicenter Clinical Trials," March 2006:

1. How the central IRB will communicate with relevant institutions, the institution's IRBs, and investigators regarding its reviews.
 2. How the central IRB will ensure that it provides meaningful consideration of relevant local factors for communities from which research subjects will be drawn.
 3. How the central IRB will assess the ability of a geographically remote site to participate in a study (e.g., whether the site has medical services appropriate to the complexity of the study).
- E. The CD, OHSRP, the DDIR and the IRB Chair must approve the decision for an NIH IRB to serve as a central IRB for a multisite trial.

20A.11 IRB RESPONSIBILITIES WHEN THERE IS A RELIANCE (AUTHORIZATION) AGREEMENT

As set forth in a reliance agreement, the IRB of Record will conform to 45 CFR 46, FDA regulations, when applicable, and the institution's written human research protections policies and standard operating procedures, including:

- A. Perform initial full board review and approval (or disapproval) at convened meetings (unless expedited review is warranted);
- B. Perform continuing review at appropriate intervals;
- C. Review and approve study amendments;
- D. Conduct review of unanticipated problems, and serious and/or continuing non-compliance;
- E. Maintain an IRB membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56;
- F. If necessary, suspend or terminate the research;

- G. Maintain appropriate protocol and IRB records, including a copy of the reliance agreement;
- H. Evaluate “local context” issues, including state, local or institutional requirements related to the protection of human subjects (see 20B - NIH IRB Responsibilities When Reviewing Local Context Considerations for Offsite Research);
- I. If an NIH IRB, the IRB will notify OHSRP of any changes to or termination of the reliance agreement;
- J. Abide by the terms of the reliance agreement;
- K. Ensure that the correct expertise is present when a protocol is reviewed;
- L. Comply with institutional policies for IRB review;
- M. Inform researchers at a relying institution of all changes to the protocol³;
- N. Comply with OHRP and FDA requirements, if applicable, for IRB registration.

20A.12 RESPONSIBILITIES OF THE RELYING INSTITUTION WHEN THERE IS A RELIANCE (AUTHORIZATION) AGREEMENT

The relying institution will:

- A. Maintain an up-to-date OHRP-approved FWA;
- B. Comply with the terms of the protocol;
- C. Notify the reviewing IRB of any changes to the research protocol or research investigators;
- D. Notify the reviewing IRB if the research is suspended or terminated at the institution;

³ IRB and institutional responsibilities are set forth in the reliance agreement itself. However, if a non-NIH investigator is relying on an NIH IRB as an AI on an NIH protocol, the NIH PI must communicate to the AI any information that is required communication for all AI's.

- E. Notify the IRB promptly of all unanticipated problems and non-compliance and cooperate with the IRB by sharing requested information about unanticipated problems or non-compliance.

20A.13 NIH PI/AI RESPONSIBILITIES WHEN NIH RELIES ON AN OUTSIDE IRB

The NIH PI/AI will, at a minimum;

- A. Conform to the human research policies and operating procedures of the reviewing institution;
- B. Obtain IRB approval for any amendments or changes to the protocol;
- C. Obtain appropriate training in human subjects research protections;
- D. Report any unanticipated problems, serious and unexpected adverse events and non-compliance to the IRB, and NIH staff as required by the NIH Human Research Protection Program (HRPP);
- E. Abide by the terms of the reliance agreement;
- F. Notify OHSRP when the research protocol has been completed.

At the time the fully executed reliance agreement is e-mailed to the NIH investigator, a copy of this SOP will also be included, and the investigator will be asked to review this section (20A.13) to ensure awareness of these responsibilities.

20A.14 RESPONSIBILITIES OF OHSRP AFTER A RELIANCE (AUTHORIZATION) AGREEMENT IS SIGNED

The OHSRP keeps a copy of the reliance agreement, the applicable protocol and supporting documentation in its database for reliance agreements. It will document any changes in the status of reliance agreements (e.g. if the agreement is amended or terminated).

20A.15 TEMPLATES FOR RELIANCE (AUTHORIZATION) AGREEMENTS

Appendices B and C to this SOP are NIH reliance agreement templates for *single* protocol agreements, approved by OHSRP, in conjunction with OGC. The template for use when NIH serves as a central IRB for a multisite protocol can be found in **Appendix D**. These templates cannot be modified without approval of the OHSRP and OGC. There is no template for program-wide reliance agreements.

REFERENCES

- A. OHRP 2008 Guidance, Engagement of Institutions in Human Subjects Research:
<http://www.hhs.gov/ohrp/policy/engage08.html>
- B. FDA Information Sheets: Non-local IRB Review:
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126423.htm>
- C. FDA Information Sheets: Cooperative Research:
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126422.htm>
- D. OHSRP website – Reliance (Authorization) Agreement Request (NIH login required): <https://federation.nih.gov/ohsr/nih/rel1a.php>
- E. FDA Guidance, Using a Centralized IRB Review Process in Multicenter Clinical Trials, March 2006:
<http://www.fda.gov/regulatoryinformation/guidances/ucm127004.htm>

LIST OF APPENDICES

Appendix A – Application for a Reliance Agreement to be Submitted Electronically to OHSRP

Appendix B – Template for Agreement for An Outside Institution to Rely on an NIH IRB

Appendix C – Template for Agreement for NIH to Rely on An Outside Institution's IRB

Appendix D – Template for Agreement When NIH Serves as a Central IRB for a Multicenter Protocol

APPENDIX A – APPLICATION FOR A RELIANCE AGREEMENT TO BE SUBMITTED ELECTRONICALLY TO OHSRP

Department of Health and Human Services | National Institutes of Health



Reliance Agreement Form

This form is to be completed by NIH investigators seeking a reliance agreement as a result of being engaged in collaborative work with a non-NIH counterpart on a single protocol. If you are seeking a programmatic agreement or assistance for some other type of work then please contact the Office of Human Subjects Research Protections directly at our main number 301-402-3444.

Section 1 - Individual/IC requesting agreement	
Date agreement needed:	<input type="text"/> <input type="text"/> <input type="text"/>
Requestor's Name:	Margaret Sanders
Contact number (xxx-xxx-xxxx):	<input type="text"/>
Role:	<input type="radio"/> Administrative Support <input type="radio"/> Principal/ Senior Investigator <input type="radio"/> Co-Investigator <input type="radio"/> NIH lead person <input type="radio"/> Other If other, explain <input type="text"/>
Is NIH Principal/Senior Investigator the same as requestor?	<input type="radio"/> Yes <input type="radio"/> No
If no, name of NIH Principal/Senior Investigator (* required fields):	
*First:	<input type="text"/>
*Last:	<input type="text"/>
*Email:	<input type="text"/>
Degrees and/or credentials:	<input type="text"/>

IC:	<input type="text"/>
Lab/Branch:	<input type="text"/>
Building/Room no.:	<input type="text"/>
Telephone (xxx-xxx-xxxx):	<input type="text"/>
Is the NIH PI/Senior Investigator an NIH employee (FTE)?	<input type="radio"/> Yes <input type="radio"/> No If no, please provide their current status/designation within NIH <input type="text"/>
Section 2 - Entity involved in this study	
<i>A separate submission is required for each non-NIH entity.</i>	
List the institution involved in this study:	<input type="text"/>
Lead Investigator at the outside Institution and credentials (MD, PHD etc.):	<input type="text"/>
Are they the study PI?	<input type="radio"/> Yes <input type="radio"/> No
Is this a multisite trial?	<input type="radio"/> Yes <input type="radio"/> No
<i>A separate submission is required for each non-NIH entity. Multi-site research/protocols refer to projects that will be conducted at more than one location. Usually a multisite study involves conduct of an entire protocol carried out at more than one medical institution or site.</i>	
Section 3 - IRB & non-NIH Institutional Information	
What institution will be responsible for the IRB review?:	<input type="radio"/> NIH <input type="radio"/> Non NIH
Name of IRB providing review (.e.g. IRB of Record):	<input type="text"/>
Provide IRB # for IRB of Record:	<input type="text"/>
Please include the following information regarding the non-NIH IRB, if applicable	
Contact name:	<input type="text"/>

Address:	<input type="text"/>
Phone (xxx-xxx-xxxx):	<input type="text"/>
Email:	<input type="text"/>
FWA #:	<input type="text"/>
AAHRPP Accreditation	<input type="radio"/> Yes <input type="radio"/> No
Will the non-NIH entity be using a sub-contractor on this protocol?	<input type="radio"/> Yes <input type="radio"/> No If yes, please specify who they will be and outline what their roles and responsibilities will be in this collaboration:
	<input type="text"/>
Institution's Signatory Official's Name:	<input type="text"/>
Title:	<input type="text"/>
Signatory Official's address, phone and email:	
Street:	<input type="text"/>
City:	<input type="text"/>
State:	<input type="text"/>
Zip:	<input type="text"/>
Email:	<input type="text"/>
Phone (xxx-xxx-xxxx):	<input type="text"/>
Section 4 - Protocol Information	
Title of Protocol:	<input type="text"/>
Protocol number:	<input type="text"/>

Study PI:	<input type="text"/>
Brief description of protocol:	<div style="border: 1px solid gray; height: 40px; width: 100%;"></div>
Protocol status with regard to IRB approval:	<div style="border: 1px solid gray; height: 40px; width: 100%;"></div>
Section 5 - Roles and Responsibilities	
Provide names of all individuals who are not at the site of the IRB of record, who will be conducting human subjects research, and who will be relying on the IRB of record. (See Section 3):	<div style="border: 1px solid gray; height: 40px; width: 100%;"></div>
What research activities will these individuals do? Check all that apply	<input type="checkbox"/> Consultants only <input type="checkbox"/> Analyze identifiable data <input type="checkbox"/> Analyze de-identified data <input type="checkbox"/> Interact with subjects & conduct research activities (informed consent, research interventions) <input type="checkbox"/> Other If other, explain: <input style="width: 100px;" type="text"/>
Where will these activities take place? (e.g. NIH, non-NIH site (list name), subject's home etc.)?	<div style="border: 1px solid gray; height: 40px; width: 100%;"></div>
Has scientific review taken place for this protocol?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't Know If yes, date: (mm/dd/yyyy) <input style="width: 100px;" type="text"/> If yes, by whom? <input style="width: 100px;" type="text"/>
Section 6 - Risk Assessment	

<p>What is the risk assessment of the entire protocol?</p>	<p><input type="radio"/> Minimal risk <input type="radio"/> Greater than minimal risk</p>
<p>What is the risk assessment of the activities that will be the subject of the reliance agreement?</p>	<p><input type="radio"/> Minimal risk <input type="radio"/> Greater than minimal risk</p>
<p> </p>	
<p>Section 7 - Population</p>	
<p>Are subjects at foreign sites or research on a Native American reservation?</p>	<p><input type="radio"/> Yes <input type="radio"/> No If yes, provide further details <input type="text"/></p>
<p>Are there vulnerable subjects(e.g. pregnant women, children, prisoners, incapacitated adults)?</p>	<p><input type="radio"/> Yes <input type="radio"/> No If yes, provide further details <input type="text"/></p>
<p> </p>	
<p>Section 8 - Funding</p>	
<p>What entity is funding this protocol?</p>	<p><input type="text"/></p>
<p> </p>	
<p style="text-align: center;"><input type="button" value="Submit"/></p>	

APPENDIX B- TEMPLATE FOR AGREEMENT FOR AN OUTSIDE INSTITUTION TO RELY ON AN NIH IRB

**Agreement between
and
THE NATIONAL INSTITUTES OF HEALTH
To Rely on an NIH IRB**

Pursuant to 45 C.F.R. 46.114, the National Institutes of Health (NIH) and _____ are entering into this agreement for NIH to conduct Institutional Review Board (IRB) review of the research protocol or activities identified below, which are jointly conducted by NIH and _____

Name of Institution Providing IRB Review (Institution A):

National Institutes of Health

Federal Wide Assurance (FWA) # 00005897, expiration date: 8/28/2018

IRB **Registration #**

Name of Institution Relying on the Designated IRB (Institution B):

Federal Wide Assurance (FWA) # _____, expiration **date:** _____

Institution B will rely on the designated NIH IRB for review and continuing oversight of its human subjects research described below. This agreement is limited to the following specific protocol(s) or research activity:

Name of Research Project/Activity:

Protocol Number(s):

Name of Principal Investigator (NIH):

Name of Investigator(s) (Institution B):

Name of NIH Principal Investigator's Institute or Center:

The review performed by the NIH IRB will meet the human subject protection requirements of Institution B's OHRP-approved FWA. The protocol(s) reviewed by the NIH IRB must include a description of the research to be conducted by Institution B. The extent to which Institution B may rely upon the review by the NIH IRB is limited to the specific activities described in the reviewed protocol. The NIH will **report changes to the protocol** to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the terms of its OHRP-approved FWA.

Both Institutions will maintain current copies of the IRB approved protocol. NIH will conduct its portion of this joint research in accord with the terms and conditions of its OHRP-approved FWA. Institution B will conduct its portion of this joint research in accord with the terms and conditions of its OHRP-approved FWA. This Agreement will be kept on file at both Institutions and will be available to OHRP upon request.

The NIH IRB retains responsibility for compliance with regulatory requirements under 45 C.F.R. 46 and 21 C.F.R. 56 (as applicable) related to the administration and operation of the IRB. These include, for example, following written procedures and maintaining records in accord with 45 C.F.R. 46.103 and 46.115, respectively. Institution B agrees that the NIH IRB may suspend or terminate approval of research that is not conducted in accordance with the NIH IRB's requirements or that is associated with unexpected serious harm to subjects pursuant to 45 C.F.R. 46.113. The NIH will notify Institution B of any **serious or continuing** non-compliance, or suspensions, or terminations of this research in a timely manner.

Institution B will ensure that before implementing a change to an NIH IRB-approved protocol its investigator will obtain NIH IRB approval for the change (unless the change is designed to eliminate an apparent immediate hazard to subjects), pursuant to 45 C.F.R. 46.103. **Institutions B is responsible for ensuring the initial and ongoing qualifications of their investigators and research staff, including required training.** Institution B retains responsibility, pursuant to 45 C.F.R. 46, including subsections .103 and .113, to promptly report to the NIH IRB, any unanticipated risks to subjects or others, and any serious or continuing **or other non-compliance** with 45 C.F.R. 46 or the IRB's requirements or determinations **as well as any restrictions placed on this joint research activity by Institution B.**

The NIH **will report, consistent with 45 C.F.R 46 and, as applicable, 21 C.F.R 56 determinations of unanticipated problems, serious and/or continuing non-compliance, and any suspension or termination of IRB approval to institutional officials, HHS, and to the FDA. This does not relieve Institution B of the obligation to report, if applicable, beyond the requirements of 45 C.F.R 46 and 21 C.F.R 56 (e.g., as a condition of funding) to institutional officials, HHS or NIH officials.**

This Agreement is effective on the date that the last official signs and may be terminated by either party at any time. If the Agreement is terminated prior to the completion of the research, Institution B will need to obtain alternative IRB review.

Signatory Officials:

X _____
Institute Name

Name:
Title:

Address

Phone:

Fax:

Email:

Date: _____

X _____

National Institutes of Health

Charlotte Holden, JD, Deputy Director

Office of Human Subjects Research Protections, National Institutes of Health

10 Center Drive

Bldg. 10, Suite 2C146

Bethesda, MD 20892

Phone: 301-402-3444

Fax: 301-402-3443

E-mail: HoldenC@od.nih.gov

Date: _____

APPENDIX C – TEMPLATE AGREEMENT FOR NIH TO RELY ON AN OUTSIDE INSTITUTION'S IRB

**Agreement between
THE NATIONAL INSTITUTES OF HEALTH
and
To Rely on the _____ IRB**

Pursuant to 45 C.F.R. 46.114, the National Institutes of Health (NIH) and _____ are entering into this agreement for _____ to conduct Institutional Review Board (IRB) review of the research protocol or activities identified below, which are jointly conducted by NIH and _____.

Name of Institution Providing IRB Review (Institution A):

Federal Wide Assurance (FWA) # _____, expiration date: _____
IRB **Registration** # _____

Name of Institution Relying on the Designated IRB (Institution B):

National Institutes of Health
Federal Wide Assurance (FWA) # 00005897, expiration date: 8/28/18

NIH will rely on the IRB of Institution A for review and continuing oversight of its human subjects research described below. This agreement is limited to the following specific protocol(s) or research activity:

Name of Research Project/Activity:
Protocol Number(s):
Name of Principal Investigator (Institution A):
Name of NIH Investigator (Institution B):
Name of NIH Investigator's Institute or Center:

The review performed by Institution A's IRB will meet the human subject protection requirements of NIH's OHRP-approved FWA. The protocol(s) reviewed by Institution A's IRB must include a description of the research to be conducted by NIH. The extent to which NIH may rely upon the review by Institution A's IRB is limited to the description of those research activities in the protocol. Institution A's IRB will follow written procedures for reporting its findings and actions to appropriate officials at NIH. Relevant minutes of IRB meetings will be made available to NIH upon request. NIH remains responsible for ensuring compliance with the reviewing IRB's determinations and with the terms of its OHRP-approved FWA.

Both Institutions will maintain current copies of the IRB- approved protocol. NIH will conduct its portion of this joint research in accord with the terms and conditions of its OHRP-approved FWA. Institution A will conduct its portion of this joint research in accord with the terms and conditions of its OHRP-approved FWA. This Agreement will be kept on file at both Institutions and will be available to OHRP upon request.

Institution A's IRB retains responsibility for compliance with regulatory requirements under 45 C.F.R. 46 and 21 C.F.R. 56 (as applicable) related to the administration and operation of the IRB. These include, for example, following written procedures and maintaining records in accord with 45 C.F.R. 46.103 and 46.115, respectively. NIH agrees that Institution A's IRB may suspend or terminate approval of research that is not conducted in accordance with its requirements or that is associated with unexpected serious harm to subjects pursuant to 45 C.F.R. 46.113. **Institution A will notify NIH of any serious or continuing non-compliance, or suspensions, or terminations of the research in a timely manner.**

NIH will ensure that before implementing a change to Institution A's IRB-approved protocol its investigator will obtain Institution A's IRB approval for the change (unless the change is designed to eliminate an apparent immediate hazard to subjects), pursuant to 45 C.F.R. 46.103. **NIH is responsible for ensuring the initial and ongoing qualifications of its investigators and research staff, including required training.** NIH retains responsibility, pursuant to 45 C.F.R. 46, including subsections 103 and 113, to report promptly to **Institution A's IRB any unanticipated risks to subjects or others, and any serious or continuing or other non-compliance with 45 C.F.R. 46 or the IRB's requirements or determinations as well as any restrictions placed on this joint research activity by NIH.** **Institution A's IRB will report, consistent with 45 C.F.R 46 and, as applicable, 21 C.F.R 56 determinations of unanticipated problems, serious and/or continuing non-compliance, and any suspension or termination of IRB approval to institutional officials, HHS, and to the FDA.**

This Agreement is effective on the date that the last official signs and may be terminated by either party at any time. If the Agreement is terminated prior to the completion of the research, NIH will need to obtain alternative IRB review.

Signatory Officials:

X _____
[name of non NIH Institution]

[Institution's Signatory Official's Name]
[Title]
[Signatory Official's address, phone and email]

Date: _____

X _____
National Institutes of Health

Charlotte Holden, JD
Deputy Director
Office of Human Subjects Research Protections, National Institutes of Health
10 Center Drive
Bldg. 10, Suite 2C146
Bethesda, MD 20892
Phone: 301-402-3444
Fax: 301-402-3443
E-mail: HoldenC@od.nih.gov

Date: _____

**APPENDIX D – TEMPLATE FOR AGREEMENT WHEN NIH SERVES AS A
CENTRAL IRB FOR A MULTICENTER PROTOCOL**

Authorization Agreement between

and
THE NATIONAL INSTITUTES OF HEALTH
To Rely on an NIH Central IRB

Pursuant to 45 C.F.R. 46.114, the National Institutes of Health (NIH) and _____ are entering into this Agreement for NIH to conduct Institutional Review Board (IRB) review of the research protocol(s) or activities identified below in section C. Division of Responsibilities.

A. Name of organization providing IRB Review: National Institutes of Health
Institutional Review Board (NIH
IRB) _____ [Insert name of NIH IRB]
Federal Wide Assurance (FWA) # 00005897, expiration date 8/28/2018
IRB Registration # _____

B. Name of institution relying on the NIH IRB: *Insert Signatory Institution Name*
(Signatory Institution)

Signatory Institution's OHRP Federalwide Assurance (FWA) Number:

Insert FWA# _____ *FWA expiration date* _____

1. A Signatory Institution's "Component Institution" is defined by the NIH IRB as meeting all of the following criteria:

- a. the Component Institution operates under a different name than the Signatory Institution but the Signatory Institution has legal authority for the Component Institution;
- b. the FWA number for the Component Institution is the same as the Signatory Institution;
- c. the local context considerations of the Component Institution are the same as the Signatory Institution;

- d. the boilerplate language and institutional requirements of the Component Institution are the same as the Signatory Institution; and
- e. the conduct of research at the Component Institution is monitored by the same office as the Signatory Institution.

List the Signatory Institution's Component Institution(s), if any, by name:

Insert Component Institution Name(s), or state "none"

2. A Signatory Institution's "Affiliate Institution" is defined by the NIH IRB as meeting all of the following criteria:

- a. the FWA number for the Affiliate Institution is not the same as the Signatory Institution;
- b. the local context considerations of the Affiliate Institution are the same as the Signatory Institution;
- c. the boilerplate language and institutional requirements of the Affiliate Institution are the same as the Signatory Institution; and
- d. the conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution.

List the Signatory Institution's Affiliate Institution(s), if any, by name:

Insert Affiliate Institution Name(s), FWA #, and FWA expiration date, or state "none"

C. Division of Responsibilities

The review performed by the NIH IRB will meet the human subject protection requirements of *Insert Signatory Institution Name's* OHRP-approved FWA. The NIH IRB will follow NIH Human Research Protection Program (HRPP) written procedures for reporting its findings and actions to appropriate officials at *Insert Signatory Institution Name*. Relevant minutes of NIH IRB meetings and supporting documents are available to the Signatory Institution upon request of the Institutional Designee or the local IRB leadership at any time. *Insert Signatory Institution Name* remains responsible for ensuring compliance with the NIH IRB's determinations and with the terms of the Signatory Institution's OHRP-approved FWA. This document should be kept on file at

the Signatory Institution and at the NIH IRB Operations Office and must be provided to the HHS Office for Human Research Protections (OHRP) upon request.

The responsibilities of the NIH are to:

- 1) Maintain NIH IRB membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56 and provides special expertise as needed to adequately assess all aspects of each study.
- 2) Maintain an FWA.
- 3) Retain IRB records for at least three (3) years after completion of the research.
- 4) Conduct initial, amendment, and continuing review of research as well as review of any other study-specific documents submitted to the NIH IRB;

_____ This agreement is limited to the following specific protocol(s) or research activity:

Name of Research Project/Activity:

Name of Principal Investigator (at Signatory Institution):

Name of Collaborating NIH Principal Investigator, if any:

Name of Collaborating NIH Principal Investigator's Institute or Center:

Name of Institutional Designee for Signatory Institution:

_____ This agreement applies to all protocol(s) or research activities submitted to the NIH IRB by the Signatory Institution.

- 5) Conduct review of local context considerations based on submission of requested local context information provided by the Signatory Institution as outlined, as applicable, in the following Worksheets (See attachments):
 - a) Initial Review Local Context Worksheet;
 - b) Continuing Review (or Update to) Local Context Worksheet; and
 - c) Study-Specific Local Context Worksheet.
- 6) Conduct review of potential unanticipated problems and/or serious or continuing noncompliance when the Signatory Institution or other entity reports an incident, experience, or outcome to the NIH IRB. This review includes reporting any unanticipated problem and/or serious or continuing noncompliance determination to OHRP, the FDA (if applicable), and the Institutional Designee for the Signatory

Institution. If the NIH IRB determines that it must report serious or continuing non-compliance determinations, suspensions or terminations or the findings of an investigation to OHRP, the FDA and/or other oversight entities, it will notify the Signatory Institution in advance. When feasible, the NIH IRB will provide the Signatory Institution the opportunity to review and comment on the report before it is sent to OHRP, the FDA or others, provided that Signatory Institution promptly provides any comments to the report. Nothing in this Agreement shall prevent the Signatory Institution from making its own report or from taking additional remediation steps at its own institution, that are more stringent than NIH IRB requirements provided such steps do not conflict with NIH IRB requirements.

- 7) Report any suspension or termination of NIH IRB approval to OHRP, FDA (if applicable), and the Institutional Designee for the Signatory Institution;
- 8) Provide institution-specific documents related to NIH IRB reviews, such as initial and continuing review approval notifications and IRB determinations related to site specific problem reports via email to the Signatory Institution's Principal Investigator and Institutional Designee, and, upon request, provide NIH IRB member roster.
- 9) Notify the Institutional Designee for the Signatory Institution immediately if there is a suspension or restriction of the NIH IRB's authorization to review a study; and
- 10) Post the NIH IRB Standard Operating Procedures on the public side of the NIH HRPP website.

The responsibilities of the Signatory Institution are to:

- 1) Comply with the NIH IRB's requirements and directives as encompassed in the publicly available NIH HRPP standard operating procedures and communications from the NIH IRB or NIH.
- 2) Report to the NIH IRB the names of any Component or Affiliate Institutions to be engaged in the covered research, if applicable, which must meet the following definitions:

a) Component Institutions are defined by the NIH IRB as meeting all of the following criteria:

- The Component Institution operates under a different name than the Signatory Institution, but the Signatory Institution has legal authority for the Component Institution;
- The FWA number for the Component Institution is the same as the Signatory Institution;
- The local context considerations of the Component Institution are the same as the Signatory Institution;
- The boilerplate language and institutional requirements of the Component Institution are the same as the Signatory Institution; and
- The conduct of research at the Component Institution is monitored by the same office as the Signatory Institution.

b) Affiliate Institutions are defined by the NIH IRB as meeting all of the following criteria:

- The FWA number for the Affiliate Institution is not the same as the Signatory Institution;
- The local context considerations of the Affiliate Institution are the same as the Signatory Institution;
- The boilerplate language and institutional requirements of the Affiliate Institution are the same as the Signatory Institution; and
- The conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution

3) Ensure the safe and appropriate performance of the research at the Signatory Institution and, as applicable, at all Component Institutions and Affiliate Institutions. This includes, but is not limited to:

a) Ensuring the initial and ongoing qualifications of investigators and research staff, including required training;

b) Overseeing the conduct of the research;

c) Monitoring protocol compliance;

d) Maintaining compliance with state, local, or institutional requirements related to the protection of human subjects;

- e) Providing a mechanism to receive and address research related concerns from local study participants and others about the conduct of the research;
- f) Investigating, managing, and providing notification to the NIH IRB of any research-specific incidence, experience, or outcome that seems to rise to the level of an unanticipated problem and/or serious or continuing noncompliance. When notifying the NIH IRB of a potential unanticipated problem and/or serious or continuing noncompliance, the Signatory Institution must provide a plan to manage the incident, experience, or outcome, including measures to prevent similar occurrences. The NIH IRB will report, consistent with 45 CFR 46 and 21 CFR 56, as applicable, determinations of unanticipated problems, serious and/or continuing noncompliance, and any suspension or termination of IRB approval of which it is aware and required to report to the OHRP and to the FDA, with a copy to the Signatory Institution. If the NIH IRB determines that it must report serious or continuing non-compliance determinations, suspensions or terminations or the findings of an investigation to OHRP, the FDA and/or other oversight entities, it will notify the Signatory Institution in advance. When feasible, the NIH IRB will provide the Signatory Institution the opportunity to review and comment on the report before it is sent to OHRP, the FDA or others, provided that Signatory Institution promptly provides any comments to the report. If the Signatory Institution is required to report beyond the requirements of 45 CFR 46 and/or 21 CFR 56 (e.g., as a condition of funding), the Signatory Institution retains responsibility to do so (e.g., promptly report to its own institutional officials, and the HHS or NIH agency head, unanticipated risks to subjects or others, and serious or continuing noncompliance with 45 CFR 46, 21 CFR 56, or the IRB's requirements or determinations.)
- g) Ensuring that before implementing a change to an NIH IRB-approved protocol, its principal investigator will obtain NIH IRB approval for the change (unless the change is designed to eliminate an apparent immediate hazard to subjects), pursuant to 45 C.F.R. 46.103.
- h) Retaining the authority to observe any aspect of the research process including observation of the consent process. The NIH IRB retains the authority to direct this to be done and has the authority to observe or have a third party observe any aspect of the conduct of the research or of the consent process.

- 4) Provide updates in a timely manner to the NIH IRB whenever a Signatory Institution Principal Investigator is replaced. The NIH IRB may require submission and approval of an updated local context form, e.g., as applicable, Continuing Review (or Update to) Local Context Worksheet, prior to finalizing the replacement Principal Investigator;
- 5) Notify the NIH IRB when a research-related regulatory deficiency has been cited on an audit that occurred during the time that the NIH IRB was responsible for research review;
- 6) Complete and submit any required local context forms, e.g., as applicable, Initial Review Local Context Worksheet, Continuing Review (or Update to) Local Context Worksheet; and Study-Specific Local Context Worksheet, and any other worksheets/forms required by the NIH IRB;
- 7) Use only the NIH IRB approved consent form and:
 - a) Obtain NIH IRB approval of changes to consent form language prior to implementation; and
 - b) Obtain NIH IRB approval of translations of the consent form prior to implementation.
- 8) Maintain study-related documents and, if required by law, or institutional or sponsor policy, a regulatory file for each study under NIH IRB purview as per local institution and sponsor policy.

D. Authorization

The Officials signing below agree that the NIH IRB provides IRB review as described in section C. Division of Responsibilities of this document for *Insert Signatory Institution Name* and, if applicable, all Component and/or Affiliate Institutions identified.

This Agreement is effective on the date that the last official signs and may be terminated by either party at any time. If the Agreement is terminated prior to the completion of the research, Signatory Institution will need to obtain alternative IRB review. In the event of any termination of this Agreement, the parties will work together to determine the effect of such termination on any research and associated research activities being conducted under the Agreement at the time of termination.

Name and contact information of Signatory Official for the relying Signatory Institution:

Signature _____ Date _____

Name _____

Title _____

Address _____

Phone: _____

Email: _____

Name and contact information of Signatory Official for the NIH:

Signature _____ Date _____

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