This document summarizes high level changes in *Policy 105 IRB Reliance and Collaborative Research* (referred to as Policy 105 in this document) that NIH investigators should be aware of, from the Standard Operating Procedures (SOPs) mentioned below. This policy describes requirements for when the NIH will serve as a reviewing IRB for multi-site research involving 1 or more institutions. This policy also describes requirements for NIH investigators when using an external IRB. This policy specifies how the NIH will comply with the NIH Single IRB Policy and the cooperative research provisions of the 2018 Common Rule (45 CFR 46). However, NIH investigators are responsible for reviewing Policy 105 and complying with the requirements of the policy.

Policy 105 IRB Reliance and Collaborative Research	**SOP 20A Obtaining a Reliance (Authorization) Agreement at the NIH**
Policy 105 supersedes:	**SOP 20 NIH HRPP Requirements for Collaborative Research** This SOP will not be replaced by an HRPP policy and will be inactivated. When inactivated, this SOP will be archived in the Policy Archive.
Policy 105 supersedes:	**SOP 20A Obtaining a Reliance (Authorization) Agreement at the NIH** When inactivated, this SOP will be archived in the Policy Archive.
Policy 105 supersedes:	**SOP 20B NIH IRB Responsibilities Reviewing Local Context Considerations for Offsite Research** This SOP will also be partially superseded by *Policy 700 International Research.* When fully inactivated, this SOP will be archived in the Policy Archive.
Policy 105 supersedes:	**SOP 20C Responsibilities When the NIH Intramural Research Program Serves as a Coordinating Center for a Multisite Trial or as the IRB of Record for a Non-NIH Coordinating Center** This SOP will not be replaced by an HRPP policy and will be inactivated. When inactivated, this SOP will be archived in the Policy Archive.
Section B.1.a – *This policy is applicable to NIH investigators when relying on a non-NIH (external) IRB for the oversight of human subjects research.*	NA
Section B.1.b. – *This policy is applicable to NIH and non- NIH investigators when the NIH IRB is the reviewing IRB for multi-site research*.	NA
Section C.1. – *The OHSRP Office of IRB Operations (IRBO) will evaluate multi-site*	SOP 20 Section 20.2 – *NIH complies with 45 CFR 46.114, and when applicable, 21 CFR*

(also referred to as cooperative research) proposals and determine whether single IRB (sIRB) review is required by federal regulation (45 CFR 46 and 21 CFR 56, as applicable) or by NIH policy (NIH Single IRB Policy). This policy has been expanded to include the NIH single IRB policy and to address the cooperative research provisions of the 2018 Common Rule (45 CFR 46). Section C.1.b. – *Exceptions to the NIH Single IRB Policy, or the new cooperative research provisions of the 2018 Common Rule, must be made through the IRBO.* NIH investigators may not seek these exceptions on their own.	*56.114. This Standard Operating Procedure (SOP) contains the NIH policy requirements for obtaining Reliance Agreements.* Neither the NIH Single IRB Policy, nor the cooperative research provisions of the 2018 Common Rule (45 CFR 46) were in effect at the time of publication. At the time this SOP was written it was at the discretion of the NIH whether to be a reviewing IRB or to cede IRB review to another institution.
Section C.1.a. – *When sIRB review is not required by federal regulation or by NIH policy, and utilization of an sIRB is requested, the OHSRP Director, IRBO Director or designee, will consider this request on a case-by-case basis.* Reliance agreements for multi-site research are now required by regulation (the cooperative research provisions of the 2018 Common Rule), and by NIH policy for research supported by the NIH, (NIH Single IRB policy). The NIH and other institutions have discretion whether to enter into reliance agreements for those collaborations that are not federally funded, or are otherwise excepted under federal regulation or NIH policy.	SOP 20A Section 20A.5 – *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.* SOP 20A – Describes that prior to the implementation of the NIH single IRB policy and the cooperative research provisions of the 2018 Common Rule, the decision to enter into a reliance agreement was at the discretion of the institution. See also SOP 20A Section 20A.6.D. – This describes that the DDIR will decide whether to enter into programwide reliance agreements.
Section C.4. – *The NIH will only cede review to external IRBs that have undergone or initiated an assessment of its quality within the past 5 years. The assessment may be accomplished through accreditation by an*	NA

external organization or through OHRP's Quality Assessment Program, or other equivalent approach. Section C.4.a. – *The OHSRP Director may waive this requirement if s/he determines that for a given study it is in the interest of the NIH that an IRB serve as reviewing IRB that has not undergone such a quality assessment, and that s/he determines that there are no significant outstanding regulatory actions or determinations against the reviewing IRB.* IRBO will confirm if this requirement has been met when assessing the request for a reliance agreement. Accreditation, or seeking accreditation, is usually an indication of a quality assessment.	
Section C.5.a. – *NIH investigators do not have the authority to sign or otherwise commit to any reliance agreement.*	NA
Section C.9.a. – *When the NIH is relying on an external IRB, the NIH PI/NIH Lead Site Investigator (referred to as the NIH PI):* • *Will ensure that all NIH requirements for the conduct of research are met, including all applicable institutional and ancillary reviews (e.g., scientific review, radiation safety committee review, etc.).* • *Will submit all required materials to the IRBO for administrative/local context review prior to submitting to the external IRB.* • *The NIH PI may not make a submission to the external IRB for review, until notified by the IRBO that the administrative/local context review is complete, and that submission to the external IRB is allowed to proceed.*	SOP 20A Section 20A.8. – *When NIH relies on an outside IRB, the following additional requirements apply:* *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).* The responsibilities listed above don't fully cover NIH institutional requirements. Policy 105 is purposefully broader than SOP 20A.

See below regarding Section E.2.a.VII.iii. which also specifies this requirement in more detail.	
Section D – Definitions - Since the implementation of the NIH Single IRB Policy, many terms of art for multi-site research and single IRB review have changed. Investigators should review and become familiar with new terms:	SOP 20A Section 20A.3. Definitions –
Cooperative Research – See "Multi-site Research."	***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."*
Lead Site Investigator – The lead investigator responsible for the conduct of research at a participating site for a multi-site protocol. At the NIH, this investigator will be referred to as the NIH PI.	
Multi-site Research – Research projects (protocols) that involve more than one institution that is engaged in, and conducting, the same human subjects research. Also referred to as "cooperative research."	***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.*
Participating Site – Is a research site involved in multi-site research.	***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.*

Reviewing IRB – The IRB responsible for reviewing human subjects research and determining that the research meets the required criteria for approval under the regulatory requirements at 45 CFR 46 and, as applicable, the pertinent Subparts of 21 CFR parts 50, 56, 312 and 812, institutional policy, and the terms of the reliance agreement(s), if any.	This term has been replaced by the more general term "Participating Site" ***IRB of Record:*** *The IRB responsible for review of research and determining that the research meets IRB regulatory requirements for approval.* ***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."* These two terms have been replaced with the term "Reviewing IRB".
Section E.1. – Responsibilities of OHSRP and IRBO – Investigators should be aware of several points covered in this section: Section E.1.c. IV. – *Ensuring, that the NIH IRB will only approve the addition of a participating site after it has received confirmation that:* *i. The institutional requirements of the relying institution have been met; and* *ii. The local context information provided has been approved by the relying institution* When serving as the reviewing IRB, the NIH IRB will not review or approve the addition of a participating site, until the NIH PI has submitted the items described in i. and ii. above.	

Section E.1.c.VII. – IRBO is responsible for the following when the NIH is relying on an external IRB: *i. Conducting administrative reviews of research protocols and consents to ensure compliance with NIH requirements (e.g., ancillary committee reviews or conflict of interest requirements)* *ii. The IRBO will issue the "NIH Institutional Review Memo" to the NIH PI, once it is satisfied that institutional requirements have been met (e.g., all applicable ancillary approvals have been completed).* Before an NIH PI may submit to an external IRB, two things have to happen: first the reliance agreement must be executed, second the PI must submit the protocol, master or site-specific consents, proof of completion of ancillary reviews, if any, proof of training, etc. to IRBO for administrative review. This is an administrative review to ensure NIH requirements are met and *is not* an IRB review. However, most external IRBs will decline to commence review without proof that local institutional requirements have been met. The "NIH Institutional Review Memo" satisfies this requirement and the external IRB will look for this memo at time of initial submission.	NA
Section E.2.a.I. – *NIH PIs are responsible for informing the IRBO, as early as possible, of the intent to rely upon an external IRB, or requesting that the NIH IRB serve as the reviewing IRB for multi-site research.* NIH has the discretion to either serve as the reviewing IRB for multi-site research or use a commercial IRB to perform this service. NIH PIs *should not* assume that the NIH IRB	NA

will be the reviewing IRB and should instead consult OHSRP as early as possible when considering which institution serve as the reviewing IRB for NIH initiated multi-site research.	
Section E.2.a.II. – *NIH PIs are responsible for working with IC leadership to ensure payment for IRB services when IRBO has granted permission for the PI to use an NIH-approved commercial IRB.* If the NIH will use the services of a commercial IRB, payment of services is the responsibility of the NIH PI and his/her IC. The PI should work with their IC to ensure that IRB review is included in the protocol budget.	NA
Section E.2.a.VII.ii. – *Ensuring, when the NIH is relying on an external IRB:* • *Review of, and compliance with, the policies and requirements of the reviewing IRB (e.g., the timely reporting of all reportable events to the reviewing IRB, amendments and, when required, continuing review.* Policy 105 is more specific than SOP 20A that the NIH PI must follow the requirements of the reviewing IRB. This change also reflects that not all reviewing IRBs are associated with another research institution (e.g., commercial IRBs).	SOP 20A Section 20A.13. – *The NIH PI will at a minimum, conform to the human research policies and operating procedures of the reviewing institution.*
Section E.1.a.VII.iv. – *That the following have been submitted to the IRBO for administrative review, including:* • *Protocol and consent(s)/assent(s);* • *All applicable ancillary committee approvals;* • *Protocol-specific local context information; and* • *Any other information as requested by the IRBO.*	NA

Section E.2.a.VII.v. – *Ensuring, when the NIH is relying on an external IRB:* • *That submission to the external reviewing IRB will not take place until the NIH PI has received the NIH Institutional Review Memo and the approved local context information from IRBO.*	NA
Section E.2.a.VII.vii. – *Ensuring, when the NIH is relying on an external IRB:* • *Submit to IRBO upon receipt all external IRB approvals, including the IRB-approved protocol and consents.*	NA
Section E.2.a.VII. viii. – *Ensuring, when the NIH is relying on an external IRB:* • *That no research activities commence until all required NIH and applicable external approvals have been received.*	NA
Section E.2.a.VIII. – *Submission to the NIH IRB of a plan for monitoring the oversight of non-NIH site(s).* • *Outline the specific research activities that will occur at the non-NIH site(s);* • *Describe the steps to ensure study and regulatory compliance by external Lead Site Investigators; and* • *Specify how the NIH PI will notify external Lead Site Investigators, in writing of the NIH IRB's review determinations.* • *Be either submitted as an amendment to an already approved protocol or be included with the initial protocol submission.*	This requirement is addressed in *SOP 20C Responsibilities When the NIH Intramural Research Program Serves as a Coordinating Center for a Multisite Trial or as the IRB of Record for a Non-NIH Coordinating Center.*
Section E.2.a.VIII.iii. – *That a participating site is not added until a reliance agreement is executed, and the NIH PI has distributed the IRB-approved materials to the participating site.*	NA
Section E.2.a.VIII.iv. – *When non-NIH investigators will conduct research at a NIH*	NA

site, that all related approvals are secured prior to commencing any research at an NIH facility.	
Section E.2.a.VIII.v. – NIH PIs are responsible to ensure*: That all participating sites are provided with the relevant policies and procedures of the NIH IRB or where to find such materials.*	NA
Section E.2.a.VIII.vi. – The NIH PI must: *Communicate to all participating sites regarding the outcome of all site-relevant NIH IRB determinations.* When the NIH is initiated the research, the IRB (internal or external) will expect the NIH PI to be the primary communicator with the study sites.	Footnote 3 in SOP 20A – 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. In SOP 20A this was largely informational to the NIH PI. In Policy 105, this is a requirement for the NIH PI.