



Frequently Asked Questions (FAQs)

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Introduction

Q: What is SMART IRB?

A: SMART IRB is an initiative developed under an award from the National Center for Advancing Translational Sciences (“NCATS”) of the National Institutes of Health (“NIH”) to support single Institutional Review Board (“IRB”) review in facilitation of multi-site human subjects research. SMART IRB includes:

- An IRB reliance agreement that permits eligible institutions that join it (“Participating Institutions”) to cede review of human subjects research to other Participating Institutions’ IRBs; and
- A set of standard operating procedures (SOPs) to guide implementation of the reliance relationship among Participating Institutions.
- A network of regional ambassadors to support adoption and implementation of IRB reliance across the nation
- Centralized online systems to support sign-on, reliance determinations, and harmonization (ongoing development)

Q: What is the SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement?

A: The SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement (the “SMART IRB Agreement” or the “Agreement”) is the IRB authorization agreement or reliance agreement that permits Participating Institutions to cede review of human subjects research to other Participating Institutions’ IRBs. The Agreement sets forth the authorities, roles, and responsibilities of Participating Institutions and their IRBs when ceding or providing IRB review. The Agreement is designed to meet the proposed regulatory requirement in the Common Rule Notice of Proposed Rulemaking (80 Fed. Reg. 53933 (Sept. 8, 2015)) for documentation of the respective compliance responsibilities of institutions and IRBs participating in an IRB reliance relationship. The Agreement was developed with the input of over 110 institutions, from 33 states, including many of the 64 funded Clinical Translational Science Award Hubs.

The SMART IRB Reliance Model

Q: I have heard about “share” and “non-share” models of reliance, as well as “one-way” and “reciprocal” models, “one-off” and “master” reliance arrangements, and a host of other models. What type(s) of reliance does SMART IRB support?

A: SMART IRB is a “non-share” model of reliance, which means that the IRB responsible for review of research on behalf of other institutions is responsible for all aspects of the IRB review. In other words, the reviewing IRB performs initial review, continuing review, review of amendments (study-wide and those specific to particular institutions), and review of reportable events. With respect to any given institution, there is a single IRB of record overseeing its participation in the research study. In addition, Participating Institutions can use SMART IRB to support one-way reliance relationships (when an institution only relies on another’s IRB or only provides IRB review) and reciprocal reliance relationships (when an institution may for one research study rely on another’s IRB and may for another research study provide IRB review). Institutions can also use SMART IRB to support reliance for a single research study or specific category of research studies or for multiple research studies as the need arises. As its full name reflects, the SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement is designed – and is flexible enough – to support a broad range of reliance relationships in facilitation of the national goal to increase utilization of single IRBs.

Q: Can SMART IRB be used to support a designated central IRB?

Yes. SMART IRB and the SMART IRB Agreement can be used to support and document a central IRB arrangement for one or multiple studies, such as a central IRB for an industry-funded trial or for a federally-funded clinical trials network or consortium. The Agreement provides that in such situations, any policies and procedures or terms of participation required by the funder, the network, or the designated central IRB, including those that affect the reliance relationship, will apply and will override any provisions of the Agreement with which they conflict. Any policies and procedures or terms of participation required by the funder, the network, or the designated central IRB must be communicated in writing to Relying Institutions.

Scope of Covered Research

Q: What types of research can be reviewed under SMART IRB?

A: SMART IRB is intended to allow reliant IRB review of US human subjects research.

The research may be externally or internally funded; the Agreement does not limit the scope of what is covered based on funding source or status. Although it is generally expected that SMART IRB will be used for US human subjects research, it could be used for international research if the parties involved in such research determine that SMART IRB and the SMART IRB agreement meet their needs and any international requirements for such arrangements.

NOTE: The Federal Food, Drug, and Cosmetic Act includes language that suggests that IRB review must be “local” in the case of FDA-regulated device studies [Section 520(g)(3)(A)(i) (21 USC 360j(g)(3)(A)(i))]. The regulations state that “the person applying for the exemption submit a plan for any proposed clinical testing of the device ...to the local institutional review committee which has been established in accordance with regulations of the Secretary to supervise clinical testing of devices in the facilities where the proposed clinical testing is to be conducted...”. As part of 21st Century Cures legislation, the FDA may eliminate the “local” IRB requirement for device studies (see section 2262, <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127013.pdf>). The SMART IRB Agreement is silent and does not preclude single IRB review of FDA-regulated device studies. Institutions may exercise discretion when reviewing and relying.

Q: Can SMART IRB be used for making and documenting determinations of exemption from IRB review?

A: Yes. Although the main purpose of SMART IRB is to cover ceding of IRB review responsibilities for research for which IRB review is required, it is recognized that currently at some institutions, IRBs also determine whether human subjects research is exempt from review under the Common Rule and other applicable federal regulations and policies. If a Participating Institution would like to have another Participating Institution’s IRB make and document exemption determinations on its behalf, the Participating Institution may use the SMART IRB Agreement for such an arrangement. In such cases, some of terms of the SMART IRB Agreement will not apply to the arrangement.

Q: One of the eligibility criteria for participation in SMART IRB is that my institution require IRB review and institutional oversight for our human subjects research regardless of funding source and regardless whether we have “checked the box” on our FWA. This requirement does not appear to have an exception for exempt human subjects research, which under the current Common Rule does not require IRB review or trigger any other regulatory obligations. Can you explain why?

A: The intent of this criterion, which is stated in Section 1.1 of the Agreement, is not to require IRB review or institutional oversight for human subjects research that is currently exempt from IRB review

and other regulatory requirements under the Common Rule (as of the date the SMART IRB Agreement was released). However, in recognition of the Common Rule NPRM proposals, which include creation of new exempt categories that will have limited IRB review and other regulatory requirements attached to them, the drafters of SMART IRB did not build an exception to this eligibility criterion for exempt research. If the Common Rule NPRM proposals are finalized in their current form, the expectation under the Agreement is that institutions will require institutional oversight, which may include limited IRB review in some cases, for the new exempt categories of human subjects research that will require such review or have other regulatory requirements attached to them.

Q: If my institution participates in SMART IRB, is it required to cede review of any or all of its human subjects research? Is my institution required to provide IRB review for other sites?

A: Unless required by policy or as a condition of participation in a study or research consortium, each Participating Institution elects on a case-by-case basis whether to cede IRB review of or provide IRB review for any research study or studies under the Agreement and whether to participate in any ceded review agreed upon by other Participating Institutions.

Q: How is it determined what specific research study(ies) will be ceded under the Agreement?

A: Each Participating Institution, in consultation with other involved Participating Institutions as needed, makes a determination whether a research study(ies) is appropriate for ceded review. No Participating Institution involved in the research is required to participate in the ceded review. If one or more involved Participating Institutions declines to participate in the ceded review, the other institutions may still participate in it.

Q: If my institution participates in SMART IRB, can it still participate in other IRB reliance agreements, including with other Participating Institutions?

A: Yes. Participation in SMART IRB does not preclude participation in any other IRB reliance agreement or arrangement with any other entity, including with other institutions that are also participating in SMART IRB. Although institutions may wish to consider switching to the SMART IRB Agreement to cover their existing reliance relationships, or those going forward, there is no requirement to do so. Institutions that participate in multiple reliance agreements with the same institutions should communicate with one another in advance of ceding review for any research study about which agreement they are using to cover and document the reliance for that research.

Eligibility to Participate

Q: Who can join SMART IRB?

A: Any institution that meets the eligibility criteria (see next question below) and agrees to the terms and conditions of the SMART IRB Agreement through execution of a Joinder Agreement (see [How To Join SMART IRB](#) below) may participate in SMART IRB.

Q: What are the eligibility criteria that an institution must meet in order to participate in SMART IRB?

A: An institution must meet the following criteria in order to become a Participating Institution in SMART IRB:

- 1) If it conducts any human subjects research, regardless of funding source, the institution must maintain an Office for Human Research Protections (“OHRP”)-approved Federalwide Assurance (“FWA”). SMART IRB views maintenance of an FWA as a baseline indicator of an institution’s agreement to be accountable for the compliance of its human subjects research program with federal and ethical norms and standards.

Additionally, the institution, by policy or otherwise, must require IRB review and provide institutional oversight of its human subjects research regardless of funding source or the scope of its FWA. Even when IRB review is not required, other institutional policies and oversight mechanisms should still exist and apply such that the exempt project is still under the “jurisdiction” of the institution and subject to its generally applicable standards. For example, many institutions provide in their policies that exempt research must still be in compliance with basic ethical standards, is subject to institutional/investigator conflict of interest policies, must be conducted in accordance with the institution’s HIPAA privacy/patient confidentiality policies, etc. These are just examples; the SMART IRB Agreement does not prescribe exactly what institutional oversight is required, just that there is some level of jurisdiction of the institution over the conduct of the project.

- 2) If it has an IRB or is an independent IRB organization, then within the 5 years prior to joining SMART IRB, the institution must have undergone or have initiated an assessment of the quality of its human research protection program (“HRPP”). SMART IRB does not proscribe the nature of the assessment; it can be a third-party assessment or a self-assessment. Accreditation through an external organization, use of OHRP’s QA Self-Assessment Tool or FDA’s Self-Evaluation Checklist for IRBs, use of the Association for the Accreditation of Human Research Protection Programs (“AAHRPP”) Evaluation Instrument for Accreditation with self-documentation of satisfaction of requirements, or another approach with a comparable, comprehensive scope of review of the HRPP that includes assessment of the IRB are sufficient to meet this criterion. Depending on the scope of audit, an audit of the institution’s IRB by a federal agency, with no major issues identified and any minor issues

corrected/resolved, may also be sufficient. The Agreement provides that Participating Institutions may obtain information about how any other Participating Institution satisfied SMART IRB’s HRPP quality assessment requirement prior to determining whether to participate in a ceded review with that institution.

Note: While OHRP no longer offers QA consultations as part of a Quality Assessment Program, completion of the OHRP QA Self-Assessment Tool (which is still available for use) is considered sufficient to satisfy this requirement.

- 3) The institution must designate at least one individual (“Point of Contact”) who will serve as the contact person for the institution with respect to matters concerning the initial and ongoing implementation of the Agreement, including decisions about ceding particular research studies.

Q: Who determines whether a Participating Institution meets the eligibility criteria?

A: Each Participating Institution, as part of its Joinder Agreement, represents and warrants that it meets the eligibility criteria for participation in SMART IRB. SMART IRB will conduct a basic process to confirm that an executed Joinder Agreement delivered to SMART IRB is complete and actually coming from the institution identified in the Joinder Agreement. SMART IRB will not substantively review how institutions have met such criteria (for example, what method the institution used to conduct the required HRPP quality assessment). Once that confirmation is complete, an institution can be activated for participation in SMART IRB.

Q: Can independent IRBs (not affiliated with an institution) participate in SMART IRB?

A: Yes. Under the Agreement, independent IRBs are referred to as “IRB Organizations.” These organizations may participate in the Agreement to provide IRB review to other Participating Institutions if they meet the applicable eligibility criteria (the second and fourth of the criteria noted in the eligibility criteria question above) and execute a Joinder Agreement. As the term “IRB Organization” is used in the Agreement, it refers to organizations that only provide IRB review (and do not themselves conduct research); therefore, for purposes of the Agreement, an institution that is an IRB Organization may not have, and is not required to have, an FWA.

Q: Can government agencies that conduct or review research participate in SMART IRB?

A: Yes. Presuming government agencies meet the applicable eligibility criteria and execute a Joinder Agreement, they or entities (such as NIH) may participate in the Agreement and rely on the IRB of another Participating Institution for review of research in which the agency is engaged or provide IRB review to other Participating Institutions through the agency’s IRB(s).

Q: Does my institution need to have an IRB in order to participate in SMART IRB?

A: No. An institution that does not have an IRB may participate in SMART IRB to rely on the IRB of another Participating Institution for review of research in which the first institution is engaged.

However, the institution that does not have an IRB may not provide review of research for other Participating Institutions. Note that if your institution normally relies on the IRB of another institution for review, and you (or another institution) wish to use that IRB for the review of research covered under the SMART IRB Agreement, then that institution would also need to join SMART IRB.

Q: My institution is a group, or part of a group of affiliated institutions with separate FWAs (for example, a university-hospital system, or a hospital system, where each institution has a separate FWA) that wants to participate in SMART IRB. Can one member of the group join SMART IRB on behalf of all of us, or does each institution need to join?

A: Each institution with a separate FWA must join SMART IRB (i.e., must be registered with SMART IRB and execute its own Joinder Agreement) in order to participate. In other words, institutions that have separate FWAs must each register and execute a Joinder Agreement to participate. This is required so that each FWA-holding institution that wishes to participate is identified and so that there is clear and simple documentation that each of them is directly agreeing to the terms of the Agreement. [Use this decision tree to help you determine how an affiliate of another institution may join and participate in SMART IRB.](#)

Q: My institution's FWA specifies that we currently rely on the IRB of another institution, with which we are affiliated but from which we are legally separate (we are distinct legal corporations). If both institutions want to participate in SMART IRB, do they both need to join?

A: Yes. Each-institution must join SMART IRB (i.e., must be registered with SMART IRB and execute its own Joinder Agreement), regardless of any pre-existing affiliations or reliance arrangements that may be in place between the institutions. This is required so that each legal entity that wishes to participate is identified and so that there is clear and simple documentation that each of them is directly agreeing to the terms of the Agreement. In this case, both institutions may join SMART IRB if they wish; however, the joining of one does not enable the other to participate in any reliance relationships under the SMART IRB Agreement. [Use this decision tree to help you determine how an affiliate of another institution may join and participate in SMART IRB.](#)

Q: My institution provides IRB review for several affiliated but legally separate institutions (distinct legal corporations). If all of our institutions want to participate in SMART IRB, do we all need to join?

A: Yes. Each-institution must join SMART IRB (i.e., must be registered with SMART IRB and execute its own Joinder Agreement), regardless of any pre-existing affiliations or reliance arrangements that may be in place between the institutions. This is required so that each legal entity that wishes to participate is identified and so that there is clear and simple documentation that each of them is directly agreeing to the terms of the Agreement. In this case, all institutions may join SMART IRB if they wish; however, the joining of one does not enable the others to participate in any reliance relationships under the SMART IRB Agreement. [Use this decision tree to help you determine how an affiliate of another institution may join and participate in SMART IRB.](#)

Q: My institution is a group, or part of a group, of affiliated institutions that are legally separate (distinct legal corporations) but are all covered under a single FWA (the FWA is held by one institution and the rest of the institutions are listed as 'components'). All the institutions want to participate in SMART IRB. Can one member of the group join SMART IRB on behalf of all of us, or does each institution need to join?

A: Each legally separate institution covered under the FWA must join SMART IRB, that is, must register with SMART IRB and execute its own Joinder Agreement. This is required so that each legal entity that wishes to participate is identified and so that there is clear simple documentation that each of them is directly agreeing to the terms of the Agreement. [Use this decision tree to help you determine how an affiliate of another institution may join and participate in SMART IRB.](#)

How to Join SMART IRB

Q: My institution has determined that it meets the eligibility criteria to participate in SMART IRB. What is the process for joining?

A: The process for joining SMART IRB involves:

- 1) Downloading and reviewing the SMART IRB Agreement.
- 2) Once you have received an invitation link to initiate the Joinder process, completing an on-line registration form to provide certain basic information about your institution that is required under the SMART IRB Agreement.
- 3) Downloading, obtaining appropriate signature, and uploading your institution's SMART IRB Joinder Agreement (see next question "What does my institution sign to join SMART IRB?").
- 4) Awaiting confirmation of activation as a SMART IRB Participating Institution.

Q: What does my institution sign to join SMART IRB?

A: The institution must execute the SMART IRB Agreement, which is done by signing a document called a "Joinder Agreement." Because the Agreement is open to participation by any institution that meets the eligibility criteria, and institutions may join at different times, there is not a single central execution document and there are no founding parties or institutions. Rather, each institution signs a separate Joinder Agreement to establish itself as a party to the terms (rights and obligations) set forth in the SMART IRB Agreement document. In the Joinder Agreement, the institution agrees to abide by all of those terms, agrees that it may accept and rely on the review of any of the IRBs of other Participating Institutions and that other Participating Institutions may rely on the review of its IRB (as applicable), and represents and warrants that it meets all SMART IRB eligibility criteria for participation.

When you are ready to join, a representative from your institution should complete the online institution registration process. This person should be someone who has the authority to represent the institution in regard to IRB reliance arrangements. The registration process will generate an institution-specific Joinder Agreement, which may be downloaded and signed by the appropriate Institution Official. The executed Joinder Agreement may then be delivered to SMART IRB by uploading an electronic file (e.g. PDF) of the signed document. NOTE: further instructions on this process will be provided when institutions receive their institution-specific link to the Joinder System; any interested parties should download the SMART IRB Agreement to be notified when sign-on is available for their institution.

The Effective Date of the Agreement with respect to any Participating Institution is the Effective Date of its Joinder Agreement, as identified in the Joinder Agreement; however, the Participating Institution's actual participation in any activities under the Agreement first requires activation of participation as described further in other FAQs. See above steps for joining SMART IRB.

Q: If two institutions have separate FWAs, can the same individual sign the Joinder Agreement for both institutions?

A: Yes, if the individual has appropriate signature authority for both institutions. This may be the case in some university-hospital affiliations, for example, where the same individual serves as an Institutional Official for both the university and the hospital. It will depend on the authority granted by each institution to the individual; such authority must be determined by the involved institutions.

Q: Can the same individual register and/or serve as the Point of Contact for more than one institution?

A: Yes, if the individual has the authority to act on behalf of both institutions with respect to participation in and implementation of the Agreement. The involved institution determines the authority granted to the individual.

Q: Once my institution has registered and signed the Joinder Agreement, can it begin participating in review and reliance activities immediately?

A: No. Although the Joinder Agreement will establish an Effective Date for the institution's participation in SMART IRB (which will be the date the institution's authorized official/signatory executes the Joinder Agreement), an institution's participation must be activated. Activation involves confirmation by SMART IRB administration that the executed and submitted Joinder Agreement is actually coming from the institution identified in the Joinder Agreement and appears to meet the eligibility criteria. Once that is confirmed, the institution will be activated to participate in ceded reviews.

The Agreement: selected provisions and annotations

Investigator Compliance

Q: The SMART IRB Agreement requires a Relying Institution to ensure that its Research Personnel are informed of and required to comply with the Relying Institution’s obligations under the Agreement regarding coordination, communication, compliance, and reporting. The Agreement also requires the Relying Institution to require its Research Personnel to comply with the Reviewing IRB’s requirements and determinations. How does a Relying Institution implement these requirements?

A: The Agreement does not dictate how Relying Institutions implement these requirements. Relying Institutions must determine for themselves how they can best ensure that their investigators and other Research Personnel are informed of the institution’s obligations when relying on an external IRB and how they will enforce these obligations internally. For example, some institutions may adopt policies and procedures for reliance arrangements, or may send written notification to investigators/personnel of specific requirements, or may require investigators/personnel to sign an acknowledgement or agreement as to specific responsibilities when they submit a protocol for ceded review.

HIPAA Privacy Rule

Q: How does the SMART IRB Agreement handle any HIPAA Privacy Rule determinations that are required for a Relying Institution that is a Covered Entity to use and disclose Protected Health Information for research?

A: Many Participating Institutions that are conducting a research study and ceding IRB review (under the Agreement, called “Relying Institutions”) are Covered Entities under the Health Insurance Portability and Accountability Act of 1996 and its privacy regulations (“HIPAA”). Such Relying Institutions may not use or disclose Protected Health Information (“PHI”) for research purposes unless HIPAA’s requirements for individual authorization, waiver/alteration of authorization, or another pathway under HIPAA is met (e.g., disclosure of a Limited Data Set).

The Agreement presumes that in most cases, the IRB of the Participating Institution providing review (under the Agreement, called the “Reviewing IRB”) will, as part of its review of a research study, make a determination on behalf of a Relying Institution that is a Covered Entity as to whether authorization is

required, whether waiver/alteration of authorization is permissible, or whether another pathway for use and disclosure of PHI is satisfied in connection with the study.

- The Reviewing IRB may determine that individual authorization is required. In these cases, the authorization language generally would be incorporated into the consent document and the Reviewing IRB would be responsible for approving a template combined consent and authorization form.
- The Reviewing IRB may grant a waiver or alteration of authorization.
- If the PHI to be used or disclosed for the research study constitutes a Limited Data Set, the Reviewing IRB may permit such use and disclosure to occur under a Data Use Agreement.

Note that the Reviewing IRB does not take on responsibility for any other HIPAA requirements applicable to the Relying Institution (such as compliance with or implementation of accounting of disclosures of PHI made by the Relying Institution pursuant to a waiver of authorization).

Q: My institution is not a Covered Entity. Can it still act as the Reviewing IRB for a Relying Institution that is a Covered Entity?

A: Yes. The Reviewing IRB does not need to be a Covered Entity or part of a Covered Entity itself in order to make HIPAA determinations on behalf of the Relying Institution to permit the use and disclosure of PHI for research. However, in recognition that some Relying Institutions may not be comfortable with a Reviewing IRB making these HIPAA determinations on its behalf (for example, when the Reviewing IRB does not regularly make such determinations), the Agreement allows a Relying Institution to request, and the Reviewing IRB to agree, that the Relying Institution use its own freestanding HIPAA authorization form (when authorization is required) or conduct the review of a request for waiver/alteration of authorization itself (when waiver/alteration is requested).

In the rare case when a Reviewing IRB is not willing to make any necessary HIPAA determinations to permit use/disclosure of PHI (for example, if an institution that is not a Covered Entity has indicated that its IRB will not perform such determinations), a Relying Institution that is a Covered Entity must make its own such determinations. If in such case a Relying Institution determines that individual authorization is required, it must use its own form of authorization language, which must be a freestanding form separate from the informed consent documents, and the Relying Institution would be responsible for ensuring the HIPAA authorization form is compliant with HIPAA’s requirements for authorizations and is consistent with the IRB-approved consent form and protocol.

Prior to participating in a determination of the acceptability of Ceded Review for a given research study, a potential Reviewing IRB must inform all Participating Institutions involved in the research if it will not perform HIPAA-related determinations.

Conflicts of Interest

Q: How are Research Personnel conflicts of interest addressed under the SMART IRB Agreement?

A: Unless the involved Participating Institutions agree on a different plan in advance for a given research study, a Relying Institution will analyze potential conflicts of interest of Research Personnel under its own conflict of interest policies. The Relying Institution will provide the Reviewing IRB with the results of its analysis, including any conflict of interest determinations, institutionally required prohibitions, and institutionally required management plans. The Reviewing IRB must consider this information in reviewing the research study on behalf of the applicable Relying Institution. The Reviewing IRB must incorporate and implement any prohibitions or management plans (such as institutionally required disclosures in consent forms) without changes, unless such changes are discussed with and accepted by the Relying Institution. The Reviewing IRB may impose additional requirements (such as further disclosures) if necessary to approve the study.

In the rare situation when the Reviewing IRB determines that implementation of a particular plan would render the study not approvable by the Reviewing IRB (for example, the Reviewing IRB determines that a disclosure statement required by a Relying Institution in a consent is misleading), and the Relying Institution does not agree to the Reviewing IRB's proposed changes (if any), the Reviewing IRB must inform the affected Relying Institution, and the study will be withdrawn from ceded review with respect to that Relying Institution (without an IRB approval/disapproval determination).

Note that institutional conflicts of interest (conflicts of a Relying Institution itself) are not addressed in the Agreement; it is expected that the Relying Institution would address such conflicts locally, prior to its consideration of any ceded review.

Local Considerations – **UPDATED**

Q: What laws and regulations must the Reviewing IRB consider in reviewing a study under the SMART IRB Agreement? Who is responsible for determining that a study is compliant with all applicable laws and regulations? **NEW**

A: The Agreement requires a Reviewing IRB to perform its review in accordance with federal human subjects protection regulations. These include the Common Rule, the FDA human subjects regulations, and any human subjects regulations of federal agencies that do not follow the Common Rule (as applicable to the study). The Agreement also requires the Reviewing IRB to make certain determinations under the federal HIPAA privacy regulations, unless the Reviewing IRB communicates to the Relying Institution that it will not make these determinations.

The Agreement also requires a Reviewing IRB to take into account any local requirements communicated to it by the Relying Institution in connection with the study. These local requirements may include applicable state and local laws and regulations; institutional policies, standards or other

local factors (including local ancillary reviews and restrictions on use and disclosure of PHI); and applicable federal laws and regulations other than human subjects protection regulations that may affect the study. An example of potentially applicable federal laws and regulations other than human subjects protection regulations is 42 CFR Part 2, regarding the confidentiality of certain substance abuse treatment records. If a study involves use/disclosure of such records, the Relying Institution would be expected to communicate any requirements applicable to its site under these regulations to the Reviewing IRB.

As a result of this allocation of tasks, the Reviewing IRB is responsible to assure that its review and the study comply with federal human subjects protection regulations. Although as part of that review it is required to consider and apply those local requirements communicated to it by the Relying Institution, the Reviewing IRB is not responsible for identifying the local requirements (including federal requirements other than the human subjects protection regulations) or for interpreting the local requirements. The Reviewing IRB depends on the Relying Institution to identify and interpret the local requirements and ultimately to determine whether the research reviewed by the Reviewing IRB meets the local requirements.

Q: How do other “local considerations” (aka “local context” issues) get addressed under the SMART IRB Agreement? UPDATED

A: A Relying Institution is required to identify, interpret and communicate to the Reviewing IRB the requirements of any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews and restrictions on use and disclosure of PHI, and federal laws and regulations other than human subjects protection regulations that are relevant to a research study for which review is being ceded under the Agreement. The Reviewing IRB is not expected to identify or interpret such requirements on its own. The Reviewing IRB is required to consider and apply any local requirements communicated to it by the Relying Institution in connection with its review of the research study. Because the Relying Institution is in the best position to identify and interpret applicable local requirements, this responsibility remains with the Relying Institution. Relying institutions are encouraged to develop appropriate procedures to ensure applicable local requirements are communicated by individuals knowledgeable about those requirements.

When written informed consent is required for a research study, the Reviewing IRB will provide informed consent documents for use by the Relying Institution/Site Investigator. The Relying Institution may customize site-specific language within the documents, e.g., the availability of treatment and compensation for research-related injury, payment/reimbursement of costs incurred by subjects for participation, and Site Investigator contact information. To the extent the Relying Institution requires specific consent language to ensure compliance with any applicable state, local or federal (other than human subjects protection) laws or regulations, it should provide that language to the Reviewing IRB.

Federal Grant Congruency Review

Q: Why does the SMART IRB Agreement require the Reviewing IRB to review the congruence of any federal grant application/proposal with the research protocol submitted to the IRB when such review is required by federal regulations or oversight agencies?

A: The intent of the congruence provision in the Agreement is to make sure that the responsibility for IRB review of the federal grant application/proposal is specifically assigned amongst institutions participating in a ceded review, and not missed. The Reviewing IRB is often in the best position to be able to compare the grant with the study protocol and address any inconsistencies, which might need to be addressed, for example, via a protocol amendment. The awardee institution is still responsible for making the certification to the applicable federal department/agency that the review has been performed.

Subject Complaints and Injuries

Q: The SMART IRB Agreement requires the Reviewing IRB to notify Relying Institutions of any findings and actions it makes with regard to “significant” subject complaints occurring at the Relying Institution or occurring at other institutions if the complaint or action could affect the rights and welfare of subjects at the Relying Institution. What is a “significant” subject complaint as contemplated by the Agreement?

A: A significant subject complaint is, generally, one that could affect the conduct of the Research. Examples might be a complaint that a subject was not provided sufficient time to read the consent form or that a blood draw occurred without informed consent. An example that would generally not rise to this level is if a subject complains about not receiving a promised parking voucher for a research visit or received the incorrect amount of study compensation. These are only examples, however, and the significance of a given complaint is to be determined by the Reviewing IRB in the context of the particular research study and other circumstances at issue.

Q: Why does the SMART IRB Agreement require Site Investigators to notify the Reviewing IRB of any subject complaints and any subject injuries? Not all complaints and injuries rise to the level of an unanticipated problem or other reportable event under federal research regulations.

A: Although complaints and injuries are not per se reportable events unless they also meet the definition of an unanticipated problem involving risks to subjects or others (or otherwise occur in connection with another reportable activity), some reliance agreements specifically require complaints and injuries to be reported to the IRB in the first instance to make sure that there is an independent judgment (other than the investigator’s or relying institution’s) as to whether they constitute unanticipated problems. In other words, some institutions view injuries, in particular, as inherently

significant such that the reviewing IRB should be informed and have the opportunity to determine whether further reporting is required. Whereas these judgments might be made entirely by investigators when the IRB is internal to the institution conducting the research, in the reliance context the IRB is not as familiar with the standards and norms of the investigators or the relying institution, and all significant complaints, research-related injuries, and other events are to be reported to the Reviewing IRB. Note that the Agreement limits subject complaints that require reporting to those that are “significant” (see above for a definition of “significant”) and injuries must be related to the research in order to require reporting to the Reviewing IRB.

Q: The SMART IRB Agreement requires a Relying Institution to ensure consistency between the approved research study protocol and consent form with the provisions of any applicable grant or funding contract for the study regarding financial coverage for research-related injuries. As an alternative, the Agreement requires the Relying Institution to ensure that in the event of any inconsistency, the approved protocol and consent form, if more protective of subjects, will control. Why does the Agreement place this responsibility for ensuring consistency with the Relying Institution, and what does it mean to ensure that the protocol and consent will control?

A: The Agreement places this responsibility with the Relying Institution because the Reviewing IRB and Reviewing IRB Institution will generally not be involved in the funding application or funding contract negotiation between the Relying Institution and the sponsor. The Relying Institution is often in the only or best position to review and negotiate the grant or contract language on financial responsibility for coverage of subject injuries as necessary to meet any requirements of the IRB and of its own institution. Aside from reviewing both the grant/contract and the protocol/consent and making sure the language in each is consistent in describing the coverage, another option is for the Relying Institution to negotiate a contract provision with the sponsor that says that to the extent there is any inconsistency, the protocol/consent language will control (the presumption behind this approach is that the protocol/consent language will generally be more protective of subjects than any contract language on the topic). This alternate approach puts the burden of a failure of consistency on the sponsor.

Investigations of Noncompliance

Q: Who investigates if there is a problem or noncompliance in research covered under the SMART IRB Agreement?

A: Both the Reviewing IRB and the Relying Institution have authority to conduct an investigation or audit of any allegation or matter relating to a research study for which review is ceded under the Agreement. Such investigations may be conducted separately or jointly. The Reviewing IRB also has the authority to request the Relying Institution to conduct such investigation. Regardless of whether it is the Reviewing IRB or the Relying Institution that conducts an investigation, the other party is required to reasonably cooperate with the investigation, and the investigating party is required to report its findings of fact to

the other. No party is required to share information that is protected by attorney-client privilege or other applicable legal privileges.

The Relying Institution must comply with any corrective actions required by the Reviewing IRB, but may also adopt its own additional corrective actions.

Reporting

Q: Who performs any required reporting of unanticipated problems, serious/continuing noncompliance, and suspension/termination of IRB approval to sponsors and oversight agencies, and how are such requirements determined?

A: The Reviewing IRB will determine whether an event falls within one of these reportable categories and whether a report is required to a regulatory agency, sponsor, funding agency, or other oversight authority. In making the determination, the Reviewing IRB will consider any regulatory requirements applicable to it or to the Relying Institution (including applicable FDA requirements), as well as the terms of the Relying Institution's FWA. Prior to participating in a determination whether to cede review of a particular research study under the Agreement, the Participating Institutions involved in the study must inform one another of whether their FWAs apply to the specific study.

Unless the involved Participating Institutions agree on an alternate reporting arrangement, the Reviewing IRB, with support of its institution as applicable, will draft and make the report and will provide the Relying Institution with an opportunity to review and comment on the report prior to its submission to the external authority. Nothing in the Agreement prohibits the Relying Institution from making its own additional report; in such case, the Relying Institution will provide a copy of that report to the Reviewing IRB. The involved Participating Institutions may agree on an alternate arrangement whereby the Relying Institution drafts and makes the report or the Reviewing IRB and Relying Institution jointly make the report.

IRB Fees

Q: My institution's IRB charges fees in connection with its review activities. The SMART IRB Agreement does not have a provision regarding IRB review fees. Does this mean it is not permissible to charge IRB fees in connection with review activities conducted under SMART IRB?

A: No. Participating Institutions providing IRB review under the SMART IRB Agreement may charge fees for such services in accordance with their usual practices and as permitted by under applicable policy (e.g., NIH Single IRB Review policy). The Agreement provides that Participating Institutions may make arrangements with one another for fees/financial coverage of IRB review services.

Insurance and Indemnification

Q: The insurance provision in the SMART IRB Agreement is very general. Why doesn't it obligate Participating Institutions to carry specific types or amounts of insurance coverage in connection with their participation?

A: SMART IRB seeks to facilitate broader participation in reliance relationships and to maximize flexibility of choice for participants. Consistent with these goals, the Agreement sets a basic expectation that Participating Institutions will have insurance coverage for their various activities (including, as applicable, the conduct and review of research), but it does not dictate the types of policies or minimum coverage levels that may accomplish this coverage.

The Agreement recognizes that different types of institutions may insure against research-related risk differently, depending on their organizational structure, the size and nature of their research program, and their relationships with their personnel and other individuals (including IRB members) who are involved. In addition, some institutions have self-insurance programs or limited coverage based on status as public or quasi-public entities, state law immunities, and other factors. The Agreement provides that Participating Institutions may obtain documentation of any other Participating Institutions' insurance coverage prior to determining whether to participate in a ceded review with those institutions. Thus, a Participating Institution can obtain the information it needs to make a study-specific decision. It is not obligated to participate in any ceded review. A Participating Institution can also agree with another Participating Institution to waive the basic requirement to maintain insurance coverage on a study-specific basis if they determine that is appropriate.

Q: Why doesn't the SMART IRB Agreement have an indemnification provision? My institution wants to be indemnified in any reliance relationship, whether it is relying on another IRB or providing IRB review for another institution.

A: As noted above, a central goal of SMART IRB is to broaden participation in reliance relationships and to help reduce potential barriers to participation. In recognition that certain types of entities, including public, quasi-public, and smaller private organizations, might find an indemnification obligation to constitute such a barrier, the Agreement does not mandate that Participating Institutions indemnify one another in connection with their activities. In addition, in light of the current open regulatory proposals regarding direct liability of IRBs and the possibility of further guidance or clarification from regulatory authorities regarding the respective responsibilities of reviewing IRBs and relying institutions, the Agreement avoids enacting an apportionment of liability that may not reflect where common understanding ultimately lands. However, in recognition that some institutions may wish to negotiate the allocation of liability among participants in advance of these developments, the Agreement does expressly provide that Participating Institutions are free to request and make agreements with other Participating Institutions for indemnification in connection with the covered Research as they deem appropriate.

It is important to be aware that the practical value of indemnification provisions in avoiding litigation and providing an immediate source of recovery may be limited, particularly in the context of a developing area such as IRB reliance agreements; participants may end up litigating about the interpretation and application of the indemnification clause along with the underlying claims for liability.

Q: Some IRB reliance agreements contain “representations and warranties” by the parties or, in some cases, disclaimers of representations and warranties. Does the SMART IRB Agreement have any of these things? What do they mean?

A: In a contract, a “representation” is a statement regarding an existing fact that is made to encourage the other party(ies) to enter the contract. If the statement is not true, the other party(ies) may be able to get out of the contract as if it never existed. A “warranty” is a promise to perform in accordance with some standard or expectation, essentially a guarantee. If a warranting party fails to so perform, the other party(ies) may be able to more easily terminate the contract or make a claim for breach of contract. Representations and warranties may be express or may be implied. Because SMART IRB does not have a central oversight or compliance body that will substantively review or verify eligibility for participation, it was determined that each Participating Institution should explicitly “represent and warrant” in the Agreement that it meets all eligibility criteria for participation. The Agreement does not contain other express representations or warranties or otherwise elevate any of the substantive obligations pertaining to provision and receipt of IRB review services over any other; the expectation is that simple agreement to comply with each substantive responsibility is sufficient to protect the Participating Institutions.

However, in contrast to some reliance agreements, the Agreement also does not contain any disclaimers of representations or warranties, express or implied. Generally speaking, when a party “disclaims” all representations, it is saying “I am not making statements of fact on which any other party should rely in deciding whether to enter this contract.” When a party “disclaims” all warranties, it is saying, “I am not promising that what I am providing under this contract will perform in accordance with any standard or function as expected – I am making no guarantees.”

Amendments to the SMART IRB Agreement

Q: Can the SMART IRB Agreement be amended?

A: The Agreement may be amended from time to time. Proposed material changes will be collected by the SMART IRB Executive Committee and will be subject to an open comment period in which all Participating Institutions may participate. Such a change might include a change to the eligibility criteria for participation in SMART IRB. Not all amendments will require re-execution of Joinder Agreements by Participating Institutions. If an amendment is finalized that does not require such re-execution, and a Participating Institution is not able to accept the terms of the amended Agreement, the Participating Institution may terminate its participation in SMART IRB as described in the SMART IRB Standard Operating Procedure (SOP) for “Ending Site Participation in SMART IRB or Specific Research.”

Q: Who is notified about updates to the SMART IRB Agreement?

A: When SMART IRB administration proposes any material Agreement amendment they will seek input from Participating Institutions during the drafting process, as follows:

- The proposed draft amendment language will be posted at SMARTIRB.org.
- All Participating Institutions (including Points of Contacts and Institutional Officials) will be notified of the proposed amendment language and provided a 30-day comment period.
- All feedback will be considered.
- A revised draft of the amendment language, if any, will be posted at SMARTIRB.org.
- All Participating Institutions (including Points of Contact and Institutional Officials) will be notified of any updates to the proposed amendment language and provided a 15-day comment period prior to the amendment being finalized.

If alternative proposals received during the feedback process are determined to be preferable to the originally proposed amendment, the updated version will be communicated back to the appropriate individuals, following the steps above.

Q: If there are changes to the SMART IRB Agreement, do we need to re-execute the Joinder Agreement?

It will be determined, on an amendment-by-amendment basis, whether Participating Institutions must re-execute the Joinder Agreement.

In cases where a Participating Institution is unable to accept the terms of the amended Agreement, the institution may terminate its participation in SMART IRB, as described in the SMART IRB Standard Operating Procedure for “Ending Site Participation in SMART IRB or Specific Research.”

Termination of Participation in SMART IRB

Q: My institution joined SMART IRB but no longer wishes to participate. How do we terminate our participation?

A: A Participating Institution may terminate its own participation in SMART IRB at any time and for any reason. The Participating Institution must give 30 days prior written notice of the termination to any other Participating Institutions with which it is involved in any ongoing research study(ies) and ceded review(s) at the time of the termination. A Participating Institution that has current studies under the Agreement for which it is the Reviewing IRB or for which it is participating as a Relying Institution may be delayed in ending its participation as necessary to ensure that appropriate arrangements have been made for alternate oversight or wind-down of the research, as applicable.

Under the SMART IRB Standard Operating Procedures (SOPs), a Participating Institution that does not have any current studies ceded under the Agreement, and is not currently serving as a Reviewing IRB for any studies ceded under the Agreement, may end its participation in the Agreement once applicable SMART IRB systems and records have been updated to reflect the change. A Participating Institution that has current studies under the Agreement for which it is the Reviewing IRB or for which it is participating as a Relying Institution may end its participation under this Agreement after 45 days, with written notice to SMART IRB (Help@SMARTIRB.org), or sooner if other arrangements have been made for open and ongoing studies affected by the discontinuation. Discontinuation of participation in the Agreement by one Participating Institution will not end the validity of the Agreement with respect to the remaining Participating Institutions.

Q: Can an institution's participation in SMART IRB be terminated by another Participating Institution?

A: No Participating Institution may terminate the participation of any other. However, a Participating Institution's participation will terminate *automatically* and immediately in the event that its FWA is suspended, restricted, terminated or expires or in the event that its IRB (if it has one) fails to remain registered with the Office for Human Research Protections. If a Participating Institution is participating in a clinical trial network or other arrangement that has its own policies or terms and conditions of reliance, those policies or terms may include bases for termination of reliance or participation *in that network/arrangement*, and those will still apply; however, if such other termination occurs, the Participating Institution may continue to participate in SMART IRB with respect to other research studies that are not part of the network/arrangement.

Q: My institution's participation or the participation of another Participating Institution with which we were involved in a ceded review has terminated. Are there any ongoing rights and obligations? What happens to any research that is still under ceded review at the time of termination?

A: When a Participating Institution’s participation in SMART IRB terminates, certain rights and obligations “survive” the termination. These rights and obligations are listed in the SMART IRB Agreement, and include: cooperation in investigations and reporting of noncompliance and problems, recordkeeping, confidentiality, and use of name. With respect to any research study/ceded review that is ongoing at the time of termination, the Agreement does not mandate a particular outcome, but the involved Participating Institutions agree to work together to determine the effect of the termination on such activities. The goal would be to transfer oversight of any ongoing research study(ies) to another IRB as soon as possible and to minimize any disruptions to such studies.

SOPs

Q: What are the SMART IRB Standard Operating Procedures?

A: The SMART IRB Standard Operating Procedures (“SOPs” or “SMART IRB SOPs”) were drafted to help Participating Institutions implement the requirements of the Agreement and their roles and responsibilities outlined in the Agreement. For example, the SOPs provide detailed guidance on carrying out communication and notification responsibilities under the Agreement.

Q: Is my institution required to use the SMART IRB SOPs?

A: No. Use of the SMART IRB SOPs is strongly encouraged, but not required. SMART IRB acknowledges that: 1) some institutions have existing policies and procedures that they apply or prefer to apply to IRB reliance relationships and 2) in some cases institutions are required as part of funding conditions or participation in clinical trial networks or other programs to use a particular set of policies and procedures to govern the reliance relationship. SMART IRB can still be used to support and document reliance in these situations. Participating Institutions may use their own policies and procedures for the reliance relationship if doing so would not render them in violation of any term of the Agreement, and must agree that if a provision of their own policies and procedures conflicts with a term of the Agreement, the Agreement will govern. For example, if a Participating Institution’s policies and procedures prohibit disclosure of IRB minutes to an institution, the Agreement’s provision regarding access to minutes must apply. However, in the instance when a Participating Institution is required by funding conditions or participation in a network/program to use particular policies and procedures for reliance, those policies and procedures will override any conflicting requirements of the SMART IRB Agreement. In all cases, Participating Institutions involved in a research study under the Agreement must communicate in writing with one another regarding what policies and procedures will apply to such study.

Using SMART IRB for a Study

Reliance Requests

Q: I want to use SMART IRB for a study I am conducting, what do I do?

A: If your institution has not signed up for SMART IRB, it will need to do so by signing a Joinder Agreement (see the FAQs about *How to Join SMART IRB*) and await activation before proceeding.

The lead principal investigator (generally the initiating or funding principal investigator) (“Overall PI”) should make a request to the SMART IRB Point of Contact (POC) of the Participating Institution of his/her primary employment or affiliation regarding reliant review for the study. The POC will need to determine if the SMART IRB Agreement and SMART IRB Standard Operating Procedures (SOPs) are appropriate to use for a reliant review request related to a research study. As needed, the POC at the institution receiving the reliant review request will consult with the POCs of other involved Participating Institutions to determine whether the research is appropriate for ceded review and, if so, to identify the Reviewing IRB and applicable SOPs that will be followed.

In some cases, such as studies conducted under a network or certain consortia, a specific Reviewing IRB may be required as a condition of participating in the research. Otherwise, no Participating Institution involved in the research is required to participate in the ceded review. If one or more institutions decline to participate in the ceded review, the other institutions may still participate in the research (unless ceding review to a particular IRB is a condition of a grant or network participation).

Selecting a Reviewing IRB

Q: How is the IRB of Record (Reviewing IRB) for a study selected?

A: The Participating Institutions engaged in a particular research study determine which IRB will provide the review. If a Participating Institution involved in the research disagrees with the selection of IRB, that institution, unless prohibited by applicable policy (e.g., NIH Single IRB Policy) or obligation (e.g., terms of participation in a consortium), may decline to cede review to that IRB and may use its own IRB (if applicable) or agree that the IRB of another Participating Institution will provide review on its behalf (unless ceding review to a particular IRB is a requirement of study participation). This may result in more than one IRB providing review for a given research study.

A Reviewing IRB is usually identified in one of the following ways:

1. Pre-determined by the study sponsor or grant.
2. Established by prior arrangement (e.g. network central IRB).
3. IRB from Overall PI’s institution.
4. Selected based on expertise in the study area (e.g. type of procedures to be performed or subject population).

Q: Is the IRB at the Overall PI's institution required to be the Reviewing IRB for a study proposed by that PI?

A: No, the IRB at the Overall PI's institution is not required to be the Reviewing IRB for that study. However, the Overall PI's home IRB has the right of first refusal to serve as the Reviewing IRB and will typically be identified as the Reviewing IRB by default, unless another Reviewing IRB has already been pre-determined by a study sponsor or grant, the Reviewing IRB has already been established by prior arrangement (e.g., a network central IRB), or an IRB is determined to be a more appropriate Reviewing IRB for a particular study (e.g., based on type of procedures to be performed, subject population, or other criteria).

Q: Can an IRB from an institution that is not conducting a particular study be the Reviewing IRB for that study?

A: Yes, under certain circumstances an institution that is not otherwise participating in the study, but is part of SMART IRB, may serve as the Reviewing IRB. This could happen, for example, in cases where the institution's IRB:

- Has already been pre-determined by study sponsor or grant.
- Has already been established as the Reviewing IRB by prior arrangement (e.g., network central IRB).
- Is selected based on type of procedures to be performed, subject population, or other criteria.
- Is selected in order to avoid any conflict of interest.

Q: What if the IRB at the Overall PI's institution declines to serve as the Reviewing IRB?

A. If the SMART IRB Point of Contact at the Overall PI's home institution (HI) reviews a request to serve as the Reviewing IRB and declines to serve as the Reviewing IRB for all Participating Institutions, the HI POC will then determine whether the HI is willing to cede review to another institution to serve as the Reviewing IRB for the Overall PI. If the HI is unwilling to cede review to another institution, the HI IRB proceeds to conduct a review of the study for its own study team or declines to participate in the research. The other Site Investigators are referred to new potential Reviewing IRBs identified by the Overall PI or by the HI POC. If the HI declines to serve as the Reviewing IRB for the study but is willing to cede review to another institution, the HI POC contacts potential alternate Reviewing IRBs identified either by the Overall PI or in advance. The Overall PI may participate in this process where necessary. Once the Reviewing IRB has been established, the SMART IRB POC (on behalf of the Reviewing IRB) will notify the Overall PI of the decision.

Q: Once oversight of a study has been ceded to the Reviewing IRB under the SMART IRB Agreement, can an institution take back IRB oversight?

A: Yes. The expectation is that when review of a research study is ceded under the Agreement, the study will remain under the Reviewing IRB's oversight authority for as long as IRB oversight is required.

However, for a particular study, if a Relying Institution determines that it must change IRB oversight of the study (e.g., the Relying Institution wants to take back review of the study to its home IRB), the Relying Institution's Point of Contact (POC) should contact the Overall PI of the study, requesting that the institution be removed as a Relying Institution. The Overall PI for the study will remove the site by submitting an amendment to the Reviewing IRB in accordance with the SMART IRB SOP on "Protocol Amendment Submission and Review Process." The Overall PI and Site Investigator for the Relying Institution should work together to ensure that appropriate alternate review and approval are in place for this institution.

Q: Can there be more than one Reviewing IRB for a study under the SMART IRB Agreement?

A: Yes. Although having a single Reviewing IRB minimizes duplicative IRB reviews to the greatest extent possible, under some circumstances it may be necessary to establish more than one Reviewing IRB. While this would not be typical, more than one Reviewing IRB may be established for the following reasons:

- Significant differences between research sites in procedures to be performed or subject populations involved could necessitate more than one Reviewing IRB, each with different areas of relevant expertise.
- If one or more Relying Institution declines to cede review to the established Reviewing IRB, additional Reviewing IRBs may be established in order to include and enable reliance for more institutions.

Q: My institution has "unchecked the box" on our Federalwide Assurance (FWA) and has agreed to serve as a Reviewing IRB for a non-federally funded, multi-site study. Can my IRB apply a flexible approach to the review of the research, such as extending the review period or reviewing the minimal risk research under an expedited category not currently identified by OHRP?

A. Unless all Relying Institutions have also "unchecked the box", the Reviewing IRB could not use a "flexible" approach to the review of the study, even if allowed by the Reviewing IRB's policy, because the Relying Institutions that have "checked the box" on their FWAs would be out of compliance with the terms of their FWAs. The Reviewing IRB should disclose any intention to apply a flexible approach to the IRB review to potential Relying Institutions as part of the reliant review process. If all Relying Institutions can comply with the flexible approach, then it can be applied.

Q: One of the eligibility criteria for participation in SMART IRB is that my institution require IRB review and institutional oversight for our human subjects research regardless of funding source and regardless whether we have "checked the box" on our FWA. This requirement does not appear to have an exception for exempt human subjects research, which under the current Common Rule does not require IRB review or trigger any other regulatory obligations. Can you explain why?

A: The intent of this criterion, which is stated in Section 1.1 of the Agreement, is not to require IRB review or institutional oversight for human subjects research that is currently exempt from IRB review and other regulatory requirements under the Common Rule (as of the date the SMART IRB Agreement was released). However, in recognition of the Common Rule NPRM proposals, which include creation of new exempt categories that will have limited IRB review and other regulatory requirements attached to them, the drafters of SMART IRB did not build an exception to this eligibility criterion for exempt research. If the Common Rule NPRM proposals are finalized in their current form, the expectation under the Agreement is that institutional oversight will be required (including limited IRB review in some cases) for the new exempt categories of human subjects research.

Local Considerations – **UPDATED**

Q: What laws and regulations must the Reviewing IRB consider in reviewing a study under the SMART IRB Agreement? Who is responsible for determining that a study is compliant with all applicable laws and regulations? NEW

A: The Agreement requires a Reviewing IRB to perform its review in accordance with federal human subjects protection regulations. These include the Common Rule, the FDA human subjects regulations, and any human subjects regulations of federal agencies that do not follow the Common Rule (as applicable to the study). The Agreement also requires the Reviewing IRB to make certain determinations under the federal HIPAA privacy regulations, unless the Reviewing IRB communicates to the Relying Institution that it will not make these determinations.

The Agreement also requires a Reviewing IRB to take into account any local requirements communicated to it by the Relying Institution in connection with the study. These local requirements may include applicable state and local laws and regulations; institutional policies, standards or other local factors (including local ancillary reviews and restrictions on use and disclosure of PHI); and applicable federal laws and regulations other than human subjects protection regulations that may affect the study. An example of potentially applicable federal laws and regulations other than human subjects protection regulations is 42 CFR Part 2, regarding the confidentiality of certain substance abuse treatment records. If a study involves use/disclosure of such records, the Relying Institution would be expected to communicate any requirements applicable to its site under these regulations to the Reviewing IRB.

As a result of this allocation of tasks, the Reviewing IRB is responsible to assure that its review and the study comply with federal human subjects protection regulations. Although as part of that review it is required to consider and apply those local requirements communicated to it by the Relying Institution, the Reviewing IRB is not responsible for identifying the local requirements (including federal requirements other than the human subjects protection regulations) or for interpreting the local requirements. The Reviewing IRB depends on the Relying Institution to identify and interpret the local requirements and ultimately to determine whether the research reviewed by the Reviewing IRB meets the local requirements.

Q: How will any outstanding concerns/requirements and/or local context issues be addressed? UPDATED

A: A Relying Institution is required to identify, interpret and communicate to the Reviewing IRB the requirements of any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews and restrictions on use and disclosure of PHI, and federal laws and regulations other than human subjects protection regulations that are relevant to a research study for which review is being ceded under the Agreement. The Reviewing IRB is not expected to identify or interpret such requirements on its own. The Reviewing IRB is required to consider and apply any local requirements communicated to it by the Relying Institution in connection with its review of the research study. Because the Relying Institution is in the best position to identify and interpret applicable local requirements, this responsibility remains with the Relying Institution. Relying institutions are encouraged to develop appropriate procedures to ensure applicable local requirements are communicated by individuals knowledgeable about those requirements.

When written informed consent is required for a research study, the Reviewing IRB will provide informed consent documents for use by the Relying Institution/Site Investigator. The Relying Institution may customize site-specific language within the documents, e.g., the availability of treatment and compensation for research-related injury, payment/reimbursement of costs incurred by subjects for participation, and Site Investigator contact information. To the extent the Relying Institution requires specific consent language to ensure compliance with any applicable state, local or federal (other than human subjects protection) laws or regulations, it should provide that language to the Reviewing IRB.

Consent Forms

Q: Can Relying Institutions use their own template consent form that includes the approved language of the Reviewing IRB or do they have to use the Reviewing IRB’s template?

A: When informed consent documents (ICDs) are required for a study reviewed under the SMART IRB Agreement, all Relying Institutions must use the Reviewing IRB’s ICD template(s) unless the Reviewing IRB agrees to review and approve a Relying Institution’s template.

Q: When is local language inserted into the consent documents?

A: When an institution agrees to rely on a Reviewing IRB for oversight of a study, it will provide that IRB with site-specific information that includes the institutional requirements and local issues. During the IRB review process, the Relying Institution will work with the Lead Study Team and/or the Reviewing Institution’s POC to provide information for the sections of the ICD that can be modified to be site-specific. Site-specific language in the ICD is generally limited to:

- Compensation for injury
- Availability of treatment for injury
- Payment or reimbursement of research costs incurred by subjects
- Local study team contact(s) for questions about the study

HIPAA authorization language is addressed separately from ICD language, and is described further in the “HIPAA Privacy Rule” section of the SMART IRB Standard Operating Procedures (“SMART IRB SOPs”).

Q: Who is responsible for ensuring that the language in an IRB-approved consent document about subject injury is consistent with the language in the grant/contract supporting the research study?

A: Because the Reviewing IRB will not be involved in the funding contract negotiation between the Relying Institution and the sponsor, it is the Relying Institution’s responsibility to review the contract language on subject injury against the consent that the reviewing IRB has approved for its site and make sure that they are consistent. Alternatively, the Relying Institution can negotiate a clause in its funding agreement that makes the sponsor effectively responsible for inconsistencies by saying that the consent form will control (if it offers broader protection than the contract).

Conflicts of Interest (COI)

Q: Whose conflict of interest policies do a Relying Institution’s Research Personnel members follow?

A: Study teams are required to follow their home institution’s policies for the reporting and management of potential conflicts of interest. The Reviewing IRB may impose additional requirements when reviewing a specific study.

Q: How do study team members from a Relying Institution communicate potential conflicts of interest and applicable management plans to the Reviewing IRB?

A: Under the SMART IRB Standard Operating Procedures, if any study team members from a Relying Institution have a potential conflict of interest (based on their institution’s policies) that is relevant to the study, this potential conflict and any related management plans must be reported to their institution’s Point of Contact (POC) and to the Lead Study Team (LST), or LST designee. The LST is responsible for informing the Reviewing IRB of this information, so that the IRB can determine how to address the conflict. The Reviewing IRB will ensure the Relying Institution’s management plans are applied and can impose additional requirements above and beyond those of the Relying Institution’s.

Q: If study team members from a Relying Institution identify potential financial conflicts of interest after the study has received IRB approval, must they disclose this information to the Reviewing IRB?

A: Yes. If the SMART IRB Standard Operating Procedures are being followed for a study, the study team must first disclose this potential financial conflict of interest (COI), as well as any applicable management plans, to their institution’s Point of Contact (POC), who will then assess whether the COI impacts their decision to cede IRB review. If the POC determines that the study can continue to be ceded to the Reviewing IRB, the study team from the Relying Institution is responsible for disclosing the COI and any applicable management plans to the Lead Study Team (LST), or designee. The LST (or

designee) will then inform the Reviewing IRB so that the IRB can determine how to address the potential conflict in regard to the study under its purview.

Q: If study team members from a Relying Institution identify potential financial conflict of interests relevant to the research reviewed by the Reviewing IRB, do they have to disclose this information to their local IRB?

A: Whether a study team must report a financial conflict of interest (COI) to its local IRB depends on that institution's policies. If the SMART IRB Standard Operating Procedures are being followed for a study, research teams must first disclose this financial COI, as well as any applicable management plans, to their institution's Point of Contact (POC), who will then assess whether the COI impacts their decision to cede IRB review.

Federal Grant Congruency Review

Q: Why are study teams required to submit federal grants for IRB review?

A: Federal regulations [45 CFR 46.103(f)] require institutions with Federalwide Assurances (FWAs) to certify that each application or proposal for non-exempt human subjects research conducted or supported by a federal department or agency has been reviewed and approved by an IRB. Part of this certification includes an assessment of whether the activities described in the grant correspond (or are congruent) with those described in the proposed or IRB-approved study. Based on this federal requirement, the SMART IRB Agreement requires Reviewing IRBs (or designees) to assure that federal grants are congruent with the research that is supported by that funding.

Q: Which IRB should review my federal grant?

A: The grant should be submitted to the IRB(s) responsible for overseeing some or all components of the research described in the grant. In cases where IRB review has been ceded to a Reviewing IRB under the SMART IRB Agreement, and the study team that holds the grant is not the Lead Study Team (LST), the study team that received the primary award is responsible for providing a copy of the grant to the LST. The LST will then submit this information to the Reviewing IRB for consideration. The Reviewing Institution may use an alternative process for a congruency determination if such responsibility is not normally performed by the whole IRB (for example, the congruency review may be delegated to a single IRB member). Nonetheless, the Reviewing IRB Institution retains responsibility for ensuring completion of the IRB congruency determination regardless of whether it holds the federal grant.

Q: Can I only submit part of my grant to the Reviewing IRB?

The Reviewing IRB (or designee) should review the entire grant submission, including budget and personnel.

Q: What do I do if not all of the aims described in the grant supporting this study will be conducted as part of this specific protocol?

Grants can have aims that span more than one study. If the proposed research is limited to only some of the aims, this should be communicated to the Reviewing IRB (or designee) as well as which aims will be covered by the research. If not all aims will be carried out in the proposed study, the study team should provide an assurance to the Reviewing IRB (or designee) that any of the aims described in the grant either are part of another IRB application that is already approved (or determined to be exempt) or will be submitted for review in future.

Q: Should the federal grant also be submitted at continuing review?

A: If a federal award was obtained in support of the research after initial IRB approval was granted, the study team should submit the federal grant to the Reviewing IRB as an amendment (change of protocol) so that the IRB can assure that the grant is congruent with the activities approved by the IRB. If the Reviewing IRB received a copy of the grant at the time of initial review, the study team is not required to provide the grant at continuing review. However, if the grant is no longer active, the Reviewing IRB should be informed of this change in funding for the research study.

Q: Should the progress report for a federal grant be submitted to the Reviewing IRB at continuing review?

A: Unless required by the Reviewing IRB institution’s policy, study teams are not required to provide the Reviewing IRB (or designee) with a copy of the progress report they provide to the funding agency. However, the progress report should be consistent with information provided to the IRB. Any changes in the study plan should be communicated to the Reviewing IRB via an amendment (change of protocol).

Study Review and Amendment Submissions

Q: What if my institution wants to see the minutes for a study we ceded to a Reviewing IRB?

A: The SMART IRB Agreement requires the Reviewing IRB to maintain and make accessible to institutional officials from Relying Institutions, upon reasonable request, and to the extent not restricted under applicable law, portions of meeting minutes relevant to the ceded research and the Relying Institution.

Q: Who is responsible for submitting amendments (changes of protocol) to the Reviewing IRB?

A: If the SMART IRB Standard Operating Procedures (SOPs) are used, the Lead Study Team (or designee) is responsible for submitting amendments to the Reviewing IRB in accordance with the Reviewing IRB’s policies. This applies to study-wide and local amendments.

If a Relying Institution requires a local amendment, that study team is responsible for alerting the Lead Study Team (or designee) and providing them with sufficient details to prepare the submission for the Reviewing IRB. In the case of personnel changes and updates to study team member conflicts of interest, the study team must also report these changes to their local Point of Contact (POC). For

personnel changes, the Relying Institution’s POC assures the Reviewing IRB that the study team member has completed required training, is qualified to participate in the study, and has adequate resources to conduct the study. In the case of updates to or identification of new potential conflicts of interest, the local POC determines whether there are additional actions required by the Relying Institution or whether this information affects the decision to cede review of the study to the Reviewing IRB.

Q: What if a change of protocol only affects one or some of the participating sites?

A: If the SMART IRB Standard Operating Procedures (SOPs) are used, the Lead Study Team (or the Reviewing IRB, where agreed upon and documented by the Overall PI and Lead Study Team) is responsible for communicating amendments and updated IRB-approved materials to *all* Relying Institutions. The Relying Institutions must comply with the applicable portions of the IRB-approved protocol and associated study materials.

Q: How are changes in study personnel handled?

A: If the SMART IRB Standard Operating Procedures (SOPs) are used, study teams from Relying Institutions will first report proposed changes in personnel to the Point of Contact (POC) at their institution, following their institution’s established procedures and policies.

The POCs at Relying Institutions must authorize submissions involving changes to a Site Principal Investigator (PI) or key personnel, in order to ensure these personnel meet the Relying Institution’s requirements.

Once authorized by the local SMART IRB POC, the Relying Site Study Team will coordinate with the Lead Study Team, who is responsible for submitting amendments to the Reviewing IRB for review in accordance with the Reviewing IRB’s policies and procedures. This includes study-wide and local amendments.

Q: Does the Relying Institution have a role in the review of amendments (changes of protocol)?

A: Yes, if the SMART IRB Standard Operating Procedures (SOPs) are applied. Although the Reviewing IRB will conduct amendment reviews and other changes in research in accordance with the SMART IRB Agreement and SOPs, applicable federal regulations, and its own policies and procedures, the Points of Contact (POCs) at Relying Institutions must authorize submissions for following types of changes:

- Changes in Site Principal Investigator (PI) or key personnel, in order to ensure these personnel meet the Relying Institution’s institutional requirements;
- Changes that appear to affect any state law or “local consideration” issues that a Relying Institution noted as part of its agreement to cede review; or
- Changes that indicate a new potential conflict of interest.

Study teams from a Relying Institution will report changes in personnel and potential conflicts of interest to their institution’s POC via the procedures and policies established by the Relying Institution.

Q: How is it ensured that all study teams participating in a study are aware of new amendments (changes of protocol) and know when the Reviewing IRB has approved them?

A: If the SMART IRB Standard Operating Procedures (SOPs) are used, the Overall PI and/or Lead Study team (or the Reviewing IRB, where agreed upon and documented by the Overall PI and Lead Study Team) are responsible for providing all participating sites with the IRB-approved versions of all study documents (e.g., consent and authorization forms, protocol, recruitment materials) at the time of initial review, continuing review, and amendments.

Q: What if an amendment (change of protocol) could be affected by the state law or other local institutional requirements from a Relying Institution?

A: If the SMART IRB Standard Operating Procedures (SOPs) are used, the Points of Contact (POCs) at Relying Institutions must authorize amendment submissions that appear to affect any state law or “local consideration” issues that a Relying Institution noted as part of its original agreement to cede review. If a study team is not sure whether an amendment is affected by state law or other local institutional requirements, they can consult with their institution’s POC. If the Reviewing IRB is unsure whether an amendment is affected by state law or other local institutional requirements, they can consult with the POC from the Relying Institution.

Study Audits, Noncompliance, and Termination

Q: Who is informed when the Reviewing IRB makes a determination of serious and/or continuing noncompliance or suspends or terminates a study?

Under the SMART IRB Agreement, the Reviewing IRB is required to promptly notify the Overall PI, Site Investigators, and Relying Institutions of any finding of serious and or/continuing noncompliance or of apparent serious and/or continuing noncompliance with applicable human subjects protection regulations or with the requirements or determinations of the Reviewing IRB pertaining to the Relying Institution or its Research Personnel or pertaining to another institution if such finding relates to or may affect the conduct of the research study or the rights or welfare of human subjects participating in the study at the Relying Institution. In addition, the Reviewing IRB will communicate the steps it deems necessary for remediation of the noncompliance. The Reviewing IRB also will determine whether any federal agencies must be notified, such as the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA), based on study funding, status of the Federalwide Assurances for the Relying Institution(s) involved (e.g., whether institutions have “unchecked the box”), and whether the study falls under FDA purview.

Q. Why does the SMART IRB Agreement require Relying Institutions to report research-related injuries if the events do not also represent unanticipated problems?

A. Although injuries are not per se a reportable event (unless they also meet the definition of a unanticipated problem), the SMART IRB Agreement specifically calls out research-related injuries as needing to be reported to the Reviewing IRB because many institutions view injuries as inherently significant enough that the IRB should know about them and make the judgment call about whether they constitute unanticipated problems, rather than leaving sole judgment of whether an injury needs to be reported to the study investigator.

Q: If the Reviewing IRB requests an audit of a study conducted at a Relying Institution, will the Relying Institution receive documentation that the audit was conducted, regardless of the result?

A: An audit of a study can be conducted by the Reviewing IRB's institution, the Relying Institution, or jointly. If conducted by the Reviewing IRB (or designee), the IRB will promptly notify the Relying Institution that it (or its designee) is conducting an audit and will report its findings of fact to the Relying Institution within a reasonable timeframe.

Q: If one of the Relying Institutions does not submit the necessary information for continuing review in advance of the expiration date, will all Relying Institutions be affected?

A: If a Relying Institution does not provide the information necessary for the Reviewing IRB to re-approve the study prior to expiration, IRB approval will expire for that Relying Institution. However, that Relying Institution's expiration will not prevent the renewal of other participating Relying Institutions that submitted the necessary renewal information in a timely manner. Upon continuing review, those Site Investigators that have provided the information necessary for the Reviewing IRB to grant a renewal of IRB approval will be notified of the approval. If IRB approval expires for a specific Relying Site Study Team, the IRB POC and Site Investigator from affected institutions will be notified separately.

The Reviewing IRB will also notify the Overall PI and Lead Study Team, of the lapse in IRB approval and any applicable corrective action plans.

Q: A subject has lodged a complaint related to a study for which IRB review has been ceded to another Participating Institution. Who is responsible for addressing the subject's complaint?

A. The Relying Institution still retains responsibility for receiving and addressing subject complaints. Significant subject complaints must be reported to the Reviewing IRB. The Reviewing IRB, in consultation with the Relying Institution at which the complaint was received, will assess the impact of the complaint on the research study and can determine if any additional action to ensure the protection of subjects' rights and welfare would be required.

Q. The SMART IRB Agreement requires Relying Institutions to report any significant subject complaints to the Reviewing IRB. What constitutes a significant subject complaint?

A. A significant subject complaint is one that cannot be resolved by the study team and suggests an increased or unexpected new risk/harm or a change to the risk/benefit ratio of the Research. Note that

the SMART IRB Agreement requires Relying Sites to follow the policies of the Reviewing IRB. Thus, if the Reviewing IRB requires that all subject complaints be reported to that committee, the Relying Institution would need to comply with this requirement.

Guidance Regarding Scope of Review Provision of the Trial Innovation Network (TIN) Letter of Indemnification (LOI) – **NEW**

We understand that questions have been raised regarding the language in the second sentence of Section II of the TIN Letter of Indemnification (LOI) stating that the Relying Institution is solely responsible for determining whether research reviewed by the Reviewing IRB meets “all other applicable *federal*” legal requirements, and whether this language is consistent with the SMART IRB Agreement. We wish to clarify these questions.

The SMART IRB team and the Trial Innovation Network team have reviewed this issue and believe that the language in the LOI is consistent with the SMART IRB Agreement and with the intended allocation of responsibilities between the Reviewing IRB and the Relying Institution.

Section 5.4 of the SMART IRB Agreement says that the Reviewing IRB’s review will be in accordance with applicable federal *human subjects research regulations / human subjects protection requirements* (emphasis added). In other words, the IRB is responsible for attending to requirements of federal human subjects regulations *only* (Common Rule, FDA, other potentially applicable human subjects regulations of non-Common Rule federal agencies). The Agreement does not require the Reviewing IRB to review research for compliance with all federal regulations generally.

For example, if a Relying Institution is subject to federal confidentiality requirements at 42 CFR Part 2 pertaining to certain substance abuse treatment records that would impose specific consent obligations on the Relying Institution in connection with a study involving such records, the Agreement does not require the Reviewing IRB to identify this issue. Rather, the Relying Institution would be responsible for identifying this issue and communicating the requirements applicable to its site to the Reviewing IRB. The Reviewing IRB would be responsible for applying this information to its review and approval of the study on behalf of the Relying Institution.

We note that Section 6.4 of the Agreement, “Local Considerations,” states that it is the Relying Institution’s responsibility to identify local context issues and requirements to the Reviewing IRB and does not currently reference federal laws or regulations. However, it was not the intent to make the Reviewing IRB responsible for the identification of the research with *all* federal laws/regulations (other than federal human subjects protection regulations). For this reason, language in Section II of the LOI was added to clarify this issue. The SMART IRB team has also posted an additional FAQ regarding this issue on the SMART IRB website.

As was noted by one of the institutions, the Relying Institution’s responsibility under the Agreement to identify and communicate requirements that affect the conduct or approval of a study at its site does require some level of ‘review’ of the research by the Relying Institution in order to be able to identify

the applicable local requirements and communicate them to the Reviewing IRB. However, we note that that is already the case with respect to the state law issues. It is NOT the intent of the LOI language to suggest that any of the regulatory review responsibilities of an IRB under the Common Rule, FDA, or other federal human subjects regulations remain with the Relying Institution; that is, the Relying Institution/Relying Institution IRB is not being asked or required to do a 'regulatory' review.