Recommendations for the Harmonization of Local Considerations

Local Considerations Working Group of the SMART IRB Harmonization Steering Committee

HARMONIZED AUGUST 2025

This document underwent a review and input process from July 2023 to September 2023 and has now been finalized.

Table of Contents

This project has been funded in whole or in part with Federal funds from the National Center for Advancing Translational Sciences, National Institutes of Health, Department of Health and Human Services, under Contral No. 75N950C00008.

Executive Summary

The Working Group identified several challenges and inconsistencies related to local considerations (aka local context) and recommended harmonization in three key areas to improve the process for providing, collecting, and reviewing local considerations:

1. Definition of local considerations.
2. The type and detail of information collected to address local considerations.
3. Assessing local considerations throughout the life of a study.

The following resources were developed in support of these recommendations:

- Institutional Profile
- Study-Specific Document
- Local Considerations Information Guidance Table
- Local Considerations Throughout the Life of a Study
- Local Considerations Responsibilities By Reliance Stage
- Considerations for Investigators Writing Multi-Site Protocols
- Single IRB Review Case Study: Addressing Variation in Institutional Assent Policies
- Template Checklists for Reviewing IRBs and Relying Institutions to Identify When to Address Local Considerations after Initial Approval of a Study

Background

What are Local Context and Local Considerations?

Federal requirements for the use of a single IRB (sIRB) for multi-site research, such as within the Common Rule and National Institutes of Health (NIH) policy, highlight the need for Relying Institutions to communicate information to the sIRB to ensure appropriate oversight for each institution. This information is often referred to as local context. The SMART IRB Reliance Agreement (henceforth SMART IRB Agreement) recognizes the importance of local considerations information and requires Relying Institutions to 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, relevant to the Research (“Local Considerations”) that would affect the conduct or approval of the Research at the Relying Institution.”

Neither phrase appears in the federal regulations governing the protection of human subjects yet collecting information about local context or local considerations is an established practice in the context of sIRB review. The Working Group uses the term local consideration rather than local context in this document because the former is defined in the SMART IRB Agreement; however, the terms are viewed as interchangeable.

The need to collect local consideration information is based on the interpretation of the Common Rule [45 CFR 46.107(a)] and FDA regulations [21 CFR 56.107(a)], which requires an IRB to be sufficiently qualified through the experience and expertise of its members (professional competence) and the diversity of its members to be sensitive to such issues as "community attitudes." Additionally, IRBs are required to be "able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice." Further, the regulations for planned emergency research with an exception from informed consent (21 CFR 50.24) require consultation with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn. These requirements suggest that a single IRB would need to know local considerations, particularly in terms of which communities to consult with and then incorporate that information into their considerations when reviewing such research.

Most sIRBs have forms and processes to collect local considerations information from Relying Institutions. Some information obtained represents generally static details about institutions (i.e., institutional profile information). Examples of static information include:

- applicability of the federal assurance,
- local requirements for implementing the HIPAA Privacy Rule,
- state and local laws,
- implementation of flexibility options regarding unregulated research, and
- select institutional policies.

Other information collected may vary by study (i.e., study-specific information). Examples of study-specific information include:

- the Relying Institution Principal Investigator (PI)[1] and study team qualifications and training,
- conflicts of interest (COI) relevant to the ceded research,[2]
- outcomes of certain ancillary reviews,[3] and
- state or local laws or institutional policies related to enrollment of vulnerable populations.

---

1 *The investigator(s) responsible for the conduct of an instance of Research at their Participating Institution, also called the Site Investigator(s) or Site PI(s).*

2 *For more detailed considerations of COI see the SMART IRB Harmonization Committee's Recommendations: Conflict of Interest Review Processes for sIRB Review.*

3 *For more detailed considerations of ancillary reviews see the SMART IRB Harmonization Committee's Recommendations: Ancillary Reviews.*

What information is collected, when it is obtained, and how it is assessed varies across IRBs. Additionally, Relying Institutions vary in whose responsibility it is to provide information and verify information provided to Reviewing IRBs.

The SMART IRB Harmonization Working Group on Local Considerations identified the following areas that would benefit from further clarification and harmonization:

1. **Defining local considerations** and distinguishing between local considerations and standard IRB review practice.
2. **Adopting universal forms and questions** to collect local consideration information and identifying the level of detail Relying Institutions/Relying PI need to provide Reviewing IRBs, including what information can be provided to Reviewing IRBs as attestations.
3. **Clarifying roles**, including:
   - Responsibilities surrounding the collection and verification of local considerations provided to the Reviewing IRB at initial review and throughout the duration of the study.
   - Developing a model workflow for sharing local considerations information.
4. **Addressing variations among institutional policies** as part of a Reviewing IRB's review process, and how research teams can enhance the sIRB review process by developing multi-site protocols or study plans that take into account potential variation in study implementation across participating sites.

Local Considerations and Standard IRB Review Practice

The Working Group distinguished between standard IRB review practice and local considerations. The standard IRB review practice requires IRBs to determine whether a study meets the criteria for IRB approval as outlined under applicable regulations. In contrast, local considerations are issues that are unique about, or specific to, a Relying Institution that the Reviewing IRB needs to be aware of to conduct an adequate review of that site, as opposed to what a Reviewing IRB should take into account to assess the study as a whole (i.e., standard IRB review practice).

Table 1 includes examples that illustrate the difference between a standard IRB review practice and a local consideration.

TABLE 1. A Comparison of Standard IRB Review Practice vs. a Local Consideration

Example	Standard IRB Review Practice	Local Consideration
Research study includes experimental drugs that could adversely affect a pregnancy	Determining how to minimize reproductive risks from drugs that can affect pregnancy, such as what forms of contraception would be acceptable.	Any limits a Relying Institution may impose on what contraception it would be willing to provide to research subjects enrolled at its site (e.g., because of religious beliefs or practices) and what language it requires to be included in the informed consent about contraception.
Informed consent content	When informed consent is required, determining the information that must be provided to research subjects, as well as the format and method of presentation.	Specific language required by institutional policy (e.g., compensation for injury language) or state law (e.g., California Experimental Participants Bill of Rights).
Subject selection and enrollment	Ensuring subject selection is equitable and that informed consent documents and forms provide information in a language understandable to the subject or the legally authorized representative. Determining whether vulnerable subjects are likely to be enrolled in the study and additional safeguards that may be needed to protect the rights and welfare of these subjects.	Participants or populations who might not be identified explicitly in a research protocol or IRB application and who could be enrolled at a site or whose records or biospecimens might be used for the research, such as those who: ▸ May have relevant ethical, cultural, or religious standards, ▸ May be vulnerable to coercion or undue influence, ▸ Are from discrete and insular communities, or ▸ May have unique legal status (e.g., American Indian/Native Alaskan tribes).

Information Collection

The Working Group identified a lack of clarity surrounding responsibilities for collecting, providing, and verifying local considerations under a reliance arrangement. Although the SMART IRB Agreement requires Reviewing IRBs to collect and evaluate local considerations information, the Working Group noted that not all Reviewing IRBs perform this activity. The Working Group noted that steps had been taken to harmonize the collection of local considerations.[4] However, significant differences continue to exist among Reviewing IRBs in the information they obtain or whether they obtain local consideration information at all. For example, some Reviewing IRBs continue to collect the CVs and resumes of study teams while others accept attestations from Relying Institution PIs or Relying Institutions that study personnel are trained and qualified to conduct the research.

The quality of information Relying Institutions provide Reviewing IRBs also varies, and gaps remain between the level of detail a Reviewing IRB expects to receive and what is actually communicated. Some Relying Institutions, for example, provide links to dense policies or state laws rather than summarizing their salient elements for the Reviewing IRB. This approach can increase the potential for a Reviewing IRB to misinterpret or fail to apply relevant local considerations during its review of a site.

The SMART IRB Agreement is generally silent on the role of the study team. However, in many cases, Relying Institution PIs and their study teams are responsible for identifying differences in study implementation, working with their institutions' reliance point of contacts (POCs) to provide information to the Reviewing IRB, and monitoring for amendments after initial IRB approval that might trigger review of new local considerations.

The Working Group also recognized that local considerations are typically obtained by Reviewing IRBs at the time of an initial review of Relying Institution. However, amendments or changes in the study can trigger the need for a Reviewing IRB to reassess the information Relying Institutions provide at the time of initial review or collect additional local considerations from Relying Institutions to conduct an appropriate review for their sites after initial review. For example, if a study is initially approved to include only adults and is amended to allow recruitment of minors, the Reviewing IRB should evaluate the local considerations collected from the Relying Institution(s) to determine whether they obtained information from each site about State and local laws or institutional policies relating to enrolling children. If this information was not collected initially, then the Reviewing IRB should go back to the Relying Institution(s) and obtain this information. Reviewing IRBs, Relying Institutions, and Relying Institution PIs need systems in place to be able to ensure relevant local considerations are taken into account throughout the life of a study.

---

4 *Examples include the SMART IRB Reliance System and the IRB Reliance Exchange (IREx) Institutional Profiles, SMART IRB Protocol-Specific Document, and Relying Site Survey.*

Recommendations for Harmonization of Local Considerations

The Working Group developed the following recommendations for harmonization of local considerations.

1. **Adopt a Harmonized Definition of Local Considerations**[5]

   The Working Group recommends the regulated community adopt an agreed upon definition of local considerations that helps identify what information is essential to be shared between the Reviewing IRB and Relying Institution to ensure Reviewing IRBs conduct appropriate reviews for all sites that rely on them. The Working Group developed a definition that pragmatically distinguishes between standard IRB review practice (i.e., what a Reviewing IRB should consider regardless of the sites it reviews for) and unique aspects of a Relying Institution that could affect the Reviewing IRB's determinations. We propose the following definition:

A local consideration is an aspect of the Relying Institution that could affect the Reviewing IRB's determinations, including the criteria for IRB approval. Local considerations may include:

- State and local laws or Relying Institution policies relevant to the study or subject population.
- Customs, beliefs, values, or practices of a distinct subject population(s) that a Relying Institution could expect to be enrolled or included (such as records or biospecimens used for the research) in a study and that may affect IRB review.
- Variations in how a study will be implemented across sites, including differences in standard of care (i.e., routine care).

The concepts of *customs, beliefs, values,* and *practices* cover a range of considerations that could be relevant to research, such as:

- Expectations around decision-making—whether it is done individually, as a family, or as a community.
- Whether oral communication is emphasized over written communication, which can affect how information is conveyed and understood.
- The level of comfort with documents being signed, especially those that appear to be official.

---

5 *During the period the Working Group met to create this harmonization document, the Office for Human Research Protections (OHRP) issued draft Guidance Use of a Single Institutional Review Board for Cooperative Research. The Working Group reviewed the OHRP definition and did not think that it contradicted the definition proposed in this recommendations document.*

- Prohibitions on the use of certain technologies, which may limit transportation modes or use of any devices used in a study, either as the focus of the research or to support participation in the research.
- Forms of contraception permitted by a belief system, which may affect eligibility requirements for a study or the description of birth control within a consent document.
- Use of health insurance, which can influence informed consent language.

Examples to further illustrate customs, beliefs, values, or practices that could be reflected in local considerations include:

- The Navajo Nation banned research using its peoples' DNA because of concerns about how that research might be used (e.g., to dispute origin stories and claims to traditional lands).
- Catholic institutions usually require specific language describing birth control options for studies that require individuals to avoid becoming pregnant or impregnating someone.
- Enrollment of people from plain communities (e.g., Amish and Mennonite) can require special consideration of recruitment methods, decision-making processes, informed consent language, costs, transportation, and technology used.
- Enrollment of Hmong elders, who often cannot read Hmong or English, will benefit from strong oral informed consent processes.
- Whether an institution provides or places restrictions on gender affirming care as part of their practice may require the Reviewing IRB to account for variations in study procedures and assessment of research risks.

2. **Harmonize the Type and Detail of Information Collected to Address Local Considerations**
   SMART IRB previously developed documents to help harmonize local considerations information: the Institutional Profile, Relying Site Survey,[6] Protocol-Specific document, and, to a certain extent, the Implementation Checklist for use of the SMART IRB Agreement. The Working Group reviewed, and revised as needed, the current information collected in these documents and took into account FDA, OHRP, and SACHRP guidance to update the Institutional Profile and Protocol-Specific document (renamed Study-Specific Document) (see Appendix 1 and 2).

---

6 *The Relying Site Survey was intended to collect key local consideration information to help the Reviewing IRB determine whether they can serve as the Reviewing IRB for that site. The Working Group evaluated the Relying Site Survey, compared it to the Institutional Profile and Protocol-Specific Document, and decided to retire this document. Instead, questions from the survey were incorporated into updated versions of the Institutional Profile and newly named Study-Specific Document.*

The Working Group recommends that Reviewing IRBs and Relying Institutions adopt these three documents to ensure consistent sharing of local considerations with the Reviewing IRB:

- The **Institutional Profile** includes information about institutions that tends to remain static, such as how to implement the HIPAA Privacy Rule, some state laws that may affect human subjects research, whether the institution has implemented the flexibility options regarding unregulated research, and institutional policies. (See Appendix 1)
- The **Implementation Checklist** will document the flexible provisions of the SMART IRB Agreement. This allows Reviewing IRBs to document whether the HIPAA Privacy Rule applies to a study and, if so, whether they will serve as a privacy board for a study; whether HIPAA authorization language will be provided to research participants via an informed consent document or a separate authorization form; and how investigator conflicts of interest will be addressed.
- The renamed **Study-Specific Document** asks Relying Institutions to provide local considerations information not captured in the other documents that may vary by the study or by research activities taking place at different site(s). (See Appendix 2)

Appendix 3 includes a table that provides guidance regarding how to complete the Institutional Profile, Implementation Checklist, and Study-Specific Document, including who is responsible for providing that information and the level of detail required. In some cases, for example, the table identifies areas where Reviewing IRBs should consider obtaining attestations as part of the reliance arrangement rather than requiring detailed information from the Relying Institution to ensure the commitments and responsibilities are being met (e.g., qualifications and training of key personnel or available resources or drug and/or device storage provisions).

3. When Local Considerations Should be Addressed and Responsibilities for the Collection and Provision of Local Considerations

The Working Group developed a recommended workflow to provide guidance regarding the stages during a study when local considerations information should be collected. There are three key points in the life of the study that should trigger the collection and review of local consideration information: study development, initial review, and after IRB approval. The table included in Appendix 4 provides more details about responsibilities related to local considerations, and the key local considerations needed at each stage. In addition, the Working Group developed a recommended workflow (Appendix 5) to provide an outline of the reliance process to identify where local considerations fits into the larger scheme of a single IRB study.

A Note on Other Considerations

The updated version of the SMART IRB Agreement issued in March 2025 (Version 3.0) includes the concept of "Other Considerations," which refers to:

> *"the requirements of any applicable federal laws or regulations or of relevant federal departments or agencies that are not readily apparent from an IRB submission or that are specific to the Relying Institution that would affect the conduct by or approval of the research or the granting of an exemption determination on behalf of the Relying Institution."*

Other Considerations were highlighted in the updated SMART IRB Agreement to address instances where there may be specific interpretations or applicability of federal laws, regulations or agency requirements other than human subjects research requirements that an IRB would need to take into account when reviewing for a Relying Institution.

For example, a study that is not specifically targeting students but may access student records at a specific Relying Institution would mean FERPA regulations would apply for that site. Similarly, a Relying Institution using a limited data set from the Centers for Medicare & Medicaid Services (CMS) would be subject to CMS regulations related to the use and distribution of that data and would require disclosure to the proposed Reviewing IRB.

Other Considerations should be addressed similarly to the recommendations for Local Considerations.

Study Development

The Working Group recognized that if a study is implemented differently across sites, this can affect sIRB review and thus can be a local consideration. Sites may vary in which populations they may enroll, what equipment they will use, their roles or the activities they will perform (e.g., a data analysis or biobanking center vs. a site that recruits research participants), or other aspects. Ideally, potential variations would be considered when a study is developed or at the time of site selection. Certain aspects of a protocol or study plan should be specific where necessary to ensure comparable data collected, but also should be written broadly enough to account for variability across sites, such as in terms of activities performed, resources available (e.g., when a site has specific equipment), and processes followed at different participating sites. If a study or protocol does not take into account potential differences across sites, the procedures or processes it describes may contradict institutional policies at some sites, which would need to be resolved.

The Working Group developed Considerations for Investigators Writing Multi-Site Protocols (Appendix 6) to help institutions and research teams address local considerations during the study development phase. Investigators can use this as a guide when creating protocols and as a basis for reaching out to potential participating site study teams to collect information about their policies, practices, and resources. Institutions also can incorporate information from this appendix into protocol templates they provide their research teams.

Initial Review

At the time of initial review, Relying Institution PIs/Relying Institution Study Teams/Relying Institutions must work together to provide Reviewing IRBs with accurate local considerations information. This allows the Reviewing IRB to appropriately evaluate each site, by taking into consideration state and local laws, as well as institutional policies, that are relevant to the research activities conducted by their study team. Reviewing IRBs should not collect local considerations information that could affect research review until a final or near final protocol or study plan has been produced.[7]

In addition to investigators writing protocols or study plans that better capture variability across participating sites, the Working Group recommends that Reviewing IRBs can rely on the fact that Relying Institutions are responsible for having policies and processes in place that ensure compliance with human subjects protections requirements and other key requirements, such as the HIPAA Privacy Rule or data security. Because Relying Institutions make certain commitments as part of a reliance arrangement, such as the responsibilities outlined in the SMART IRB Agreement, Reviewing IRBs can a) obtain assurances from Relying Institutions about certain compliance areas (e.g., qualifications and training of key personnel) and b) approve protocols or study plans that allow research teams to implement some local institutional procedures, even if those policies differ by institution.

We provide the following examples to illustrate how Reviewing IRBs could obtain assurances from Relying Institutions and depend on Relying Institution policies for certain aspects of a study to address variations across sites without the need to collect such details as part of local considerations.

- **Example 1: Variation in Electronic Platforms Supporting Informed Consent**
  Institutions differ in what electronic platforms are available to them or permitted by institutional policy to be used in support of informed consent. Consequently, an investigator describing a study's informed consent process in a protocol or IRB application should build in flexibility regarding what platforms may be used. In this situation:
  - The protocol does not need to specify the electronic informed consent but instead describes key characteristics any platform used must have (e.g., part 11 compliance or meets HIPAA security standards), which could apply to a range of systems.
  - The Reviewing IRB can conduct an adequate review of the informed consent process and data confidentiality based on the characteristics the electronic informed consent platform must have.
  - Relying Institutions would be responsible for ensuring that any platform they use for that study complies with the features and functions approved by the Reviewing IRB as well as their institutional policies.

7 *This is because the study-specific local considerations are likely to change based on aspects of the protocol. Prematurely collecting local considerations based off an incomplete protocol may mean that the IRB needs to recollect local consideration information, hence duplicating effort.*

- **Example 2: Variation in Assent Policies and Processes**
  A responsibility of the Reviewing IRB is to determine whether assent will be required for a study and, if so, from which children assent would be obtained based on their ages, maturity, and psychological state. In addition, the Reviewing IRB would be expected to review and approve any language that would be used to obtain assent, which could vary by the child's age and maturity. However, institutions may differ on when assent is obtained, what language and forms are used in support of the process (e.g., children are presented with different approaches and documents depending on their age), and whether it is documented.
  To accommodate variations across sites in their assent approaches, the research protocol could be written to reflect, and the Reviewing IRB could approve, the following:
  1. Allow sites to choose whether to have a child sign a form.
  2. Approve multiple assent processes that can be tailored based on the child's age and maturity such as:
     - A waiver of assent for children too young or not sufficiently mature to engage in the assent process or a waiver of assent for a subset of children based on their psychological condition.
     - Allowing study teams the option to ask a child to sign an assent form or document the assent process without the child's signature based on their institution's requirements, but identifying a default position in cases that an institution does not specify how assent must be documented.
     - Approving assent scripts and/or forms for different ages or maturity levels and providing recommendations for study teams when each form might be appropriate, but allowing the study team to use the script or form that they deem appropriate for a specific child based on applicable institutional policy or state or local laws.

Appendix 7 provides an expanded analysis of sIRB issues related to assent, including distinguishing between standard IRB review practice and local considerations.

After IRB Approval

The Working Group identified review of local considerations after IRB approval as a particular challenge for sIRB arrangements. Changes to the protocol, recruitment materials, or other study materials (e.g., the addition of a new subject population) may introduce new local considerations that affect or require IRB review. We recommend:

- Reviewing IRBs identify categories of changes that should trigger a review of information collected as part of the local considerations process. Then determine whether additional information needs to be obtained from the Relying Institution to conduct an adequate review for that site. The addition of a new population may require the IRB to incorporate relevant state or local law or institutional polices into its review.
- Relying Institutions develop guidance for their study teams regarding what changes in research, events, and other information may impact local considerations and may require input from their institution's HRPP (e.g., a new COI management plan relevant to the research).

Appendix 8 provides template checklists that Reviewing IRBs and Relying Institutions can use to identify amendments or other events that should prompt an assessment of the local considerations information to determine whether additional communication between Reviewing IRBs and Relying Institutions is necessary.

Appendix 1.

INSTITUTIONAL PROFILE

Updated August 2025

Institutional, Local, and State Requirements
Working Group of the SMART IRB Harmonization
Steering Committee

Introduction

Purpose

The SMART IRB Institution Profile captures institutional information that is **independent** of a specific protocol. An institution's SMART IRB Point of Contact (POC) should complete this profile to (1) document institutional, local, and state requirements that would apply to all protocols; (2) refer to in conjunction with a completed SMART IRB Study-Specific Document) during the ceding and review of a specific protocol; and, if applicable, (3) document information about the institution and its IRB(s). A potential Reviewing IRB may refer to this profile during initial determination of whether to serve as the Reviewing IRB. Likewise, potential Relying Institutions may refer to this information when determining whether to cede IRB review to an institution for a specific protocol.

Instructions

1. An institution's POC should record the appropriate responses (and sub-responses) to each question.
   a. Complete each text box, as applicable.
   b. Select **one** appropriate response from each drop-down list.
   c. For each "yes" response, provide additional details, as applicable.
2. An institution's POC should update the information on this form on an annual basis and as needed to ensure accuracy.

Notes

- **Institution Name(s).** Because a Reviewing IRB may not be familiar with your institution, it is important to include all alternate names, abbreviations, and acronyms by which the institution may be known to avoid confusion and/or potential delays in approvals or correspondence.
- **Components.** When listing all components under your institution's FWA, indicate in the text field whether the components are considered separate legal entities.
- **State Laws and Local Requirements.** Provide details for any state laws and/or local requirements that would be applicable to **all** protocols, (e.g., IRB reporting requirements for all studies).
- **Flexibility.** Many institutions have implemented flexibility options with regard to review and approval of research at their institutions. Examples of flexibility include establishing additional exempt categories, extending IRB approval dates, and/or expanding expedited review categories. If your institution has implemented flexibility options, provide details for the Reviewing IRB.

Institutional Profile

All institutions should complete this form and update it on an annual basis to ensure accuracy.

1. Name of Institution

2. List all other names by which the institution is known.

3. List all organizations that are considered components under this institution's FWA.

4. Identify any affiliations this site has, such as a university, clinic, or hospital.

- *If any of the sites are within a network or system, identify all sites with separate Federal Assurances.*

5. Does your state law or institutional policy require you to apply the Common Rule to all studies?
☐ Yes ☐ No

6. Does your state law or institutional policy require you to apply any of the subparts (B, C, or D) of the HHS regulations at 45 CFR part 46 that provide additional protections for certain populations in research to all studies, when applicable?
☐ Yes ☐ No If yes, indicate the subpart(s) your institution applies.

7. Are there any local considerations (e.g., customs, beliefs, values, or practices of distinct subject populations(s)) that could be expected to apply to research conducted by the institution?

8. Provide any additional information that may affect the IRB's review of research at your institution. Some examples may be California Bill of Rights, Virginia law that requires application of the Common Rule to all research, restriction of any vulnerable populations, etc.

9. Identify the age of majority for your state or territory.

10. Is your institution willing to serve as an IRB of record (Reviewing IRB) for other institutions?
☐ Yes ☐ No ☐ It depends ☐ Not applicable

11. Name of the institution's IRB(s), if applicable.

12. As a Reviewing IRB, would you be willing to serve as the Privacy Board for other institutions?
☐ Yes ☐ No ☐ It depends ☐ Not applicable

Appendix 2.

STUDY-SPECIFIC DOCUMENT

Institutional, Local, and State Requirements
Working Group of the SMART IRB Harmonization
Steering Committee

Introduction

Purpose

The SMART IRB Study-specific Document captures institutional information that is **specific** to a given protocol. A Reviewing IRB may use this document to (1) collect applicable institutional, local, and state requirements, and to (2) document how the IRB has reviewed and approved a protocol for the Relying Institution.

Instructions

1. The Relying Institution's SMART IRB POC should work with their Site Investigator (Relying Institution PI) and/or designated study team point of contact (Relying Institution PI's POC) to identify and record the appropriate responses (and sub-responses) to each question. ***The Relying Institution PI should complete as many items as possible then forward the document to their institution's SMART IRB POC, who will verify all items.***
   a. Complete each text box, as applicable.
   b. Select **one** appropriate response from each drop-down list.
   c. For each "yes" response, provide additional details, as applicable.
2. The Relying Institution's SMART IRB POC will share the completed Study-specific Document with the proposed Reviewing IRB, and update this document throughout the history of the study.
3. The Reviewing IRB should retain a copy of the completed Study-specific Document.

Notes

- **Local (Context) Considerations.** To help with the Reviewing IRB's determination to serve in such a capacity and to appropriately orient the Reviewing IRB to the Relying Institution, please provide a basic overview of the local community (i.e., cultural, demographic, and economic characteristics, languages spoken, local educational and/or literacy concerns, and religious, social, and political considerations) as it relates to the protocol being reviewed. This will help the Reviewing IRB ensure that appropriate methods are in place for conducting research within the Relying Institution's community.
- **HIPAA.** Because each institution may interpret preparatory research provisions differently, and because some researchers may be considered employees or members of a covered entity while others are not, the Reviewing IRB will require confirmation on whether a Relying Institution will require a HIPAA waiver to disclose protected health information and allow the Relying Institution PI and/or study team to contact and recruit individuals into the study.

Study-Specific Document

A Relying Institution's SMART IRB Point of Contact (POC) should complete this form in conjunction with the local study team. The Relying Institution PI should complete as many items as possible then forward the document to their institution's SMART IRB POC, who will verify all items.

1. Protocol Title

2. Site Name

Relying Institution Investigator (Relying Institution PI)

3. Name:

4. Email:

5. Phone:

*Relying Institution PI's **point of contact (POC)***

6. Name:

7. Email:

8. Phone:

9. Will the study be implemented differently at your site due to a limited role (e.g., your site serves as a data analysis center or biospecimen repository)?
☐ Yes ☐ No If yes, provide details.

10. Do any of the site's study team members have financial conflict of interests (COIs) related to this study?

☐ No
☐ Yes, and a management plan has been developed.
☐ To be determined; COI review will be performed by the Reviewing IRB.
☐ For federal agencies: The Agency or Department engaged in this study has completed COI analyses required by its procedures (based on federal law and policy) and participation of its investigator(s) in the research is permissible.

If yes, provide summary of conflict and management plan, or attach documentation.

If yes, provide the name and contact information for the appropriate POC (e.g., Research Integrity Officer) for questions related to the determination and/ or local management plan.

11. The Relying Institution PI/Relying Institution confirms that all resources are available to conduct our portion of the study.
☐ Yes ☐ No If yes, please describe:

12. Relying Institution PI/Relying Institution confirms that any drugs/devices used for this research study will be stored and managed as described in the study plan and in compliance with my institution's policy.
☐ Yes ☐ No

13. Relying Institution PI/Relying Institution confirms that all individuals conducting the research are qualified to perform any tasks delegated to them, have received adequate training on how to conduct the delegated tasks, were provided with an adequate understanding of the study, and that the Relying Institution has adequate resources to carry out this research study.
☐ Yes ☐ No

14. Does your state law, local law, or institutional policy require that the recruitment at your site be implemented differently from what is outlined in the study plan?
☐ Yes ☐ No If yes, describe in detail the difference that must be implemented at your site:

15. Does your state law, local law, institutional policy, **or standard of care (routine care) or local practice** require that the study be implemented differently at your site than from what is outlined in the study plan?
☐ Yes ☐ No If yes, describe in detail the difference that must be implemented at your site:

16. Does your state law, local law, or institutional policy require that the **consent process, use of a short form, and translation of consent form** be implemented differently at your site than from what is outlined in the study plan?
☐ Yes ☐ No If yes, provide details.

17. Does your local/state laws or institutional policy impact or require changes to what is outlined in the study plan for any of the following populations?

- **Minors** (For example, your site may differ: assent process, pregnancy testing in minors, wards of state, emancipated minors, who is able to assess the capacity to consent, etc.)
  ☐ Yes ☐ No ☐ N/A (no minors to be enrolled)

  If yes, describe in detail the difference that must be implement at your site:

- **Adults with impaired decision-making capacity and their legally authorized representative (LAR)** (For example, your site may differ: who can obtain informed consent, who serves as an acceptable LAR, identifying capacity to consent, etc.)
  ☐ Yes ☐ No If yes, describe in detail the difference that must be implement at your site:

- **Pregnant persons**
  ☐ Yes ☐ No If yes, describe in detail the difference that must be implement at your site:

- **Prisoners** (For example, your site may differ categories of research in which prisoners may participate.)
  ☐ Yes ☐ No If yes, describe in detail the difference that must be implement at your site:

- **Other** (ex. Students, employees, etc. Your site may differ in who can conduct studies on students or employees.)
  ☐ Yes ☐ No If yes, describe in detail the difference that must be implement at your site:

18. Is there anything additional related to state law, local law, or institutional policy that impacts this particular study (e.g. AI policy)?
☐ Yes ☐ No If yes, please describe:

19. Does your institution have any **required language** that must be incorporated into the **consent form**? For example: compensation in the event of research-related injury, pregnancy testing in minors, or genetic testing.
☐ Yes ☐ No If yes, please describe the sections that must be altered and include the required consent language for this study:

20. Are there any site-specific **ancillary reviews** that could affect the IRB review and/or approval at your site and need to be addressed by the Reviewing IRB?
☐ Yes ☐ No

If yes, what is the current overall status of review and approval by the applicable ancillary commitee(s)?
☐ Pending ☐ Complete

If pending, provide details (i.e., outcome, anticipated date of review) or attach documentation.

21. Is the Relying Institution a HIPAA Covered Entity?
☐ Yes ☐ No

If yes, will you require the Reviewing IRB to serve as Privacy Board:
☐ Yes ☐ No

If you are accessing PHI and requesting a partial or full waiver/alteration of HIPAA authorization, explain how your request meets the following criteria:

- Use or disclosure of PHI involves no more than a minimal risk to the privacy of participants
- Research could not be practicably conducted without the waiver and access to PHI
- Researcher has a plan to protect the PHI from improper use and disclosure
- Researcher has a plan to destroy identifiers at the earliest opportunity

Appendix 3. Local Considerations Information Guidance Table

This table identifies responsibilities related to providing various types of local considerations, and describes the level of detail that should be provided, as well as when and how that information should be communicated. All constituents must work together to ensure accurate local consideration information is provided. The Relying Institution Principal Investigator (PI) should work in consultation with the Relying Institution. Thus, when the table references Relying Institution PI, it assumes they have consulted with the appropriate person at the Relying Institution, as applicable. It is especially critical that Relying Institution PIs review the protocol or study plan and communicate to the Lead Study Team, Reviewing IRB, and Reliance Point of Contact (POC) any differences in local protocol implementation or study conduct throughout the life of the project. Relying Institutions will need access to an IRB-approved or near-final protocol or study plan in order to provide local considerations information to the Reviewing IRB.

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
Available resources and facilities to conduct the study	Relying Institution PI should consider whether they have the resources and facilities required to participate in the research at the time of deciding to be involved in this study. Relying Institutions should confirm whether their study team has adequate resources and facilities to perform the research through their internal formal review process.	Prior to or during initial IRB review for a site.	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 3. Local Considerations Information Guidance Table (cont'd)

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
State and local laws or institutional policies around implementation/ conduct of the protocol or study plan (e.g., site uses different imaging mode or equipment)	Relying Institution PI and/or in conjunction with the Relying Institution.	Prior to or during initial IRB review for a site.	**Resource**: Use SMART IRB Study-Specific Document.
Institutional policies around differences in standard of care (routine care) or local practices	Relying Institution PI and/or in conjunction with the Relying Institution.	Prior to or during initial IRB review for a site.	**Resource**: Use SMART IRB Study-Specific Document.
Federalwide Assurance (FWA)—whether the box is checked requiring the Relying Institution to apply the Common Rule (and any or all of its Subparts) to some or all human subjects research.	Relying Institution.	Prior to or during initial IRB review for a site.	**Resource**: Use SMART IRB Institutional Profile.
State and local laws or institutional policies around data access, storage, sharing, confidentiality, privacy, and security of information and specimens	Relying Institution PI and/or in conjunction with the Relying Institution.	Initial IRB review for the site.	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 3. Local Considerations Information Guidance Table (cont'd)

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
State and local laws or institutional policies around recruitment (e.g., address patient contact prior to consent)	Relying Institution.	Initial review for that site and after initial approval when amendments affect recruitment.	**Resource**: Use SMART IRB Study-Specific Document.
Drug/device storage or management	Relying Institution PI in conjunction with the Relying Institution.	Initial review for that site and after initial approval when amendments affect drug and/or device storage or management.	**Resource**: Use SMART IRB Study-Specific Document.
Individual researcher conflict of interest (COI)	Relying Institution.	Initial review for that site and after initial approval when COI management plans change or new personnel are added who have COI management plans relevant to the ceded research.	**Resource**: Use SMART IRB Study-Specific Document.
Eligibility to conduct research (e.g., credentials, qualifications, trainings, adequacy of the research site)	Relying Institution.	Initial review for that site and after initial approval.	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 3. Local Considerations Information Guidance Table (cont'd)

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
HIPAA Privacy Rule: determinations and authorization language	Relying Institution.	Initial IRB review for the site.	**Resource**: Use SMART IRB Implementation Checklist to provide information on HIPAA determinations and actions; HIPAA authorization language and consent forms. Use SMART IRB Institutional Profile and SMART IRB Study-Specific Document.
HIPAA Privacy Rule: approach to screening and recruitment of potential participants (i.e., partial waiver of HIPAA authorization vs. activities preparatory to research)	Relying Institution.	Initial review for that site and after initial approval if a recruitment method changes to require information from protected health information from a new source.	**Resource**: Use SMART IRB Institutional Profile.
State and local laws or institutional policies that affect informed consent content	Relying Institution.	Initial review for that site and after initial approval when substantive changes are made to the informed consent language, especially areas known to be covered by institutional policy (e.g., compensation for subject injury).	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 3. Local Considerations Information Guidance Table (cont'd)

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
Non-English speaking participants (e.g., short forms, translation of the consent)	Relying Institution.	Initial IRB review for the site and after initial approval if a non-English speaking population is included in the study for the first time and will be enrolled at that site.	**Resource**: Use SMART IRB Study-Specific Document.
Minors (e.g., age of majority, assent policy, pregnancy testing, wards of state, emancipated minors)	Relying Institution.	Initial IRB review for the site and after initial approval if a new population of children will be enrolled or study procedures added that may trigger state or local laws or institutional policies.	**Resource**: Use SMART IRB Study-Specific Document.
Individuals with impaired decision-making capacity/ legally authorized representative (LAR)	Relying Institution.	Initial IRB review for the site and after initial approval if study procedures added that may trigger state or local laws or institutional policies.	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 3. Local Considerations Information Guidance Table (cont'd)

Local Considerations	Who is responsible for providing local consideration information to the Reviewing IRB?	When should the local consideration information be provided to the Reviewing IRB?	Which SMART IRB resource(s) can I use?
State and local laws, or institutional policies relevant to the study or subject population that may be enrolled by the Relying Institution Study Team, e.g., customs, beliefs, values, or practices of a distinct subject population(s) that may be included in the research.	Relying Institution PI in conjunction with the Relying Institution.	Initial review for that site and after initial approval when a new study population may be included in the research.	**Resource**: Use SMART IRB Study-Specific Document.
Ancillary reviews	Relying Institution.	Initial review for that site and after initial approval when an amendment is likely to trigger additional institutional reviews (e.g., changes in study drugs or devices, addition of or change in radiation exposure).	**Resource**: Use SMART IRB Study-Specific Document. See also the SMART IRB Recommendations for the Harmonization of Ancillary Reviews for changes/events that may trigger ancillary reviews after sIRB approval.
Other	Relying Institution.	Initial IRB review for the site and after initial approval if study changes trigger state or local laws or institutional policies.	**Resource**: Use SMART IRB Study-Specific Document.

Appendix 4. Local Considerations Throughout the Life of a Study

STAGE: STUDY DEVELOPMENT

RESPONSIBILITIES

- The investigator(s) developing a protocol or study plan should consider the compatibility of study procedures and planned participant population with potential participating sites.
- Investigators at potential participating sites should evaluate protocols or study plans to determine whether their site is a good candidate for the research and, if so, identify any differences that may need to be incorporated into study documents and communicate them to the Overall PI (and, if applicable, the Lead Study Team).
- Institutions should provide protocol or study plan templates (similar to the protocol-specific addenda that some institutions have developed) and guidance for their research teams that take into account multi-site research and single IRB review (e.g., how to address variations in recruitment approaches across institutions or study procedures).

KEY LOCAL CONSIDERATIONS INFORMATION AT THIS STAGE

- Protocols and study plans should be written to take into account variations across participating sites, including: institutional standards of care, available equipment and facilities, study population likely to be enrolled, recruitment process and materials, informed consent process, and data security.
- When informed consent is required, template consent documents should accommodate language affected by institutional policy (e.g., compensation for injury, contraception permitted), differences in study costs, variations in study procedures across sites (e.g., differences in equipment, devices, or drugs used), and study team contact information.

Appendix 4. Local Considerations Throughout the Life of a Study (cont'd)

STAGE: INITIAL IRB REVIEW OF A SITE

RESPONSIBILITIES

The Reviewing IRB:

- Must have a method to collect and consider information about how Relying Institutions will implement a study to make the required determinations for approval under applicable regulations, such as 45 CFR 46.111 or 21 CFR 56.111.
- Must have a mechanism to integrate local considerations into its review, especially if a specialized position or team (e.g., a reliance team or reliance specialist) collects that information.
- Should conduct reviews taking into account potential permissible variation across sites, such as in recruitment materials, informed consent and assent processes, and locally required informed consent language (e.g., compensation for injury, costs, contact information).
- If HIPAA applies for a study, must collect information about whether Relying Institutions are HIPAA covered entities and whether they wish for the Reviewing IRB to serve as Privacy Board on their behalf.

Relying Institutions:

- Must provide Reviewing IRBs with sufficiently detailed information about relevant institutional policies, state and local laws, and other local considerations that may affect the Reviewing IRB's assessment of that site.
- Should ensure ancillary reviews that could affect IRB review (e.g., COI) are completed before IRB review of its site is conducted and communicate relevant information to the Reviewing IRB.
- Should ensure their research teams are qualified and have adequate resources and facilities to conduct the study and provide such attestations to the Reviewing IRB.
- Should ensure appropriate drug and device management and storage at sites under their purview.

Relying Institution PIs/Relying Institution Study Teams Must:

- Provide Reviewing IRB (working closely with the Relying Institutions POC) with information about implementation of the study at their site(s) that differs from what is described in the protocol.
- Obtain sign off (e.g., by a reliance specialist or IRB personnel at their home institution) for any institutionally-required language that must be included in applicable consent documents.

Appendix 4. Local Considerations Throughout the Life of a Study (cont'd)

STAGE: INITIAL IRB REVIEW OF A SITE

KEY LOCAL CONSIDERATIONS INFORMATION AT THIS STAGE

Relying Institutions may need to provide the following to the Reviewing IRB, such as through the SMART IRB Institutional Profile and SMART IRB Study-Specific Document:

- State and local laws that may affect IRB review of a participating site(s).
- Whether a Relying Institution applies the Common Rule to some or all of its human subjects research.
- Institutional policies that may affect the informed consent process, content, or other documentation.
- Conflict of interest management plans relevant to the study and put in place by the Relying Institution.
- Attestations from the Relying Institution regarding the adequacy of study team qualifications and training as well as resources and facilities available to conduct the study.
- Compliance with institutional data security requirements.
- Completion of relevant ancillary reviews.
- Information about any variations in study implementation at a Relying Site not captured in the protocol or study plan.

Reviewing IRBs and Relying Institutions can use the SMART IRB Implementation Checklist to document whether a Reviewing IRB plans to serve as a HIPAA Privacy Board, and if so, how the Relying Institution implements the HIPAA Privacy Rule (e.g., interpretation of the preparatory to research provision, requirement for a separate authorization form).

Appendix 4. Local Considerations Throughout the Life of a Study (cont'd)

STAGE: AFTER INITIAL IRB APPROVAL

RESPONSIBILITIES

- Reviewing IRBs should consider whether an amendment may require, prior to its review and approval, either a) re-review of each Relying Institution's local considerations information; or b) communication with the Relying Institution POC and/or the Relying Institution Study Team to obtain additional local considerations information.
- Relying Institutions and Relying Institution Study Teams should monitor changes in research, personnel updates, or new information that may require the provision of new or updated local considerations information to the Reviewing IRB.
- Relying Institutions should provide guidance to their Study Teams regarding changes of protocol that may trigger local context considerations.

KEY LOCAL CONSIDERATIONS INFORMATION AT THIS STAGE

- Updates to or new conflict of interest (COI) management plans relevant to the ceded research.
- Types of amendments that could affect local considerations, such as:
  - The addition of new populations, sub-studies, unique recruitment strategies, pregnancy testing in minors, or new drugs or devices.
  - Changes to types of contraception permitted.
  - See Appendix 7 for additional considerations.

Appendix 5: Local Considerations Responsibilities By Reliance Stage

Role	Feasibility	Reliance Execution	Local Considerations Review	After Site Approval
Reviewing IRB	Ensure you can meet the requirements of the Relying Institution by reviewing their Institutional Profile.	▸ Create a reliance package: – Collect local considerations using the Study-Specific Document. – Identify how you will implement the flexible terms of the SMART IRB Agreement using the Implementation Checklist. – Create a Communication Plan.	Review Study-Specific Document received from Relying Institution.	▸ Identify categories of changes that should trigger a review of local considerations. ▸ If a change or reportable event occurs, determine whether additional information is needed from the Relying Institution.
Relying Institution	Ensure Institutional Profile is up to date.	▸ Review all reliance documents. ▸ Provide institutional local considerations in consultation with local study team.	Answer Reviewing IRB questions about local considerations, if requested.	▸ Answer Reviewing IRB questions about local considerations, if requested. ▸ Monitor and communicate to the Reviewing IRB and study teams any updates to local considerations that could impact research review by an external IRB or research conduct by study team(s).

Appendix 6. Considerations for Investigators Writing Multi-Site Protocols

When writing multi-site protocols, researchers are encouraged to take into account potential variation across participating sites to ensure that the protocol accurately reflects how the study will be implemented. Protocols and study plans should be written broadly to account for variability in what study procedures will be performed at participating sites, any differences in how sites perform certain procedures (e.g., subject recruitment or the informed consent process), and any differences in subject populations that will be recruited (e.g., to achieve diversity, equity, and inclusion).

The following list reflects key areas of potential variability across sites that should be considered when developing protocols. Not all areas apply to all studies. Research teams might also build questionnaires that can be provided to sites to capture differences in implementation based on the potential variations identified.

Potential Variation	Examples of Questions to Capture Differences Between Sites
Recruitment procedures	▸ How will subjects be identified? ▸ Who will approach potential subjects? ▸ How will potential subjects be approached? ▸ Are there any restrictions on who can be recruited for this study? ▸ Are there any restrictions about who can approach some or all research participants? ▸ Are there any restrictions on language that is permitted in recruitment materials?
Informed consent and assent processes	▸ Are there any languages other than English that potential subjects might read and speak that could influence translations of informed consent documents that may be required? ▸ Are there any restrictions or requirements regarding who can obtain informed consent? ▸ Are there any specific requirements or restrictions regarding electronic informed consent platforms that can be used?

Appendix 6. Considerations for Investigators Writing Multi-Site Protocols (cont'd)

Potential Variation	Examples of Questions to Capture Differences Between Sites
When children are subjects	▸ What are the policies that affect the assent process or forms? ▸ Are there any specific requirements regarding pregnancy testing in children? ▸ Are there any specific requirements for reporting child abuse?
When adults with impaired decision-making capacity are subjects	▸ What are the specific requirements regarding who assesses capacity to provide informed consent? ▸ What are the specific requirements regarding who may act as a legally authorized representative (LAR)? ▸ Are there any specific requirements regarding the methods used to assess capacity to provide informed consent?
Where study procedures occur	▸ Are the procedures described in the protocol as standard of care (or routine care) NOT considered standard of care (or routine care)? ▸ Would there be any differences in supportive, rescue, or prophylactic therapies used from what is described in the protocol at your site? ▸ What are the locally available resources or equipment for ensuring necessary medical or professional intervention or equipment will be provided in the event of adverse events or unanticipated problems involving subjects? ▸ Are there any differences in how biospecimens would need to be collected from what is described in the protocol? ▸ Are there any differences in how data or biospecimens would need to be stored or shared from what is described in the protocol? ▸ Are there any differences where study procedures will occur (e.g., in clinics, in homes or in the community) from what is described in the protocol?

Appendix 6. Considerations for Investigators Writing Multi-Site Protocols (cont'd)

Potential Variation	Examples of Questions to Capture Differences Between Sites
Drugs	▸ Are there any differences in the drugs available (e.g., brands, formulations used, route administered) from what is described in the protocol? ▸ Are there any differences in how drugs would be dispensed from what is described in the protocol?
Devices	▸ Are there any differences in the devices available from what is described in the protocol? ▸ Are there any differences in how study devices would be stored from what is described in the protocol?
Contraception	▸ Are there any limitations on forms of contraception that would be permitted or available?
Laboratory tests	▸ Are there any differences in what laboratory tests would be performed or who performs them? ▸ Would results or other information from laboratory tests performed for this study be added to medical records?
Radiographic or other imaging assessments	▸ Would there be any differences in imaging devices or other equipment used from what is described in the protocol?

Appendix 7. Single IRB Review Case Study: Addressing Variation in Institutional Assent Policies

The Working Group considered how sIRB review related to assent for minors determinations differs from when a local IRB reviews a study on behalf of its research team. What follows is an analysis of what are local considerations vs. standard IRB review practice for determining whether assent is required, and if so, how variations in institutional assent policies and practices can be addressed on a study-wide basis, rather than through site-specific determinations.

What is the local considerations challenge?

Institutions vary in their assent policies and practices, such as when it is required and whether it is documented, the content and format of assent forms, and the expected assent process by child's age, which can affect IRB review.

What local considerations for assent should be collected from Relying Institutions and/or study teams?

- State and local laws that establish age of majority.
- Institutional policies that affect any applicable assent process.
- Populations likely to be enrolled at a site or by a study team that could affect the assent process, such as in terms of language or religious or cultural considerations.

What are the Reviewing IRB's responsibilities related to assent?

- Determining whether assent will be waived for a study or a specific site(s).
- If assent is not waived, determining whether any children who may be enrolled in a study are capable of providing assent.
- Collecting and considering local consideration information provided by Relying Institutions.

How can Reviewing IRBs proactively address a range of institutional policies and practices?

- When assent is required for a study, approve a range of options and associated documents to account for variability in institutional policies and preferences, such as:
  - Identifying a default position regarding whether written assent is required, but allowing research teams to obtain written documentation of assent in accordance with their institutional policies and guidelines and approving documents that enable a written assent process.
  - Approving assent scripts and/or forms for different ages and providing recommendations for study teams regarding which children they would suit (e.g., children with beginner vs. intermediate vs. advanced reading skills), but allowing the study team to use the script or form that they deem appropriate for a specific child based on applicable institutional policy or state or local laws.

What can research teams be encouraged to include in their multi-site studies to assist Reviewing IRBs in making assent determinations that are responsive to differences in Relying Institution policies and practices?

When assent is expected to be required, research teams should proactively work to understand site requirements for assent and variations in practice based on local or state laws or institutional policies. The comprehensive assent plan proposed in the protocol should account for this variability, detail the options that may be used and under what circumstances they may be exercised including:

- From which children assent will be obtained.
- If assent will be obtained from only some children:
  - When and why assent would not be required.
  - The process to determine whether a child is capable of assent.
- What information will be communicated to the child and how?
  - Depending on the age range of children who will be enrolled, consider creating multiple templates that research teams can choose from to tailor the assent approach to the individual child and describe this process for the IRB (e.g., an oral assent script or written assent form).
    - This could include, when appropriate, presenting some children with the parental permission form that they co-sign with their parents or guardians.
  - The process that will be used to determine the information communicated to each child, including using a written assent form.
- Will written assent be documented and the process to document assent.
- Whether and how parental permission will be obtained.
  - If permission will be obtained from individuals other than parents, who will be allowed to provide permission?
- The process used to determine these individual's authority to consent to each child's general medical care, as applicable.
- Re-consent processes for children who become adults or emancipated minors.

Appendix 8. Template Checklists for Reviewing IRBs and Relying Institutions to Identify When to Address Local Considerations after Initial Approval of a Study

These template checklists serve as guides for Reviewing IRBs and Relying Institutions to identify when amendments, events, or other updates might trigger a local consideration that could affect IRB review for a specific site. When events or amendments identified in the checklists occur:

a) Reviewing IRBs may need to review local considerations they collected (e.g., via the Institutional Profile, Study-Specific Document, and Implementation Checklist) to ensure they are taking into account relevant information in their review of that site; and

b) Relying Institutions need to determine whether they must communicate new or updated local considerations information to the Reviewing IRB.

Reviewing IRB

	Amendment Content
☐	Addition of a new subject population, especially children, pregnant women, prisoners, individuals with impaired decision-making capacity, LGBTQIA, other potentially vulnerable subject populations
☐	Addition of non-English speakers
☐	Significant change in recruitment method
☐	Addition of genetic testing
☐	Addition of testing for an infectious disease
☐	Addition of pregnancy testing or collection of information about pregnancy status
☐	Providing research results to participants
☐	Addition of or change in contraception used in the study
☐	Change in study drug or device storage or distribution
☐	Addition of a new drug or device that could affect billing
☐	Change in informed consent language that is commonly affected by institutional policy, such as compensation for injury language and study costs
☐	Addition of a new consent process

Relying Institutions

	Event
☐	Change in state or local law or institutional policy that could affect a ceded research study
☐	Change in study personnel, including the site Relying Institution PI (PI)
☐	New or additional ancillary review required that could affect IRB review
☐	New or changes in conflict of interest
☐	New or changes in funding
☐	If the Relying Institution is serving as the HIPAA Privacy Board, changes that could affect HIPAA authorization language that are not consistent with any IRB-approved informed consent language
☐	Changes in research activities taking place at the Relying Institution

CONTRIBUTING AUTHORS

John Baumann, PhD (retired)
Indiana University

Jenni Beadles, MEd, CIP
Assistant Director for Single IRB
Mass General Brigham

Nichelle Cobb, PhD, CIP
Senior Advisor for Strategic Initiatives
AAHRPP

David Forester, JD, MA, CIP
Chief Compliance Officer
WIRB-Copernicus Group (WCG)

Tiffany Gommel, MS, CIP
Director, IRB Operations, NIH

Stacey Goretzka, CIP (retired)
Medical University of South Carolina

Lubabah Helwani, MA, CIP
Principal Analyst
University of California, Los Angeles

Janelle Maddox-Regis, MS
Associate Director IRB Reliance Program
Johns Hopkins University

Eric Mah, MPH, EdD
Associate Dean, Clinical & Translational Research, University of California, San Diego

Ada Sue Selwitz, MA
Executive Integrity/Compliance Advisor
University of Kentucky

Emily Serdoz, MPA
Manager of Translational Research
Vanderbilt University

Megan Singleton, JD, MBE, CIP
Associate Dean for Human Research Protection & Director of the Human Research Protection Program
Johns Hopkins University

Jessica Ripton, MPH, CIP
Director, External Relations, Policy & Quality
Boston Childrens Hospital

Shannon Sewards, MA, CIP
Director, Human Research Protection Program
Administrative Director
Dartmouth Health IRB

SMART IRB HARMONIZATION STEERING COMMITTEE LEADERSHIP

Barbara E. Bierer, MD
Director of Regulatory Policy, SMART IRB
Co-chair, SMART IRB Harmonization Steering Committee

Josh Fessel, PhD, MPH
Division of Clinical Innovation,
National Center for Advancing Translational Sciences (NCATS), National Institutes of Health
Co-chair, SMART IRB Harmonization Steering Committee

Polly Goodman, CIP
Senior Associate Director of Regulatory Affairs Operations, SMART IRB

Aaron Kirby, MSc
Director, Regulatory Affairs Operations, Harvard Catalyst
Operations Officer, SMART IRB Harmonization Steering Committee