Evaluation Framework for the NIH Single IRB Policy

September 13, 2019

This report contains findings and proposed next steps from the Single IRB (sIRB) Evaluation project team assembled by the Clinical Trials Transformation Initiative to support an NIH workgroup developing a comprehensive plan for the evaluation of the NIH sIRB policy. Its contents, and views expressed, are solely the responsibility of the authors and do not necessarily represent their employers, the official views of US Department of Health and Human Services, the Clinical Trials Transformation Initiative, the National Institutes of Health, or EnDyna Inc.

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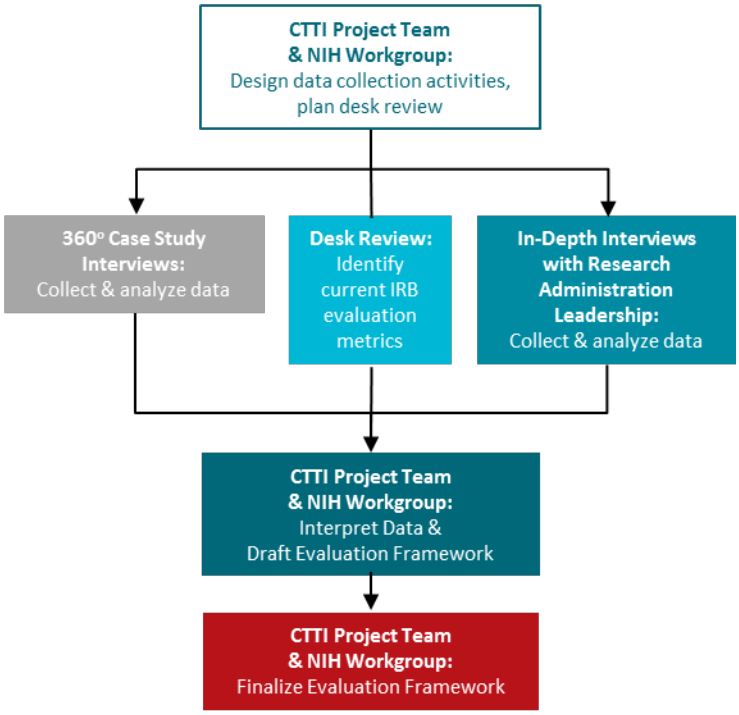
Introduction

Activating high-quality clinical trials is critical to advancing science and improving and saving lives. The Institutional Review Board (IRB) review process has been criticized for delaying clinical trial activation.[1-4] In 2014, when the National Institutes of Health (NIH) issued its draft single IRB (sIRB) policy, its stated intent was "to enhance and streamline the process of IRB review and reduce inefficiencies so that research can proceed efficiently without compromising ethical principles and protections."[5] The Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research was released in June 2016.[6] As of January 25, 2018, with limited exceptions, U.S. sites participating in multi-site, non-exempt, human subjects research that receive funding from the NIH are required to use a sIRB of record for ethical review required for the protection of human subjects.[7]

Additional information about the goals of the NIH policy was provided in an October 2017 presentation from the NIH Office of Extramural Programs.[8] These goals are:

1) enhance and streamline IRB review for multi-site research,
2) maintain high standards for human subjects protections,
3) allow research to proceed effectively and expeditiously,
4) eliminate unnecessary duplicative IRB review,
5) reduce administrative burden, and
6) prevent system inefficiencies.

Figure 1: Project Overview



On April 17, 2018, EnDyna, Inc., as part of an Office of Extramural Programs support services contract, released a request for proposals to develop a comprehensive evaluation plan for the NIH sIRB policy in collaboration with a policy evaluation workgroup.[9] The NIH workgroup is led by the Office of Extramural Programs and includes representatives from several NIH Institutes and Centers.

The Clinical Trials Transformation Initiative (CTTI) project team consisted of national experts in human subject protections, evaluation, and clinical research (see Appendix 1 for team member listing). The CTTI project team prepared a proposal in response to the RFP. The team's collective experience includes evaluating government policies, serving as principal investigator (PI) on NIH-funded research, participating as IRB members, administering IRBs and research programs, and holding leadership positions on the Secretary's Advisory Committee on Human Research Protections (SACHRP) and the Public Responsibility in Medicine and Research (PRIM&R) Board of Directors.

To ensure that the experts on the CTTI Project Team had a comprehensive assessment of available resources to support development of the evaluation framework (Figure 1), the project team reviewed

existing data sources and designed supplemental data collection activities. See the Data Collection Summary and Appendices 1 and 2 for full details. The three data collection activities were:

1) a desk review of existing sIRB/central IRB evaluation methods, with a literature review prepared by NIH Library services staff and the NIH workgroup;
2) 360° case study interviews at two universities that have implemented the sIRB policy as both the reviewing sIRB and the relying institution; and
3) in-depth interviews with research administration leadership.

In addition to the frequent CTTI project team teleconference discussions and check-ins with the NIH workgroup, an in-person meeting on July 31, 2019, brought the CTTI and NIH groups together to discuss and interpret the data collected in the context of creating the evaluation framework. Through additional CTTI project team teleconference meetings after the in-person meeting, this report was finalized.

Project Team Considerations and Conclusions

After an assessment of the available literature and of the sIRB processes at a sample of institutions that were following the NIH sIRB policy, the CTTI project team concluded that an evaluation of the direct impact and effectiveness of the policy would require clear definition of key data points and a case-control approach before the evaluation's implementation. Attributing outcomes directly to the policy is challenging in a clinical research environment where the sIRB model was already being implemented in response to the sIRB policy and other sponsor preferences; in preparation for the sIRB policy and Common Rule requirements; and due to pre-policy requirements of some NIH networks and National Cancer Institute studies.[7,10-15]

Although an evaluation to measure whether the NIH sIRB policy alone has enhanced and streamlined IRB review is not recommended, the CTTI project team observed and recommends the following specific actions for NIH to assist the IRB community with widespread sIRB implementation and ongoing evaluation.

1. **Define critical time points and factors in the sIRB review and approval process that all NIH grantee institutions serving as an sIRB should regularly measure**. The sIRB policy is in a relatively early stage of implementation, and the in-depth interviews confirmed the CTTI project team's experience that there is wide variation in how the policy is implemented by institutions (see the Table in section 4.3 of qualitative data report). Retrospective data are available for long-performing sIRBs such as the National Cancer Institute–funded and NIH-funded trial networks and initiatives,[10,14,16-18] but these implementation examples use discordant definitions and time point collection methods. Although the time and effort to establish reliance agreements have been included in some prior comparisons of IRBs and sIRBs, measurement of other administrative demands, such as the need for lead study team communication between sites and time needed to enter information into the sIRB system on behalf of relying sites, is less common.[19-21] The CTTI project team strongly believes that establishing standard definitions and approaches to time point collection and process expectations would be valuable, not only to assess the effectiveness of using sIRB, but also to establish much needed consistency within and between institutions.

2. **Routinely collect and share established metrics with NIH Institutes and grantee institutions to promote a continuous learning environment and best practices.** Most IRBs have

addressed their internal "quality" through quality improvement (QI) program self-assessments, accreditation, and/or staff and investigator training.[22,23] These QI efforts allow for assessment of human research protection program (HRPP)/IRB qualifications and procedures and potential compliance with regulations. However, they do not provide the ability to assess efficiency or effectiveness specifically for sIRB reviews, and they offer limited comparisons across programs. Creation of well-defined quantitative and qualitative IRB- and sIRB-specific metrics, and routine collection and reporting, are needed to assess the efficiency of sIRB review. Analysis of the metrics is important to understanding how sIRB is being implemented, to identify best practices and standards, to identify unnecessary administrative burden, and to help grantees improve human subject protections while managing changes in business practice.

3. **Engage a diverse group of NIH grantee institution representatives** to address actions 1 and 2 above. The stakeholders should include a mix of large and small NIH grantee organizations, independent IRBs, multi-site study investigators and study staff, policy organizations, and other relevant parties to develop consensus practices that are feasible for all organizations.

The assumption, supported by previous comparison studies of local IRBs and sIRBs,[1,19-21] is that implementation of the sIRB model—particularly for studies subject to full board review—will reduce overall IRB member effort and time, since fewer full boards will review the same protocol across multiple sites. However, it is important that IRB review time not be the only factor considered. Details on how implementation is occurring should also be included, along with time and effort for other parts of the process, such as establishing reliance agreements; communications between lead study teams, sites, and the sIRB; and entering information into the sIRB system on behalf of relying sites. The CTTI project team recommends metrics focused on benchmarking and process improvement, as there is little agreement on metrics to measure the quality of IRB review.[24-26]

The CTTI project team recommends that the best use of resources moving forward is to develop a learning system to measure and improve the sIRB process and realize the goals of the sIRB policy. This report describes the suggested next steps and provides a framework for their implementation. These steps include engaging stakeholders; developing a foundational database to identify the population of organizations implementing the sIRB policy; developing, testing, and deploying an instrument to evaluate sIRB functions and establish and measure metrics across NIH grantee institutions and sIRBs; and using the results to continually improve the sIRB process.

Suggested Next Steps for the NIH

Engage Stakeholders

It is imperative that those implementing the sIRB model for multi-site studies be involved as key participants in communicating their needs and suggesting areas for improvements in implementation of, or enhancements to, the sIRB policy. A group of stakeholders from a mix of large and small NIH grantee organizations, independent IRBs, multi-site study investigators and study staff, policy organizations, and other relevant parties should be created to advise on every step of the process described below. A series of meetings could be used, but other methods of ongoing community dialogue should be considered in order to include organizations that may lack the resources to attend in-person meetings.

Develop a Foundational Database of Organizations Implementing the sIRB Policy

It is unclear what organizations currently serve as sIRBs in accordance with the sIRB policy. A database of planned or active sIRBs is needed. There is no comprehensive list of reviewing sIRBs and relying institutions, and the absence of such a list makes it difficult to identify the population to query in any evaluation. The list could be developed from existing or new data fields on the R&R Other Project Information Form already used for all grant applications, or collected during the Just-in-Time period when a prime awardee indicates whether they are serving as the sIRB of record, relying on the IRB of a sub-awardee institution or NIH program central IRB, or contracting with an independent IRB. Only collecting the minimum necessary additional information, and doing so within an existing process, will minimize the burden of creating this database.

Proposed Evaluation of sIRB Functions Across NIH Grantee Institutions and IRBs

Purpose of Evaluation

The CTTI project team recommends that a survey* instrument be developed—with broad input from NIH grantee institutions and stakeholders—and used to globally evaluate sIRB functions in order to create a learning system that continuously improves the sIRB process and furthers the goals of the policy. Working group expertise, validated by the qualitative data collection, was used to identify key questions and potential metrics (see Tables 1-7) to guide the creation of the proposed survey instrument. The survey should be pilot tested to assess the practicality and adjust the questions and definitions of metrics and milestones as needed. The final survey would then be deployed, and assessment of survey responses would be used to understand the way the sIRB model is being implemented, to identify best practices and standards, to identify unnecessary administrative burden, and to help grantees improve human subject protections while managing changes in business practices. Standard metrics and measures established through the survey should then be collected annually by the NIH, NIH Institutes, implementing organizations, and/or other relevant groups to be used for continuous improvement of the sIRB process.

Target Sample

The sIRB database should be used to select a representative sample of NIH grantee institutions implementing the sIRB policy to take part in the pilot and final surveys. Surveyed organizations at both

*The Paperwork Reduction Act requirements, to receive permission from the Office of Management and Budget (OMB) before surveying more than 10 or more people, will need to be considered if the evaluation is implemented by a government agency.

stages should include institutions of varying sizes and levels of NIH funding, conducting different types of research, and with different levels of experience using the sIRB model.

Type of Evaluation

The proposed evaluation framework borrows its underlying evaluation approach from the "expertise-oriented" approaches.[20] Because there is no baseline for evaluating IRB or sIRB efficiency or effectiveness for multi-site clinical trials, this evaluation should be used to compile and share nationwide sIRB processes and metrics, establish standards where appropriate, and identify areas where changes and improvements are feasible. Organizations in the process of implementing the sIRB policy will also benefit from access to the survey results to use in their own QI programs.

Evaluation Methods

The survey should consist of a set of guided assessments that ask grantee organizations to share their practices and processes. Selected organizations should be asked to collect information from their own experiences as sIRBs, the experiences of relying institutions, and the experiences of lead study teams under their grants. The information that the self-assessments provides to the NIH and participating organizations about the implementation of the sIRB policy is expected to assist in systemic improvement. The survey should be piloted, modified, and released to selected grantee organizations.

Consideration should be paid to, and consensus of stakeholders should be obtained on, the way the questions in the survey are asked. One of the challenges identified during this work is the wide variability in how different organizations define terms and tasks and how they are implementing the sIRB policy. Comparing data across institutions will, therefore, require deliberate up-front work developing the instructions for the survey. At a minimum, (1) key terms should be clearly defined; (2) quantitative data to support certain metrics (ie, time to approval) may require the development of detailed help text; and (3) an effort should be made to limit free text where possible, with look-up fields or drop-down menus provided where appropriate to ease reporting and analysis. Adjustments to annual surveys should be made to add or remove elements as sIRB measures and processes become standardized or questions about implementation are no longer relevant.

Given the approaching compliance date for the sIRB requirement in the Common Rule, the NIH should leverage its leadership and experience by working with other Common Rule agencies and the Office for Human Research Protections (OHRP) to implement the survey, promoting consistency and best practices in the use of sIRBs. Standard definitions and milestones established through the survey should be established as national standards for IRBs.

Key Evaluation Questions and Methods Crosswalk

The goals of the NIH sIRB policy were used as the domains to guide the development of the in-depth interview guides (see Appendix A of Appendix 1). As mentioned above, CTTI project team expertise, validated by qualitative data, was used to create the key questions organized by policy goal domains in Tables 1-6, and to collect organization information from the survey population in Table 7. The questions in Tables 1-7 are not intended as final survey questions, but to provide a framework of the key information to be gathered.

Timeline

If information about organizations that are implementing the sIRB model is already available at the NIH from sIRB plans or other sources, creation of the foundational database could begin immediately and be completed in 2 to 6 months. If a collection mechanism is needed, this process may take up to a year.

While the database of involved institutions and organizations is being developed, the preliminary survey should also be built. Questions should capture the practices of organizations involved in the sIRB mandate, organized by the domains described below. It is likely that several different and overlapping questions will need to be tested in the preliminary survey in each domain to find those that will be most consistently understood and reliable. Professional organizations such as the Association of American Medical Colleges (AAMC), PRIM&R, the Association for the Accreditation of Human Research Protection Programs (AAHRPP), established regional networks, the National Center for Advancing Translational Sciences (NCATS), and others could be approached for partnership.

Once this evaluation instrument is created, it should be pilot tested with a small group of grantee organizations drawn from the database of sIRB implementing organizations. The results of this test should inform selection of questions and framing for the final survey, which should then be deployed on an annual basis to assess progress in reaching the goals of the sIRB policy.

The specific metrics that will be included in the final survey should be publicly released in order for grantee organizations to begin planning for data collection ahead of the required collection period. Early public release of stakeholder-informed metrics and definitions would allow for the best evaluation results, as institutions would be better prepared for the collection. For example, if the survey is to be deployed in January 2021, it could be released in June or July of 2020. This approach is similar to how changes in Public Health Service regulations on conflicts of interest in federally funded research were evaluated in a national study.[27] One year before the effective date of the rule, the metrics that were going to be collected were announced, allowing institutions to prepare and provide the best possible data.

The stakeholder community should continue to be involved in reviewing the survey results, defining standard definitions for efficiency and effectiveness measures, determining where development of standards and tools would be useful for the research community, and suggesting improvements or changes to the policy.

Conclusion

While the project team agreed that it would be infeasible to conduct a definitive evaluation of the direct impact and effectiveness of the NIH sIRB policy due to multiple factors, NIH could and should lead the way, in partnership with other Common Rule agencies, in the ongoing evaluation of the implementation and process improvement of the sIRB model. This effort includes, but is not limited to, the development of standards and best practices based on the evaluation. NIH leadership has previously been effective in developing required training programs for human subjects research and standards for review of potential conflicts of interest, even for organizations outside the Public Health Service funding environment. We hope the NIH will take the same leadership role in the implementation and continuous improvement of the sIRB model.

Tables: Key Evaluation Questions and Methods Crosswalk

Table 1: Goal 1 Crosswalk - Enhance and Streamline IRB Review for Multi-site Research

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
What activities does the institution consider to be included in sIRB review?	Initial ethical review of the protocol, review of consent form, ancillary reviews, continuing review, local considerations.	X	X	
What are the roles and responsibilities of the Human Research Protection Program (HRPP)/IRB staff when serving as the **reviewing** IRB?	• Number of full-time employees (FTEs) required to serve as sIRB • Titles and roles of employees in the sIRB process • Amount of time (hours) spent by these employees on sIRB activities	X		
Describe how, if at all, resource allocation has changed for the HRPP/IRB when the institution is serving as the **reviewing** IRB?	• Change in number of HRPP/IRB staff handling sIRB process (FTEs in 2017, 2018, 2019, and 2020) • Changes in roles of employees	X		
What activities does the institution consider to be part of local institutional review (reviews occurring at the **relying** institution)?	• Departmental review, ancillary reviews, HIPAA, other	X	X	
What are the roles and responsibilities of the HRPP/IRB staff when **relying** on an outside IRB?	• Number of FTEs required for relying site institutional review activities • Amount of time (hours) spent on sIRB activities		X	
Describe how, if at all, resource allocation has changed for the HRPP/IRB when the institution is **relying** on an outside IRB?	• Change in number of HRPP/IRB staff handling sIRB process (FTEs in 2017, 2018, 2019, 2020) • Changes in roles of employees	X	X	
What are the roles and responsibilities of lead study team when: submitting initial protocol to sIRB, communicating with other sites about sIRB submissions, other activities specifically related to the sIRB process?	• Number of FTEs required to complete IRB submissions and communicate with sites about sIRB submission • Amount of time (hours) spent on sIRB activities. • Change in site staff due to need to conduct sIRB activities in 2017, 2018, 2019			X
How, if at all, is the process for serving as the **reviewing** sIRB standardized? Process for serving as relying institution?	Which standardized processes or systems are being used?	X	X	
In what ways, if any, could the sIRB process be enhanced and/or streamlined?		X	X	X
How, if at all, is the process different depending on type of study (large multi-site clinical trials vs socio-behavioral/minimal risk research)?	Multi-site interventional trials vs socio-behavioral/minimal risk research?	X	X	

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
In what ways, if any, has variability in research process and conduct changed with implementation of the sIRB mandate?	Ask for each process below: • Reliance • Submission process/Initial Review • Addition of sites • Institutional review/ancillary reviews • Informed consent forms • Events reporting	X	X	X

Table 2: Goal 2 Crosswalk - Maintain High Standards for Human Subjects Protection

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
How does the **reviewing sIRB** obtain local considerations/context from relying institutions relevant to the study, including information related to vulnerable populations?	Written policies or procedures, reliance agreement specifications, other process	X		
In the past 12 months, how many selected study sites (relying institutions) have dropped out of a research study before sIRB review?	Number and reason for drop-out: unresolved issues around local considerations, inability to agree and execute reliance agreement, refusal to rely on sIRB	X		
How is the **reviewing** sIRB selected for a multi-site study?	• IRB characteristics, availability of expert scientific reviewer(s). • Is level of vetting dependent on risk level of study?		X	X
Is participant/patient/non-researcher viewpoint represented with the use of a sIRB?	How is viewpoint incorporated? Has the amount of input changed with sIRB review compared to multiple local IRB reviews? Note: Participating grantee organization should request viewpoint of non-research IRB member with research participant experience.	X	X	
How are unanticipated problems involving risks to subjects or others handled by the **relying** institution? By the **reviewing** sIRB?	Does institution have policies in place for reporting events specifically in sIRB model? How are differences in reporting requirements tracked? Has amount of work required changed for PI?	X	X	X
How are allegations of serious or continuing noncompliance handled by the **relying** institution? By the **reviewing** sIRB?	Who writes the corrective and preventative action plan? Who is responsible for reporting to regulatory agencies? Who is responsible for determining whether an activity constitutes serious or continuing noncompliance? Is there an appeal process? Who is responsible for reporting possible noncompliance to the sIRB?	X	X	
What suggestions, if any, would help institutions maintain high standards for human subjects protection in sIRB review?		X	X	X

Table 3: Goal 3 Crosswalk – Allow Research to Proceed Effectively and Expeditiously

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
How does the sIRB interact with relying institutions, the study lead PI, and local investigators?	• Who is responsible for collecting site reports for submission to the reviewing sIRB? • If an eIRB system is used, who is responsible for entering information for research sites? • Who is responsible for reporting unanticipated problems involving risks to subjects or others and possible noncompliance to the reviewing sIRB?	X	X	X
What suggestions, if any, would allow research reviewed by an sIRB to proceed more effectively and expeditiously?		X	X	X
What kinds of training programs for implementation of the sIRB mandate does the institution have?	• Who receives training? • Who provides training? • What additional training programs would be helpful?	X	X	X
Describe the process for ensuring necessary institutional reviews are occurring.	Who gives the final approval for research to start at site?		X	
Suggested review time metrics included below. Consider if it is feasible and worthwhile to collect and report separately for studies undergoing expedited review and full board review. Proportion of studies of each type are collected in Organization Profile (Table 7). Specific definitions should be established in the next step of the process.				
For NEW submissions over the past 12 months, describe the median time required for approval of non-exempt human subject research at your institution when your institutional IRB is reviewing research NOT subject to sIRB requirements	Provide the median time for the following: • Time from submission to the office responsible for processing human subject research applications to final approval to conduct research at your organization • Time from submission to the office responsible for processing human subject research applications to IRB review • Time from IRB review to final approval	X		

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
For NEW submissions over the past 12 months, describe the median time required for approval of non-exempt human subject research at your institution when your institutional IRB is serving as the sIRB on a multi-site study	Provide the median time for the following: For your site • Time from submission to the office responsible for processing human subject research applications to final approval to conduct research at your organization • Time from submission to the office responsible for processing human subject research applications to IRB review • Time from IRB review to final approval For relying sites • Time to complete IRB Reliance Agreement • Time from submission to the office responsible for processing human subject research applications to approval for the relying organization • Time from submission to the office responsible for processing human subject research applications to IRB review • Time from IRB review to final approval	X		

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
For NEW submissions over the past 12 months, describe the median time required for approval of non-exempt human subject research at your institution when you are the prime and you have chosen to subcontract the sIRB on a multi-site study to a commercial IRB or are utilizing a NIH network IRB.	Provide the median time for the following: For your site • Time from submission to the office responsible for processing human subject research applications to final approval to conduct research at your organization • Time from submission to the office responsible for processing human subject research applications to IRB review • Time from IRB review to final approval For relying sites • Time to complete IRB Reliance Agreement • Time from submission to the office responsible for processing human subject research applications to approval for the relying organization • Time from submission to the office responsible for processing human subject research applications to IRB review • Time from IRB review to final approval	X		
For NEW submissions over the past 12 months, describe the median time required for approval of non-exempt human subject research at your institution when you are a **relying site**	Provide the median time for the following: For your site • Time from submission to the office responsible for processing human subject research applications at your institution to final approval to conduct research at your organization • Time to complete IRB Reliance Agreement • Time from submission to your institution to the relying IRB • Time from submission to the relying site to IRB review • Time from IRB review to final approval	X		

Table 4: Goal 4 Crosswalk - Eliminate Unnecessary Duplicative IRB Review

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
To what extent, if any, has the sIRB process eliminated duplicative IRB review?	IRB review of the protocol	X	X	X
What, if anything, could the sIRB process do to eliminate duplicative review?	Communication processes about which parties are completing which reviews	X	X	X
What IRB reviews are occurring at relying institutions (in purview of IRB, not other ancillary reviews)?	Who is conducting reviews? Is informed consent reviewed? If reviewed, before or after approved by sIRB?		X	
What documents are collected and stored at relying institutions?	• Informed consent, protocol, approval document from sIRB, investigator training and qualifications, other? • Purpose of collection: reference/documentation at relying institutions, used for ancillary reviews, other purpose.		X	

Table 5: Goal 5 Crosswalk - Reduce Administrative Burden

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
What, if any, additional burdens does the sIRB process create at relying institutions? At institutions serving as the reviewing IRB?	How many different authorization agreements are being used? How many different eIRB systems are being used?	X	X	X
How, if at all, might the administrative burden be reduced? At the relying institution? At the reviewing sIRB?	Document sharing systems, access for external personnel to sIRB electronic system, communication tracking systems	X	X	X

Table 6: Goal 6 Crosswalk - Prevent Systemic Inefficiencies

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
What, if any, systemic inefficiencies are created by the sIRB process?		X	X	X
How, if at all, is the sIRB process standardized across reviewing institutions?		X	X	X
How, if at all, might current inefficiencies be reduced or eliminated?		X	X	X
How, if at all, have IRB/HRPP policies, practices, and/or eIRB systems been updated due to the sIRB model? At the relying institution? At the reviewing sIRB?	• Practices removed, practices added/building? • Software changes? • What have the costs been to implement these changes?	X	X	

Table 7: Organization Profile Crosswalk

Key Evaluation Questions	Data	Source		
		Reviewing sIRB	Relying Institution	PI
Type of organization? • Reviewing IRB organization type? • Relying institution organization type? • Principle investigator/Lead study team organization type?	Academic institution; hospital; independent IRB; dedicated research facility; VA facility; governmental organization; contract research facility, or sponsor	X	X	X
Number of NIH funded multi-site studies for which the organization is serving as the reviewing sIRB? For NEW submissions over the past 12 months	Total number of pending/open NIH funded studies where organization is serving as the sIRB? • expedited review, full board review	X	X	
Number of NIH funded multi-site studies for which the organization is relying on an external sIRB?	Total number of pending/open NIH funded studies where organization is relying on an external IRB? • expedited review, full board review	X	X	
Total number of reliance agreements for NIH multi-site studies for which the organization is serving as the sIRB? Relying institution?	Total number of reliance agreements for pending or open studies	X	X	
Total number of electronic IRB systems used by PI/study teams?	Number of different eIRB systems used (PI)			X

Data Collection Summary

Desk Review Summary

Metrics currently collected by institutions, IRBs, and other groups to evaluate the performance and effectiveness of local IRBs and sIRBs were collected through a literature review; presentations at the 2018 Advancing Ethical Research Conference; and correspondence with established NIH sIRBs/central IRBs, academic IRBs, and multicenter study coordinating centers. The list of metrics collected and sources are included in Appendix 2. Metrics are grouped into five categories: volume, review time, staffing, costs, and quality.

Review Time: Time from IRB submission to IRB approval is often collected internally at HRPPs/IRBs and is compiled and reported by AAHRPP[32] and the Clinical and Translational Science Award (CTSA) Program Common Metrics.[16] There are also studies that compare review times between sIRBs and local IRBs.[1,14,19-21] To capture the full picture of the sIRB process, institutions have started collecting total HRPP/IRB review time (see Desk Review Metrics: Appendix 2), though total review time definitions vary. For example, some start from the request to rely and others start with HRPP/IRB submission. Similarly, end date definitions range from IRB approval of the main protocol to IRB approval of all relying sites. At this time, available review time benchmarks are limited to those collected by AAHRPP and the CTSA program. They are not sIRB-specific and do not include time for reliance agreements or local institutional reviews.[16,32] The IRB Reliance Exchange (IREx) reports full time-to-approval metrics for lead and relying member institutions starting with when sites are contacted to begin the reliance process through the time they are reviewed by the sIRB. Local (ie, relying) institution review dates, time with the IRB, and time with the study team are also measured.[17]

Volume: Volume of HRPP/IRB submissions is commonly collected and separated by level or review and type of submission (eg, full board review, expedited review; and initial, continuing review, and other). Volume metrics specific to sIRBs include the total number of studies relying on an external IRB, the number of requests for an IRB to serve as the sIRB or to rely on an outside IRB, and the total number of reliance agreements (which may be fewer than the number of relying studies if a single reliance agreement covers multiple studies).

Staffing and Costs: The total number of full-time equivalent staff is a standard metric collected by IRBs. More recently, some IRBs that are transitioning to the sIRB model have implemented time tracking programs for their employees to record staffing costs related to sIRB review.[29-31] Although costs are mainly calculated using staff time, other costs, such as upgrading or changing information systems needed for sIRB review, are also measured.

Quality and Effectiveness of IRB Review: Little information is collected on the effectiveness or quality of IRB and sIRB review.[3,24-26] Assessment of qualifications, procedures, and compliance with HRPP regulations are completed through accreditation or certification by third parties or OHRP QI program self-assessments. They do not provide the ability to assess the effectiveness of IRB or sIRB reviews or compare the quality of review across IRB programs. Post-review surveys of researchers are used by IRBs and HRPPs to identify areas for QI.[26] The absence of significant findings on external inspections or audits have been used as criteria for assessing quality when selecting an sIRB.[28] Groups have suggested conducting studies to determine the impact of common effectiveness surrogate measures—such as IRB composition, staffing, decision making, review times, regulatory compliance, and auditing—on the protection of human subjects.[24,25] However, standardized outcome measures were not established before the effective date of the NIH sIRB policy.

Most of the available literature on sIRB use and evaluation focus on quantitative methods and are primarily collected only at the institution or network level, with limited aggregate data reporting or specific measures for

sIRB review. Existing sources of compiled data on IRB operations and review time, the AAHRPP and the CTSA Common Metrics program, are limited to member organizations (n=254, n=58 respectively in 2018) and are not specific to the use of sIRBs.[16,22] Measurement of components specific to the sIRB process are being collected by individual institutions and initiatives such as IREx.[17,29-31] However, the definitions and time points used to define IRB and sIRB review times vary across organizations. Creation of well-defined IRB- and sIRB-specific metrics, and routine collection and reporting, are needed to assess the efficiency of sIRB review. Standard outcome measures are not available for assessment of the effectiveness of IRB and sIRB review or to compare quality across programs.[24-26] Development and pilot testing of reliable measures of IRB and sIRB effectiveness are needed before an assessment of the effect of sIRB on enhancing IRB review and maintaining high standards for human subjects protection can be completed.

Qualitative Research Summary

A qualitative descriptive study was conducted using in-depth interviews with (a) individuals at two universities that have implemented the sIRB process as both a reviewing sIRB and a relying institution (referred to as 360° case study interviews); and (b) research administration leadership who represent academic, independent, and health center–based IRBs and institutions (n=34). The objectives of the interviews were to describe key stakeholder experiences in implementing the NIH sIRB policy, describe steps involved in operationalizing the sIRB process at IRBs and institutions, and identify potential metrics to evaluate the implementation of the NIH sIRB policy. **The qualitative findings summarized here and fully described in the report found in Appendix 1 informed the development of the NIH sIRB evaluation framework.** The final deliverable is the evaluation framework.

In brief, the main findings that informed the development of the evaluation framework are:

1. Generally, most participants believed that the sIRB model improves, or has the potential to improve, inefficiencies associated with the local IRB model (ie, IRB review at each site) by creating consistency in the review process, standardizing documents produced for a study, reducing workload for staff at relying sites, and reducing overall duplication in ethics reviews. Most participants described that implementing the NIH sIRB policy has not streamlined ethics review when their institution has served as the sIRB; however, it has streamlined the amount of involvement of their IRBs when they are a relying institution. In addition, reviews are still required by the relying institution. These include privacy reviews and determinations, ancillary reviews, and activities related to compliance and oversight.

2. Most participants believed that the sIRB process typically becomes more efficient, or has the potential to become more efficient, once systems are created, systematic processes are followed (eg, use of common reliance agreements), and institutions gain experience and IRBs establish working relationships.

3. The sIRB model also creates new inefficiencies due to unclear roles and responsibilities for staff and institutions; a lack of systems and processes for implementing the sIRB process (eg, retooling IRB workflows, incompatibility of IRB software, and inability of relying sites to directly access the reviewing IRB's electronic systems); and added workload, particularly for investigators who must now submit the same documents to both reviewing and relying IRBs.

4. There was variation in the order and specific manner in which the sIRB steps are implemented across and within institutions (see section 4 “Process Mapping” of the qualitative data report). The steps included:
    a) The PI identifies a need for a sIRB plan.
    b) The PI and/or site investigators submit the study protocol to their own institution; the protocol is submitted to the reviewing institution as the sIRB (if their own institution is not the reviewing IRB).
    c) The relying and reviewing institutions negotiate reliance agreements.
    d) The relying institution completes ancillary reviews.
    e) The relying institution provides information on local context.
    f) The reviewing institution conducts the ethics review.
    g) The reviewing institution approves the study protocol, and the relying institution provides institutional approval.
    h) The institution(s) (the relying institution or the reviewing IRB) notifies the study teams of the protocol and institutional approvals.
    i) The institution(s) (the relying institution or the reviewing IRB) conducts post approval oversight, monitoring, and auditing.

5. Concerns were raised about the need for extensive monitoring and reporting to ensure that the high standards for human subjects protections are maintained when using a sIRB process.

6. “Shadow reviews”—in which relying IRBs still provide an ethics reviews—are being conducted by some institutions.

7. The development and use of resources and tools, such as the NCATS Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB, are helpful and assist in standardizing the process.

8. Additional processes and systems are needed and will improve the efficiency of the sIRB process (eg, establishing a well-defined definition of local context and having a central repository for institutional information).

9. Study participants’ experiences with research do not appear to have changed with the use of sIRBs.

Numerous current and new metrics were suggested for evaluating the sIRB process. Similar to the findings of the desk review, current metrics measure time in each step of the review process. Some participants reported measuring time spent pre-reviewing documents before IRB submission and time for PI training on the sIRB process. Measurement of the volume of IRB submissions and communications between IRBs and investigators were also reported. A few quality metrics were noted, including the number of modifications requested, the percentage of initial study applications approved by the reviewing IRB, and the number of errors in approved documents found by relying sites. It was noted that quality metrics will be important in evaluating the sIRB process and should continue to be developed. Suggested metrics include number of staff and time spent on sIRB activities; costs of required infrastructure changes; determining what activities are being conducted by the reviewing IRBs and relying institutions; number of communications between parties involved; and satisfaction surveys. Participants noted that the ability to collect standard metrics could be improved by the use of standardized processes and increasing the ability of relying sites to access the sIRB software system or portal. (see Section 5.0 “Metrics” of the qualitative data report for all proposed metrics.)

Definitions

Ancillary review[33] – Review conducted in coordination with IRB review to ensure that risks associated with the research are minimized and compliance requirements are met. Areas of ancillary review include radiation safety, institutional biosafety (recombinant DNA/gene transfer studies), embryonic stem cell oversight, scientific review committees, conflict of interest, IT security, clinical trials office, genomic data sharing institutional certification, environmental health and safety, nursing, and research pharmacy/controlled substances. Ancillary reviews can be deferred to the reviewing IRB with some exceptions. The responsible party should be specified in a reliance agreement or study-specific addendum.

Lead study team – Group responsible for communications, coordination, and document management associated with the use of a sIRB across all sites in a multi-site study. The overall PI should identify who will take on the role of the lead study team. This may be the PI's own study team, a coordinating center, both, or a contract research organization.

Local considerations – Any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews, relevant to an instance of research.

Reviewing sIRB – The IRB of record, which provides the ethical review for all sites participating in a particular multi-site study, for the duration of the study. Also known as the sIRB.

Relying institution – The participating institution that will rely on (ie, cede IRB review to) an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying institution. The NIH sIRB policy refers to these institutions as "participating sites."

Research administration leadership – Individuals in leadership positions (eg, IRB chairs, regulatory administrators) who have implemented the sIRB process (as a reviewing IRB, a relying institution, or both) either at an academic institution or with an independent IRB.

sIRB plan – A written description of how the multi-site study will comply with the NIH sIRB policy. The plan is required to be submitted as an attachment in the grant submission. Required components are available at https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm.

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Appendices

1. Findings from Qualitative Research to Inform the Framework
2. Desk Summary Metrics Listing

Developing an Evaluation Framework for NIH's Single IRB Policy:

Findings from Qualitative Research to Inform the Framework

FINAL REPORT: September 12, 2019

TABLE OF CONTENTS

1. Background

As of January 25, 2018, all U.S. sites participating in multi-site, non-exempt, human subjects research that receive funding from the National Institutes of Health (NIH) are required to follow the NIH's single Institutional Review Board (sIRB) policy.[1]

The NIH selected the Clinical Trials Transformation Initiative (CTTI) at Duke University to partner with the NIH's sIRB policy evaluation workgroup on the development of a framework for evaluating the implementation of the NIH sIRB policy. CTTI convened a group of human research protections and clinical research experts to serve on the CTTI project team to collaboratively design a qualitative descriptive study, develop data collection materials, assist in interpretation of results, and contribute to development of the evaluation framework.

This report describes the qualitative research CTTI conducted to inform the development of the NIH sIRB evaluation framework. The final deliverable is the evaluation framework.

2. Overview

This section describes who was involved in the research; the objectives; the overall design, methods, and analysis; eligibility criteria; and how participants were recruited and selected. It also provides a general framing for how the data were collected. Detailed information on the sample size and the demographic characteristics of the participants is provided in the next section. Detailed information on data collection and analysis—as well as findings from the interviews—is provided in the Process Mapping, Metrics, NIH Goals, and Other Findings sections of the report.

2.1. CTTI Social Science Team

- **Principal Investigator**:
  - Amy Corneli, PhD, MPH: Lead CTTI Social Scientist; Associate Professor of Population Health Sciences, Duke University School of Medicine
- **Interviewer and Project Leader**:
  - Kevin McKenna, MPH: Assistant CTTI Social Scientist; Research Program Leader, Department of Population Health Sciences, Duke University School of Medicine
- **Data Analysts**:
  - Kevin McKenna, MPH
  - Emily Hanlen, MPH, MEd: Research Program Leader, Department of Population Health Sciences, Duke University School of Medicine
  - Brian Perry, MPH: Associate CTTI Social Scientist, Senior Research Program Leader, Department of Population Health Sciences, Duke University School of Medicine
- **Research Assistant:**
  - Adora Nsonwu, BA: Clinical Research Specialist, Sr., Department of Population Health Sciences, Duke University School of Medicine

2.2. CTTI Project Team

- **Senior Project Manager:**
  - Sara Calvert, PharmD: Senior Clinical Project Manager, CTTI
- **CTTI Team Members**:
  - Laura Cleveland, BS: patient representative, member of the National Cancer Institute's Central IRB
  - Cynthia Hahn: President of Integrated Research Strategy, LLC
  - Eric Mah, MPH: Executive Director of Clinical Research Operations, University of California, San Diego
  - Rita O'Sullivan, EdD, MA: Associate Professor; Evaluation, Assessment, and Policy Connections; School of Education; University of North Carolina at Chapel Hill
  - Helen Panageas, BA, CIP: Director of IRB Operations, New York University School of Medicine
  - Heather Pierce, JD, MP: Senior Director for Science Policy and Regulatory Counsel, Association of American Medical Colleges
  - Stephen Rosenfeld, MD, MBA: Chair, Secretary's Advisory Committee on Human Research Protections

2.3. Research Objectives

- Describe key stakeholder experiences in implementing the NIH sIRB policy
- Describe steps involved in operationalizing the sIRB process at IRBs and institutions
- Identify potential metrics to evaluate the implementation of the NIH sIRB policy

2.4. Study Design and Methods

The study design was a qualitative descriptive study[2-3] using two approaches:

A. 360° case study interviews (CSIs) at two universities. The 360° CSI approach uses in-depth interviews to solicit the unique perspectives of individuals engaged in various roles in the sIRB process at a single institution.

B. In-depth interviews with representatives from multiple institutions. Interviews were conducted with research administration leaders who represent academic, independent, and health center–based IRBs and institutions.

2.5. Eligibility Criteria

A. 360° CSIs:
   - The two participating universities must represent research institutions of different sizes, and public versus private.
   - Each institution must have had experience serving as both a reviewing IRB and a relying institution for NIH-funded multi-site studies.
   - Each individual must have had some engagement with the sIRB process.

B. In-depth interviews with research administration leaders:
   - Each individual must have had some engagement with the sIRB process.

2.6. Participant Recruitment and Selection

A. 360° CSIs:
   - After a review of multiple institutions, a large academic research institution and a midsize academic research institution were selected and invited to participate; one institution was public and the other institution was private.
   - Of the two selected institutions, the CTTI project manager worked with the IRB leadership at each institution to identify individuals who represented the various roles associated with implementing the sIRB process at that institution. Each individual was invited to be screened for the interviews.
   - CTTI used the following process to purposefully select[4] individuals to participate in an interview:
     - Screening information was reviewed (e.g., role, length of time in the role, previous experience), and the screened individuals with the most relevant experience were selected to participate.
     - Individuals were selected to represent the variety of roles engaged in implementing the sIRB process (e.g., research administration leaders, IRB chairs, reliance agreement officers, investigators, study/regulatory coordinators).
     - Investigators and study/regulatory coordinators were selected to represent a variety of research areas (e.g., clinical, behavioral).

- The IRB leadership representative at the institution was also interviewed.

B. In-depth interviews with research administration leaders:
   - The CTTI project team members identified potential leadership representatives from multiple institutions to invite for participation based on their professional networks.
   - The CTTI project manager reviewed the proceedings of Public Responsibility in Medicine and Research (PRIM&R) Advancing Ethical Research Conferences and identified leadership representatives to invite for participation.
   - Identified individuals were purposefully selected[4] to represent a variety of research environments, including academic, independent, and health center–based institutions.

2.7. Data Collection and Analysis

A trained interviewer conducted one-on-one in-depth interviews with the participants. One participant—an investigator—requested to be interviewed together with a study coordinator; therefore, one dyadic interview was also conducted. Most of the interviews were conducted in person, either at the 360º CSI university or at the PRIM&R AER conference in November 2018. We chose to conduct interviews at PRIM&R AER because it is a large professional conference for those working in human subjects protections, research ethics, and oversight; therefore, it provided an opportunity to efficiently conduct face-to-face interviews with many eligible participants. All other interviews were conducted by telephone. Demographic information was collected from each participant.

One of three question guides was used to correspond with the role of the participant: (1) research administration leadership representatives, (2) institution and other IRB representatives, and (3) investigators and study/regulatory coordinators (Appendix A). The interviews followed the same overall format, though questions varied based on the participant's role. The interview began with the participant reviewing a research map displaying the various steps and roles involved in implementing the sIRB process (except for the interviews with investigators and study/regulatory coordinators). Participants discussed the flow of activities and their similarity to or difference from the processes followed at their own institutions. Participants were then asked to describe their experiences with implementing the sIRB process, focusing on whether they believed the NIH goals were being met and reasons why or why not. The six NIH goals[5] are:

- Goal 1: Enhance and streamline IRB review for multi-site research
- Goal 2: Maintain a high standard for human subjects protection
- Goal 3: Allow research to proceed effectively and expeditiously
- Goal 4: Eliminate unnecessary duplicative IRB review
- Goal 5: Reduce administrative burden
- Goal 6: Prevent systemic inefficiencies

Questions eliciting participants' perceptions of how the sIRB process could be evaluated were woven into the discussion of each NIH goal (except Goal 6) and asked independently (e.g., current and suggested baseline metrics). The interviews concluded with participants describing their perceptions of the top benefits and burdens of the sIRB process, based on their experience, as well as benefits to research participants. Questions about costs were not asked based on a decision made by the CTTI and NIH teams during research development. All interviews were audio-recorded and professionally transcribed verbatim according to a transcription protocol.[6] Additional information about data collection is provided in the Process Mapping, Metrics, and NIH Goals sections of this report.

After each interview, the interviewer completed a non-identifiable debriefing form to summarize the key information learned. The CTTI project team and the NIH workgroup used this summary information to engage in ongoing discussions about the draft evaluation framework while the data were being formally analyzed.

Applied thematic analysis was used to fully analyze the data[7] (except the process map data; see the Process Mapping section for more details). Using NVivo 12,[8] two analysts applied structural (a priori) codes to segment the participants' narratives into conceptual categories. Next, the analysts identified and applied content (emergent) codes to the text for each of the structural coding reports. To ensure consistent application of the codes, analysts conducted intercoder reliability assessments of the content codes as applied to 20% of transcripts for each question guide. Discrepancies in coding were resolved through discussions between the analysts; transcripts were recoded and the codebook revised accordingly. Analysts summarized each content code in analytical memos, which also included a code frequency table and illustrative quotes. Additional analytic steps are described in the Process Mapping, Metrics, and NIH Goals sections of this report.

We provide the frequencies of all coded responses for each topic to allow the CTTI project team and NIH workgroup to be informed of the full range of responses. We then provide detailed information on the most frequent responses for each topic. In addition, following the CTTI methodology,[9] we describe findings for all domains that were explored as part of the interviews rather than reducing the description to the most common themes overall. This approach allows members of the CTTI project teams, who are experts in the field, to be fully informed of all results so they can assist in the interpretation of the data.

2.8. Ethics

The IRB of the University of North Carolina at Chapel Hill determined this research to be exempt from further IRB review. As a means of protecting participant privacy, the approved protocol stated that neither transcripts from the interviews nor any other identifiable study data will be shared with the broader CTTI and NIH teams. All participants were provided with an informational sheet before study participation, which explained the study in detail, including its purpose, risks, and benefits.

3. Study Population

This section describes the final study population.

Qualitative, in-depth interviews were conducted with a total of 34 individuals. The participants included:

- 13 research administration leadership representatives (e.g., IRB executives, IRB directors or associate directors, IRB chairs, institutional officials) of multiple academic, independent, and health system–based IRBs;

- 10 research administration leadership representatives (e.g., IRB directors or associate directors, IRB chairs), institutional representatives (e.g., directors of human protection programs), and other IRB representatives (e.g., reliance agreement officers) from the two 360° CSI universities; and

- 5 investigators and 6 study/regulatory coordinators from the two 360° CSI universities.[£]

Demographic information about the study population is shown in Tables 1 and 2 below.

[£] A dyadic interview was conducted with an investigator and study coordinator. Therefore, a total of 11 investigators/study coordinators participated in the interviews; 10 transcripts represent those interviews.

Table 1: Demographic Characteristics of 360° Case Study Interview Participants	
All participants (n=21)	**No. (%)**
Current role at institution	
IRB director or associate director	2 (10)
IRB chair	2 (10)
IRB representative (e.g., reliance agreement officer, quality improvement officer)	2 (10)
Institutional official (e.g., director of human research protections, director of quality control, attorney)	4 (19)
Investigator	5 (24)
Study/regulatory coordinator	6 (29)
Length of time in current role	
Less than 1 year	2 (10)
1 to 2 years	4 (19)
3 to 4 years	4 (19)
5 years or more	11 (52)
Years engaged in the sIRB process	
Less than 2 years	6 (29)
2 to 3 years	5 (24)
4 to 5 years	1 (5)
More than 5 years	9 (43)
Investigators and study/regulatory coordinators (n=11)	**No. (%)**
Type of multi-site research conducted[1]	
Clinical	9 (82)
Socio-behavioral	2 (18)
Health systems research	1 (9)
Implementation science	2 (18)
Bioethics	1 (9)
Other[2]	2 (18)
Number of studies using sIRB[3,4]	
1 to 2	4 (44)
3 to 5	3 (33)
6 to 15	1 (11)
More than 15	1 (11)

[1]Participants could give more than one answer when applicable.
[2]Includes observational and biomarker research.
[3]Data not available for two participants—from network study/regulatory coordinators.
[4]All investigators and study coordinators were engaged in NIH-funded, multi-site research.

Table 2: Demographic Characteristics of Research Administration Leadership Representatives (n=13)	No. (%)
Type of institution	
Academic institution	6 (46)
Independent IRB	3 (23)
Heath system	4 (31)
Current role at institution	
IRB executive (e.g., chief executive office, vice president)	3 (23)
IRB director or associate director	3 (23)
IRB chair	2 (15)
IRB administrator	1 (8)
Institutional official (e.g., director of regulatory affairs, director of research compliance)	4 (31)
Length of time in current role	
1 to 2 years	1 (8)
3 to 4 years	1 (8)
5 years or more	11 (85)
Years engaged sIRB process[1]	
2 to 3 years	2 (15)
4 to 5 years	2 (15)
More than 5 years	9 (69)
Role of institution in single IRB process	
Reviewing IRB	3 (23)
Reviewing IRB and relying institution	10 (77)

[1]All research administration leadership representatives were engaged in NIH-funded, multi-site research.

4. Process Mapping

4.1. Overview

The CTTI social science team used process mapping to identify and describe actions that have been taken by institutions to operationalize the sIRB process. Process mapping offers a holistic view of the implementation of new processes and procedures.[10-11] The CTTI project team, in collaboration with the NIH workgroup, will use the process mapping findings to position metrics for evaluating the implementation of the NIH sIRB policy.

4.2. Methods

Preparation: The CTTI project team created a sIRB process map for reviewing IRBs based on a sIRB process map from the University of Utah (https://irb.utah.edu/guidelines/sirb/relying-on-uu-sirb.php). The process map displays the steps and roles involved in implementing the sIRB process (Appendix B).

Data collection: Process mapping was included as part of the 23 in-depth interviews conducted with the following two participant groups:

Group A: Research administration leadership representatives (e.g., IRB executives, IRB directors or associate directors, IRB chairs, institutional officials) of academic, independent, and health system–based IRBs (n=13)

Group B: Research administration leadership representatives (e.g., IRB directors or associate directors, IRB chairs) and institutional and other IRB representatives (e.g., directors of human protection programs, reliance agreement officers) from the two 360° CSI universities:

- University A (research administration leadership representatives, n=3)
- University B (research administration leadership representatives, n=1; institutional and other IRB representatives, n=6)

At the beginning of the in-depth interviews with research administration leadership representatives, participants reviewed a printed color copy of the sample sIRB process map and described how the flow of activities at their own institution and/or partnering institutions are similar to or different from the sample process map. As applicable, participants focused on activity flow in their experience when serving as a reviewing institution and as a relying institution (only for academic and health system–based institutions). Differences were marked on the printed copy of the sample process map.

At the beginning of the 360° CSIs with the institutional and other IRB representatives and with one research administration leadership representative,[ϒ] the interviewer presented the sample process map and explained the differences in activity flow between the sample process map and the process used at the participant's institution, as described during the previous interviews with research administration leadership representatives. These participants then described their perspective on the flow of activities and their role in the overall sIRB process.

[ϒ]Due to the sIRB leadership structure, one research administration leadership representative was interviewed at a 360° CSI university using the question guide for institutional and other IRB representatives.

Data Analysis: All narratives on the process map were coded with a single code, grouping together all text related to the process map. Narratives were differentiated by respondent ID numbers. For the research administration leadership interviews conducted across multiple institutions (Group A), the CTTI social science team reviewed data (i.e., the marked process map and the transcript narrative) from each interview and summarized the implementation differences the participant described for operationalizing the sIRB process. For the 360º CSIs (Group B), the CTTI social science team first grouped data from all interviews conducted with representatives from the same institution (e.g., all data from representatives from University A were grouped together). Then, the team reviewed the data from each university collectively and identified and summarized the process followed for implementing the sIRB process at each university. All summaries were then combined, resulting in the final summary presented below.

4.3. Findings

Participants confirmed steps and described additional steps that their institution implements when carrying out the sIRB process. The order of these steps varied across and within institutions.

The steps included:

1. The principal investigator (PI) identifies a need for a sIRB plan.
2. The PI and/or site investigators submit the study protocol to their own institution; the protocol is submitted to the reviewing institution as the sIRB (if their own institution is not the reviewing IRB).
3. The relying and reviewing institutions negotiate reliance agreements.
4. The relying institution completes ancillary reviews.
5. The relying institution provides information on local context.
6. The reviewing institution conducts the ethics review.
7. The reviewing institution approves the study protocol, and the relying institution provides institutional approval.
8. The institution(s) (the relying institution or the reviewing IRB) notifies the study teams of the protocol and institutional approvals.
9. The institution(s) (the relying institution or the reviewing IRB) conducts post-approval oversight, monitoring, and auditing.

Listed below are highlights of the processes participants described, with additional information on participants' perceptions and suggestions and potential implications.

Topic	Various processes	Perceptions, suggestions, and potential implications
Initiate sIRB plan	• The lead PI contacts their own IRB about initiating a sIRB plan, either as part of the NIH application process or after funding is anticipated. ○ If during the application process, the PI's IRB helps write the sIRB section of the application, including budget implications. • The lead PI does not contact their own IRB about initiating a sIRB plan but contacts the reviewing institution. As a result, the relying institution first learns of the study after being contacted by the reviewing institution.	• Investigators do not yet fully understand the sIRB process; some PIs contact external IRBs (i.e., the reviewing IRB) before informing their own institution that they want to rely on another IRB for ethics review. • Large amounts of time and effort are expended during the NIH application process, considering how few applications are funded. Identifying the sIRB should not be part of the application process. • When evaluating the sIRB process, time and effort spent on the sIRB plan during NIH application preparation should be included. • All institutions involved must be notified so they can determine whether they are willing to participate in the sIRB process for the specific study in their specific roles. • Some IRBs conduct feasibility assessments or other reviews to determine whether their IRB or the relying institution has the capacity to review the study protocol and whether the institution or the PI has the capacity to implement the protocol. The risk of the study is also considered.
Initial protocol submission	• Relying institutions request that the protocol be submitted to their own IRB's electronic system. • Relying institutions refer to study protocols as "external IRB applications" when the protocols are submitted to their own IRB while also being reviewed by a reviewing IRB. Documentation is also requested (e.g.,	• When external institutions or investigators are unable to submit directly to the reviewing institution's electronic IRB software, a liaison is needed to facilitate the process. • This liaison is often the lead study team.

Topic	Various processes	Perceptions, suggestions, and potential implications
	approved protocols, letters, consent templates, conflict of interest disclosures). • Some relying institutions can submit protocols directly to the reviewing IRB's electronic system; some systems do not have this capability. • IRBs have the PIs gather information from all sites and upload it into the IRB software—or have sites upload information directly themselves.	

Reliance agreements	• Study protocols must be finalized and submitted to the IRBs before institutions will begin reliance agreement negotiations.
	• Study protocols must be approved before the initiation of reliance agreement negotiations.
	• Institutions will begin reliance agreement negotiations before the study protocol is finalized and submitted to the IRB—or at any other time during the review process.
	  ○ Protocol review and reliance agreement negotiations can occur simultaneously.
	  ○ Reliance agreements are not finalized until after the study is approved.
	• The institution requires the PI to complete a reliance request survey.
		• Institutions want to know what they are committing to reviewing or relying on another institution to review; and to determine the risk of the study and whether they want to rely on another institution. Thus, they want to see the protocol before reliance agreement negotiations.
		• For NIH-funded research, IRBs may start the reliance agreement negotiation process earlier than for non–NIH-funded research because of the NIH sIRB policy.
		• Having established master agreements saves time.
		• Using standard documents saves time.
		• Using the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB platform streamlines the process, because all parties use the same documents; otherwise, institutions use different processes, which slows the process. Some institutions require the use of SMART IRB agreements.
		• Some institutions have created their own reliance agreement template and require others to use it.
		• Individualized reliance agreements are becoming less relevant because more institutions are using SMART IRB.

Topic	Various processes	Perceptions, suggestions, and potential implications
		• There is a preference for all sites to use the same reliance agreement—otherwise the process is far longer. • Having master agreements in place between institutions speeds up the process. Having master agreements covering multiple protocols is also used. Having individual reliance agreements for each study is time consuming. • Some use SMART IRB or master agreements, and then only an additional flex agreement may be needed for details. The master agreement can also cover a series of protocols in a certain therapeutic area (e.g., oncology). • Different kinds of reliance agreements can be used. A study-specific agreement is referred to as the Institutional Authorization Agreement (IAA), and a comprehensive agreement is called the Master Jurisdiction Agreement (MJA), where a wide range of details are negotiated.
Ancillary reviews	• Various ancillary reviews (e.g., conflict of interest disclosures, institutional training, ensuring that institutional policies are followed) are conducted by the relying institution. • Ancillary reviews also include internal reviews that are required at the institutional level before submission of the study protocol to the respective IRB (e.g., departmental reviews, broader research unit reviews, specialty reviews for vulnerable populations). ○ PIs can start completing ancillary reviews as soon as they receive the notice of award.	• Relying sites often want the protocol approved before they take the time to complete ancillary reviews. • Internal pre-reviews should not be included in any metrics evaluating the sIRB process because there are institutional standards for all study protocols. • Relying institutions still have responsibilities and tasks to complete. The reviewing IRB cannot be in charge of everything. Reviews and activities are perceived as a shared responsibility: relying sites conduct the research, monitor implementation, report information; the reviewing site provides oversight. The relying site is still responsible for all pre-reviews before IRB submission.

Topic	Various processes	Perceptions, suggestions, and potential implications
	• Ancillary reviews can be completed at the same time as the ethics review. • Ancillary reviews are initiated and completed after the study protocol is approved by the relying institution. • Ancillary reviews can also include reviews conducted after the ethics review and before institutional sign-off. • PIs have access to local IRB software, so can gather the results of ancillary reviews and report this information to the reviewing IRB.	
Local context	• Local context can include institution-specific and protocol-specific information. • Information about local context is not requested until study protocol is approved. • Information about local context is requested before or during the ethics review of the study protocol by the reviewing IRB. • Obtaining local context information is part of the reliance agreement process. • During the review of the study protocol (focused on providing approval for the parent site), local context information can be collected from the sites, and sites are approved as an amendment.	• Relying sites often want the protocol approved before they take the time to complete the local context information, because the latter can be time-intensive. • It is better to collect local context information early in the process. • Sites should be informed that they will be asked to provide local context information once the study protocol is approved at the parent institution. • Information is typically limited to institutional policies and state laws; it should be kept on file and not re-created each time. Some requests are more specific and are related to the study protocol, such as site resources and conflict of interest disclosures. • There is a lack of consistency in how local context is interpreted at relying sites, which results in inconsistency in the information collected. • There is no standardized process for collecting information on local context.

Topic	Various processes	Perceptions, suggestions, and potential implications
Protocol approval	• The reviewing IRB approves the protocol for its own site (i.e., the parent site), then approves it for the other sites. Alternatively, the reviewing IRB approves the protocol without including the sites. The sites are then approved as amendments. • The reviewing IRB reviews and approves the study protocol for sites in batches—whichever sites are available for review at a given time—continuously reviewing and approving new sites. • The reviewing IRB does not approve the protocol until it receives word from the relying institution that all ancillary reviews are complete.	• There is a perception that IRB approval for the parent site is easier because it is the PI's institution. This is due to parent protocol approvals that can be obtained at the same time that all local context information requests are being completed by sites. Sites are then approved as amendments. • Usually information for all sites is not ready at the same time. Thus, simultaneous review of the parent protocol and all sites usually does not occur. • The overall process is generally much more streamlined when the institution is relying on another IRB rather than serving as the reviewing IRB. • Some relying IRBs do not collect documentation from the reviewing IRB that the protocol from their institution was approved (i.e., the protocol approval letter).
Notification of approval	• IRBs communicate directly with the PI or point of contact; the PI or point of contact communicates with all sites. • IRBs communicate directly with the PI and all sites.	• Institutions need systems to communicate with all sites involved, not only the study PI.
Post-approval oversight, monitoring, and auditing	• Monitoring includes personnel updates, conflict of interest disclosures, ethics trainings updates, revisions to HIPAA requirements, adverse event reviews, compliance, and amendments to informed consent documents. • No plan is specified for post-approval monitoring. • The reviewing IRB monitors the informed consent changes and other pre-identified	• Decisions must be made about roles, responsibilities, reporting, and rules of the relying institution and the reviewing IRB after the protocol is approved. • It is up to the institution's preference whether to put all amendments into the local IRB software.

Topic	Various processes	Perceptions, suggestions, and potential implications
	tasks, with the relying institution monitoring local aspects, such as personnel updates, conflict of interest disclosures, and ethics training.	

5. Metrics

5.1. Overview

The CTTI social science team gathered data about suggested metrics for evaluating the sIRB process from a variety of individuals who are engaged in the sIRB process in different roles. Together with the NIH workgroup, the CTTI project team will use the data to inform which metrics will be proposed or included as examples as part of the sIRB evaluation framework.

5.2. Methods

Data collection: During the in-depth interviews, questions related to metrics were asked of all 34 participants:

- Research administration leadership representatives (e.g., IRB executives, IRB directors or associate directors, IRB chairs, institutional officials) of academic, independent, and health system–based IRBs (n=13)
- Research administration leadership representatives (e.g., IRB directors or associate directors, IRB chairs), institutional representatives (e.g., directors of human protection programs), and other IRB representatives (e.g., reliance agreement officers) from the two 360° CSI universities (n=10)
- Investigators (n=5) and study/regulatory coordinators (n=6) at the two 360° CSI universities[¥]

The specific questions asked about metrics varied based on participants' roles. Research administration leadership representatives were asked to share their insights on the following:

- Current metrics measured by institutions
- Potential baseline metrics
- Required changes to current procedures and systems to collect sIRB metrics
- Metrics for evaluating NIH sIRB goals 1 through 5
- Process and impact evaluation metrics

Investigators, study/regulatory coordinators, and all other IRB and institutional representatives were asked about the following:

- Metrics for evaluating NIH sIRB goals 1 through 5
- Process and impact evaluation metrics

Analysis: All narratives related to metrics were first coded with structural codes, based on the question topic (e.g., current metrics, baseline metrics). Next, all proposed metrics described within these structural areas were coded inductively with content codes, based on the emerging overall topic (e.g., time metrics). All metrics mentioned by participants, regardless of their frequency, were summarized by their structural and topical areas and are shown in the tables below.

[¥] A dyadic interview was conducted with an investigator and study coordinator. Therefore, a total of 11 investigators/study coordinators participated in the interviews; 10 transcripts represent those interviews.

5.3. Findings

5.3.1 Metrics Currently Measured by Institutions

Participants described numerous metrics currently collected at their institutions:

Metric	Sub-metrics and additional information
Time	Time spent reviewing documents for completeness before IRB submission
	Time spent training the PI on the sIRB software
	Turnaround time between each step in the review process, including amendments: • Time from PI sign-off on the submission to the start of internal/departmental review • Time from the start of internal/departmental review to release to the IRB • Time from request for modifications to response from the PI • Time for completion of ancillary reviews • Time from submission to the IRB to decision by the IRB by review type (i.e., exempt, expedited, or full board review) • Time from submission to the IRB to assignment to a meeting (for protocols requiring full board review) • Time from initial approval to release of approved documents to the sites • Time from initial approval to first site added • Time from initial approval to all sites added
	Time spent for post-approval monitoring and review of additional submissions: • Time between submission of continuing review application and decision • Time between submission of unanticipated event report and response
Number and type of submissions and communications between IRB and investigator	Not applicable[∝]
Quality	Number of modifications requested by the reviewing IRB
	Number of times the relying site finds errors in approved documents
	Percentage of studies approved at initial review

[∝]No additional sub-metrics were provided.

5.3.2 Suggested Potential Baseline Metrics

Participants suggested that current metrics could be used for baseline comparators. Some participants commented that quality metrics, rather than time metrics, are more important to capture and evaluate for change. Suggested baseline metrics are:

Metric	Sub-metrics and additional information
Time to completion of each necessary step in the review process through site initiation	Not applicable
Quality	Number of modifications requested
	Number of protocol deviations reported
	Access to the reviewing IRB's meeting minutes
	Relevant expertise of the reviewing IRB members
	Knowledge by relying site staff of reviewing IRB reporting policies
	Ability to appropriately report and respond to adverse events
Percentage of full-time staff effort needed	N/A
Time for presubmission requirements	Time spent completing reliance agreements
	Time spent gathering documents from sites
	Time spent training staff on sIRB requirements
Number of submissions and communications between staff and IRB	Not applicable
Communication between sponsor and IRB	Amount of time sponsor takes to respond to questions or requested changes from the sIRB vs the local IRB
Number of sIRBs the institution currently relies on	Not applicable

5.3.3 Metrics for Evaluating the NIH sIRB Goal 1

Goal 1 is to enhance and streamline IRB review for multi-site research. Suggested metrics are:

Metrics	Sub-metrics and additional information
Time*	Time between every touchpoint
	Time spent setting up reliance agreements
	Time spent gathering and reviewing documents before submission
	Time between submission of initial protocol to sIRB and issuance of a decision
	Time spent submitting and approving amendments to add each or all relying sites to the protocol
	Time between IRB approval and first subject accrual
	Turnaround time for responding to unanticipated events

Metrics	Sub-metrics and additional information
Number of communications between reviewing and relying sites	Not applicable
Degree of compliance to agreed communication plan	Not applicable
Percentage of full-time staff effort required to submit and review documents	Not applicable
Financial costs	Not applicable
Expertise of staff submitting and reviewing documents	Not applicable
Relying site feedback	Satisfaction survey of sIRB process and result
	Willingness of institutions to use sIRB when not required
	Interpretation of the reliance agreement by the relying IRB
Number of modifications required	Not applicable
Process changes at reviewing IRB	Not applicable
Number of small sites participating in studies that require ancillary reviewers	Not applicable
Number of convened meetings	Not applicable
Number of full board review items (as opposed to expedited reviews)	Not applicable

* Notes regarding time metrics:

- Several participants said that, when comparing time metrics, studies must be grouped by IRB determination (i.e., exempt, expedited, non-exempt) and other characteristics, such as therapeutic area and risk to participants.
- The level of familiarity with the sIRB process must be considered when comparing sites on time metrics, because the time to complete activities will decrease as sites become more familiar with the process.

5.3.4 Metrics for Evaluating the NIH sIRB Goal 2

Goal 2 is to maintain a high standard for human subjects protection. Suggested metrics are:

Metrics	Sub-metrics and additional information
Staff qualifications	Track roles, number of staff needed, and qualifications of staff completing and reviewing local context forms
	Track completion of required trainings
	Document type of person (e.g., IRB role) who provided local context information
Accessibility	Access to relevant state laws

Metrics	Sub-metrics and additional information
	Ability of relying and reviewing IRBs to directly communicate
Spot checking	Inclusion of local context in key areas and time points throughout the protocol (e.g., initial review, continuing review, audits)
Input from relying IRB	Survey of relying sites about inclusion of local context in final protocol
Time	Time required to respond to request for local context
Track updates	Track updates to standard institutional information
Confirm provision and inclusion of local context	Documentation by relying sites of the provision of local context information to the reviewing IRB
	Documentation by the reviewing IRB of the consideration and inclusion of local context, if any, and justification for not including local context information, if applicable
	Documentation by relying sites of approval of inclusion of local context in the final protocol

5.3.5 Metrics for Evaluating the NIH sIRB Goals 3 through 5

Goals 3 through 5 are for research to proceed effectively and expeditiously, to eliminate unnecessary duplicative IRB Review, and to reduce administrative burdens.

Participants gave suggestions for evaluating changes in the time requirements for a sIRB model compared to a local IRB model:

Metrics/process	Sub-metrics and additional information	
Compare review time between sIRB and local models*	Track time for every stage of the process	Time to complete reliance agreements
		Time to complete review of amendments
		Time to review continuing review documentation
		Time to study start-up
		Time from notice of award to study start-up
	Compare time from submission to approval	Clarity about when the clock starts (e.g., when the application is opened, or when all documents are submitted)
	Compare anticipated start date to actual start date	Frequency of IRB meetings and expected IRB turnaround times
	Compare historical measures of time spent at sites converting from local to sIRB review	Not applicable
	Compare studies of similar phase, therapeutic areas	Not applicable

Metrics/process	Sub-metrics and additional information	
	Compare turnaround times at each site for every stage of the process	Not applicable
	Aggregate time spent from all of the sites involved	Not applicable
Compare the number of IRB submissions at all sites between sIRB model and local model	Not applicable	
Conduct a satisfaction survey with staff familiar with both local IRB model and sIRB model	Not applicable	

* Notes regarding time metrics:

Participants indicated that the following considerations will influence any evaluation of time:

- Degree of familiarity with the sIRB process
- How often the institutions work together
- Competing priorities (e.g., some reviews take precedent)
- Availability of staff at the reviewing IRB
- Whether sites are required to submit duplicative information to the local IRB

Participants noted a number of challenges in comparing metrics across trials and/or types of IRBs:

- Comparing time metrics across different types and phases of trials, because of the varying complexity of the trials
- Comparing an academic sIRB to a commercial sIRB, because of the greater availability of resources and experience at commercial IRBs
- Tracking the preliminary work completed before IRB submission

Participants gave suggestions for evaluating the division of roles and responsibilities:

Metrics/process	Sub-metrics and additional information
Basic institutional metrics*	List of external IRBs reviewing studies conducted at the institution
	List of investigators who rely on external IRB review
	Number of studies relying on external IRBs
Change in burden for staff at relying institutions	Number of local IRB activities performed when institution is relying on another IRB

Metrics/process	Sub-metrics and additional information
Consistency in and adherence to reliance responsibilities	Adherence to work expectations agreed upon and described in the reliance agreement (e.g., roles of the reviewing IRB and relying institution)
Degree for which local context is reviewed or included in reviewing IRB review	Not applicable
Time	Time spent completing review process
	Time spent processing serious adverse events
Change in number of safety events or subject complaints	Not applicable
Qualifications of staff assigned to responsibilities	Not applicable

* Participants described that different metrics are needed for different types of studies (e.g., phase 2 vs phase 3) and that there is a need to poll institutions on how they are already conducting evaluations.

Participants gave suggestions for evaluating the sharing information between institutions:

Metrics/process	Sub-metrics and additional information
Time spent*	Time between communications (e.g., between institutions, between the reviewing IRB and the PI)
	Time between each stage of the review process
	Stoppage time between internal/departmental review and IRB submission
	Time spent reviewing protocol at relying site
Degree that reviewing IRBs and relying institutions can communicate directly	Relying sites can submit directly to reviewing IRB rather than through an intermediary at the reviewing institution (which is particularly important for adverse event reporting and other time-sensitive notifications).
Feedback from staff at participating institutions	Level of direct access to information vs relying on others (e.g., enrollment numbers)
	Timeliness of communications
	Time and effort spent by IRB analysts processing reliance and non-reliance studies
	Efficiency of email vs other communication channels
	Thoroughness of information provided
	Type of information disseminated
	Whether the reviewing IRB met the criteria for ethical review as perceived by the relying institution
Frequency of communication between reviewing IRB and relying institution	Number of modifications made to submissions from relying institutions
	Number of times incomplete forms are submitted
Degree of redundancy	Completing different copies of the same forms
	Number of duplicate submissions at relying and reviewing IRBs

Metrics/process	Sub-metrics and additional information
Degree to which study teams retain and utilize information from trainings	Not applicable
Post-approval monitoring	Degree to which site PIs follow reviewing IRB requirements
Delayed review due to settling on reliance terms	Not applicable

* Notes regarding time metrics:

Participants indicated that the following considerations will influence any evaluation of time:

- Degree of familiarity with the sIRB process
- Standardization of and consistency in using forms
- The number of relying sites (e.g., with more sites, more time is needed for the reviewing IRB for review)
- Percentage of full-time staff devoted to the process per study

Participants also discussed that:

- Infrastructure to support monitoring of communication timeliness must be created, because it cannot be monitored through email.
- The time spent negotiating reliance agreement is not necessarily associated with a better agreement.

Participants gave suggestions for evaluating the administrative burden:

Metrics/process	Sub-metrics and additional information
Time burden	Time spent on administrative review at every stage of the process
	Time spent compiling and submitting all necessary documents
	Time spent getting systems and processes up and running
Amount of work	Number of communications per site
	Number of amendments
	Number and type of submissions per full-time employee per month
	Number of clicks (to process an IRB submission electronically)
	Number of documents processed per site in a multi-site study
Staff feedback	Survey of site staff about their level of confidence in the reviewing IRB
Personnel	Percentage of full-time employees needed
	Role and experience of full-time employees involved
Cost of developing electronic infrastructure	Not applicable
Training	Time spent training
	Number of training sessions needed
Costs charged for paying overhead	Not applicable

Participants also said that differences in the types of studies must be considered when measuring the effectiveness of the sIRB process.

5.3.6 Process Evaluation Metrics

Participants offered the following process evaluation metrics:

Metric	Sub-metrics and additional information
Time*	Time spent setting up reliance agreements
	Turnaround time for issuing decisions on amendments to add sites
	Time from initial submission of protocol to decision
	Time between sIRB approval to first subject accrual
	Time spent preparing for sIRB submission
	Time required for training staff
Personnel costs	N/A
Feedback from staff	Satisfaction surveys with all study and IRB staff involved
	Focus groups to determine how to improve processes
	Staff completion of work journal to record observations and experiences
Percentage of full-time effort required to train investigators on sIRB processes and review additional amendments per study	Not applicable
Number of sIRB submissions by type	Not applicable
Number and complexity of communications or consults between reviewing IRB and study staff	Not applicable
Number of sites participating	Not applicable
Adherence to new sIRB standard operating procedures and agreements	Not applicable
Number of new or revised policies with which staff must be familiar	Not applicable
Number of sIRB-related training sessions required and attended by staff	Not applicable
Role of staff (e.g., seniority) assigned to review or relying activities	Not applicable

* Notes regarding time metrics:

Participants identified numerous factors that may influence time metrics. These include:

- Different types of studies, which may require more or less time
- Level of familiarity with the sIRB process

Some participants suggested measuring time in number of hours rather than number of days to obtain a more precise measurement of effort.

5.3.7 Impact Evaluation Metrics

Participants offered the following impact evaluation metrics:

Metric	Sub-metrics and additional information
Compare review and implementation timelines of similar studies using a sIRB vs multiple IRBs	Not applicable
Feedback from all IRB and study staff involved	Not applicable
Feedback from research participants during and after the study	Not applicable
Percentage of full-time effort required for sIRB review vs multiple IRB review	Not applicable
Variability between IRBs	Differences between sites' consent forms
	Variability in IRB decisions after reviewing the same protocol
Number of sites using a sIRB when not required	Not applicable
Differences in cost for sIRB review vs multiple IRB review	Not applicable
Number of adverse events reported	Not applicable
Number of protocol deviations reported	Not applicable
Determination of whether benchmarks are being met	Not applicable
Impact of publications from studies using sIRB	Not applicable

5.3.8 Participant Experience Metrics

Some participants offered metrics related to how study participants' experiences may differ between studies that use the local IRB model and those that use the sIRB model:

Metric	Sub-metrics and additional information
Number of study participants who contact the sIRB directly	Not applicable
Review of screening and enrollment logs to measure success rate and reasons for refusal	Not applicable
Gathering study participant feedback	Feedback from study participants comparing expectations of participation based on consent material and experience participating in the study
	Knowledge and attitudes survey about study participants' awareness of multi-site trials and sIRB review
	Determination of participant preferences for and understanding of sIRB-approved consent material vs local IRB–approved consent material

Some interview participants said no feedback is needed about study participants' experiences with the sIRB process because study participants are generally unaware of IRB review procedures.

5.3.9 Required Changes to Current Procedures and Systems

Some participants indicated that no changes would be needed to their institution's current system to begin documenting metrics to evaluate the sIRB process. Other participants described necessary changes. Suggested changes are:

Suggested changes	Process
Greater use of SMART IRB to reduce burden and effort needed to facilitate reliance agreements	Not applicable
Create new tools and resources	Comprehensive list of documents to facilitate sIRB review process
	Comprehensive list of data queries and associated data points in tracking systems (e.g., tracking hours on a task rather than days)
	Formal sIRB institutional policies and systems to for storing information (e.g., document repositories)
	Comprehensive list of questions for investigators to determine whether reliance is appropriate and the reviewing IRB is qualified to serve as the IRB of record
Greater access to sIRB software	Guest access to the sIRB software for relying sites to more easily communicate with the lead site
	Opportunity to submit more than one amendment at a time and track their progress separately
Systems to track relevant metrics after approval	Not applicable

Participants also described steps that need to be implemented before local context information can be measured. These are:

1. Defining standard local context information vs study-specific local context information
2. Standardizing institutional profiles for basic local context information (e.g., contact information in consent forms, relevant state laws).
3. Creating an easily accessible institutional profile and keeping it updated.
4. Providing study-specific information in addition to institution- and state-specific information (e.g., study-related special populations, standard of care, and clinic culture).

6. NIH Goals

6.1. Overview

The CTTI social science team gathered data on participants' experiences in implementing the sIRB policy as they relate to the NIH sIRB goals. The six goals are[5]:

- Goal 1: Enhance and streamline IRB review for multi-site research
- Goal 2: Maintain a high standard for human subjects protection
- Goal 3: Allow research to proceed effectively and expeditiously
- Goal 4: Eliminate unnecessary duplicative IRB review
- Goal 5: Reduce administrative burden
- Goal 6: Prevent systemic inefficiencies

The findings described here provide the CTTI project team and the NIH workgroup with a holistic view of how institutions operationalize the sIRB policy, as well as participants' perceptions of the effectiveness of the sIRB process, based on their hands-on implementation experience. The CTTI project team and the NIH workgroup will use these data to inform the sIRB evaluation framework as appropriate.

This study was not designed to evaluate the NIH's sIRB policy but rather to gather stakeholders' viewpoints on the implementation of the sIRB process, so that the CTTI and NIH teams can develop an evaluation framework grounded in stakeholder experiences.

6.2. Methods

Preparation: The CTTI social science team developed a research grid that lists domains and subdomains to explore under each of the NIH sIRB goals and questions linked to the domains and subdomains. The CTTI and NIH teams reviewed and provided feedback on the research grid, which was used to inform the development of the three interview guides, one each for research administration leadership representatives, institutional and other IRB representatives, and investigators and study/regulatory coordinators (Appendix A).

Data collection: During the in-depth interviews, participants were asked questions related to the six NIH sIRB goals, focusing on how participants operationalized aspects of the goal. Questions also explored whether participants believed the NIH goals were being achieved, including reasons why or why not. Questions about goals 1, 2, and 6 were asked independently. Questions about goals 3, 4, and 5 were combined given the similarity of the goals. Research administration leadership representatives and institutional and other IRB representatives were asked multiple questions related to each NIH goal. Investigators and study/regulatory coordinators were asked a subset of questions about each goal as they related to their roles (as reflected in various sample sizes in the findings sections).

Participants were also asked questions about (1) selecting a sIRB (investigators and study/regulatory coordinators only), (2) the top benefits and burdens of the sIRB policy, and (3) how the sIRB process affected the experiences of study participants. Those findings are described in the next section.

At the beginning of each interview, the interviewer provided the following definition of two terms to ensure consistency of terms throughout all interviews:

- "When I refer to a reviewing IRB, which is also known as the single IRB, I mean the IRB of record for a particular multi-site study for the duration of the study."

- "When I refer to a relying institution, I mean the IRB or institution that will rely on an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying IRB's institution. The NIH's single IRB policy refers to these institutions as 'participating sites.'"

The study sample included the following groups:

- Research administration leadership representatives (e.g., IRB executives, IRB directors or associate directors, IRB chairs, institutional officials) of academic, independent, and health system–based IRBs (n=13)

- Research administration leadership representatives (e.g., IRB directors or associate directors, IRB chairs) and institutional (e.g., directors of human protection programs) and other IRB representatives (e.g., reliance agreement officers) from the two 360° CSI universities (n=10)

- Investigators (n=5) and study/regulatory coordinators (n=6) at the two 360° CSI universities[¥]

Analysis: After coding of the interview transcripts, text from the content coding reports were reviewed for overarching themes and organized into emergent thematic groups. See the Overview section of this report for more details on the analysis.

6.3. Findings

6.3.1 NIH sIRB Goal 1

Goal 1 is to enhance and streamline IRB review for multi-site research.

Participants described their perspectives on whether the sIRB process has enhanced and/or streamlined the IRB process for multi-site research, focusing on:

1) The entire review process, including ethics and ancillary reviews and all processes necessary for a protocol to start data collection (asked of investigators and study/regulatory coordinators only)
2) Ethics review (asked of research administrator leadership, institution, and other IRB representatives)
3) Activities beyond ethics review, such as ancillary reviews (asked of research administrator leadership, institution, and other IRB representatives)

6.3.1.1 The Entire Review Process

Ten investigators and study/regulatory coordinators described whether they believed the entire review process has been streamlined.

[¥] A dyadic interview was conducted with an investigator and study coordinator. Therefore, a total of 11 investigators/study coordinators participated in the interviews; 10 transcripts represent those interviews.

Investigators and study/regulatory coordinators (n=8) gave the following reasons for believing the sIRB process <u>has streamlined</u> the entire review process. These reasons include:

- Efficiency of the review process (n=5)
- Standardization of documents (n=3)
- Familiarity with the overall process (n=3)
- Availability of a standardized timeline across all project sites (n=2)
- Less local IRB involvement (n=2)
- Improved overall process (n=1)
- Faster process once reliance agreements were finalized (n=1)
- Simple informed consent changes for site-specific needs (n=1)

For "**efficiency of the review process**," an investigator offered insight into the shift the sIRB process has provided, from the extensive time it previously took for the same protocol to be approved by multiple entities to a more streamlined process:

> It can take sometimes forever to get things settled because you're going from one IRB then sending your already approved IRB to another site. They're basically trying to carbon copy it through their IRB. And as you know, everybody's institution is a little bit different. So, they make their amendments. It's a lot of amendments and then back—a lot of back and forth. It seems like a never-ending process. So, the idea of being able to streamline that is really nice. And also to be able to keep your protocol really tight.

For "**standardization of documents**," participants, all speaking from a reviewing perspective, said:

> But overall, with other changes, and it comes especially important around when we do a protocol amendment, if we had to wait for the informed consent form changes for every university across all sites to approve, we would be implementing a protocol amendment. It would take either a very long—if you have to wait on everyone or the protocol is active in some sites and not others. I mean, it really simplifies the whole process. — Joint Investigator/Study Coordinator Interview

> And I think knowing that we're using current materials, and that everything we're doing is currently approved and it all happened at the same time, which is another benefit. — Investigator

For "**familiarity**," participants in the joint investigator/study coordinator interview said they expect the process to be more efficient over time due to becoming more familiar with the process:

> I think we were one of the first. So the reliance on other sites for some sites took a while, but I can imagine that the now single IRB mechanism is so widely or much more widely utilized, that would speed things up.

Investigators and study/regulatory coordinators (n=8) described numerous reasons for believing the sIRB process <u>has not streamlined</u> the entire review process. These reasons include:

- Lack of a standard process (n=4)
- Lack of infrastructure to implement the new policy (n=4)
- Limitations associated with conducting ancillary reviews (n=2)
- Reviews that were or appeared to be duplicative (n=2)
- Roles that were not clearly defined (n=2)
- Lack of guidance on implementing the new process (n=1)
- Lack of forms and templates to help with the process (n=1)
- Additional workload with the sIRB model (n=1)
- Too much involvement from participating sites when consent forms were being created (n=1)

For "**lack of a standard process**," investigators and study/regulatory coordinators, most speaking from a reviewing perspective, said:

> I think our department needed a better strategy to be able to use the IRB correctly and know what was needed right off the bat for the study. That would've shortened that timeframe quite a bit. And then subsequently knowing what we needed from the other sites, because there was definitely some delay in that. — Investigator

> I think some of the other institutions would really struggle with how to do that, what's the infrastructure that's needed? I mean, there was no chart, there was no organizational graph on how this should work. — Study Coordinator

Similarly, for "**lack of infrastructure**," participants described a lack of tools for implementing the new policy, lack of portals for relying sites to submit consent forms and access updated documents, and limited information for how local sites should handle local oversight vs what the reviewing IRB handles. Participants said:

> There were processes talked about that would do that, but none of them were put in place. So, the policy far preceded the infrastructure to be able to implement it. That seems to be the hiccup. — Regulatory Coordinator

> The institution that is serving as our sIRB has a portal that we can log into...That is how we submitted our consents and stuff like that, which seems great, but it was pretty bare minimum that we could input in there and pretty minimal information that we could pull out of there. So, I think that that is potentially another issue. Like, the only two people that have access to it are the study PI and one coordinator, but in reality there's a lot more people involved in the study than just those two people. — Study Coordinator

6.3.1.2 Ethics Review

Twenty-three research administrator leadership representatives and institutional and other IRB representatives described whether they believed the ethics review process has been streamlined.

Research administration leadership representatives and other IRB and institutional representatives (n=7) described the following ways in which the sIRB process <u>has streamlined</u> ethics review:

- Decreased workload for the relying institution (n=6)
- No ethics review required for relying sites (n=5)
- Improved efficiency of the ethics review process (n=3)
- Availability of standardized documentation (n=3)
- Availability of a standardized timeline across all project sites for ethics review (n=2)
- Incorporation of local context as part of ethics review (n=1)
- Familiarity with collaborators (n=1)

For "**decreased workload**," participants said the sIRB process reduces the overall workload and the workload of others when institutions rely on another IRB. Participants said:

> When we are the relying IRB, it certainly lessens our workload across the life of the study, because we have that one touchpoint. — Institutional/Other IRB Representative

> I think it's really just kind of the overall administrative burden has been moved from multiple sites to one site, and then that one site is able to oversee all aspects of the review is kind of the overall streamlining. — Institutional/Other IRB Representative

Participants, all speaking from a relying institution perspective, said that having **"no ethics review"** for relying sites helps to streamline the overall ethics review process. Research administration leadership representatives said:

> …if you're relying on an external IRB for ethical and regulatory review, yeah, you streamlined your process because you're not doing it.

> If we're relying on another IRB, we don't do an ethics review. So, it has streamlined it that way.

> So, we don't do an IRB review at all, obviously. We don't send it to a chair or anything. It's an administrative confirmation. And we have to sign consent form inserts that our staff confirms. And then we coordinate ancillary reviews. It's really a completely administrative review process and acknowledgment of request to rely. These are studies that are completely out of our ethics review process.

Research administration leadership representatives and other IRB and institutional representatives (n=15) indicated that there were no improvements or benefits in terms of the sIRB streamlining ethics review. Ten described the following ways in which the sIRB process has not streamlined ethics review:

- Increased workload (n=6)
- Local IRB involvement (n=2)
- Lack of standardized consent forms for relying sites and common IRB application for all participating sites (n=1)
- Lack of infrastructure resulting in study team being unprepared to implement the new policy (n=1)
- General lack of guidance on the sIRB process (n=1)

For "**increased workload**," participants, all from a reviewing IRB perspective, said:

> If we're the reviewing IRB, though, it's absolutely more. —Institutional/other IRB representative

> We've had three FTEs taken away from other things. And then when we are the single IRB, those three FTEs definitely help with that, but it's just a pant-load of work.—Research administrator leadership representative

> If we are the reviewing site, it's put more work on us because we're reviewing for multiple sites and having to juggle having new forms and templates and communication requirements to send things out to relying sites. — Research Administration Leadership Representative

Participants said that **"local IRB involvement,"** creates more difficulty with finalizing consent forms and reviewing the IRB application. A research administration leadership representative said, from a reviewing perspective:

> One of the difficulties in acting as a single IRB of record is still all the institutions want their own quirky consent form language, which is difficult to manage.

6.3.1.3 Beyond Ethics Review

Twenty-two research administrator leadership representatives and institution and other IRB representatives described whether they believed the process beyond ethics review has been streamlined.

Research administration leadership representatives and other IRB and institutional representatives (n=6) described the following ways in which the sIRB process has streamlined the process beyond ethics review:

- Efficiency of the process beyond the ethics review (n=3)
- Development and review of conflict of interest forms (n=1)
- Standardized study timelines (n=1)
- Monitoring systems associated with adverse events or vulnerable populations (n=1)

For "**efficiency**," participants said the sIRB review process makes the overall IRB process go faster. A research administration leadership representatives said:

> Yeah. I think it has allowed sites to get up and running quicker, in terms of enrolling subjects, simply because there are very few things you can negotiate when you're using a single IRB. You can't modify the consent form to any great extent.
>
> It's making it easier for us as the reviewing IRB. Whereas we used to have this process where we replicated some parts of their internal review or made these notifications, more and more organizations are saying, "Oh, you don't have to do that anymore. We're not going even send the study to you until it's clear to have an IRB review. We've done all our internal processes."

Research administration leadership representatives and other IRB and institutional representatives (n=19) described the following ways in which the sIRB process <u>has not streamlined</u> activities beyond ethics review:

- Lack of infrastructure, systems, and processes (n=6)
- Increased workload (n=5)
- Ancillary reviews (n=4)
- Workflow between different members of the team or different sites to communicate about and oversee local issues (n=3)
- Need for more information gathering (n=3)
- Lack of familiarity with the process and expectations of the policy (n=2)
- Compliance with an array of policies and requirements from different institutions (n=2)
- Reliance on other sites (n=1)
- Cost for reviews associated with the new policy (n=1)
- Use of auditing to oversee work at relying sites to ensure compliance (n=1)

For "**lack of infrastructure, systems, and processes**," participants discussed the large administrative reviews that happen for reviews beyond the ethics review at their site, regardless of whether they are a reviewing IRB or a relying institution. Participants said:

> And then also, I think there's a technology aspect to it as well, in that a lot of the sites don't have IRB management systems or IT systems that allow external sites to access it, and so there's kind of an administrative hurdle that we have to get through with submitting those documents.
> — Institutional/Other IRB Representative
>
> And so I think because of the way institutional IRBs are set up and the need for having a lead site or a coordinating site be the real—the chokepoint or funnel for information. You know anything that needs to be properly reported has to go through that coordinating center. So, you need more resources on the study team side of the lead site to facilitate everything. — Research Leadership Administration Representative

For “**increased workload**,” participants spoke about tasks that were not considered part of the ethics review. Tasks included serving as the privacy board for HIPAA, reviewing amendments, loading documents into IRB software systems, and having to spend excessive time soliciting information like local context from participating sites or obtaining an additional ethics consult. A research administrator leadership representative said:

> The only way do that is to create another process to solicit that information. I can give you an example where we had a full ethics consult where we have a study that we think does have some hot issues and we wanted the input from all of the reliance sites about what their thoughts were. The only way to do that was to effectively do it up front before the IRB completed its review was to organize a separate ethics consult day. So, that was, again, additive. We did an entirely additional ethics consult, where we had representatives be able to weigh in on what their concerns would be before the protocol was reviewed.

For “**ancillary reviews**,” participants spoke about the time necessary for the extensive review from the local site and related entities. An institutional/other IRB representative said:

> When people hear single IRB, they think only a single review. So, when we have to do radiation safety, and we’re having to do it at 15 sites, it takes time. Single IRB doesn’t streamline that. Single IRB couldn’t streamline that.

In addition, eight research administration leadership representatives and other IRB and institutional representatives simply said that there were no streamlining changes beyond ethics review with the sIRB model. Research administration leadership representatives said:

> Not related to this process. We’ve done our own streamlining but not related to this.

> In terms of ancillary reviews, I don’t believe there’s an impact.

6.3.2 NIH sIRB Goal 2

Goal 2 is to maintain a high standard for human subjects protection.

During the interview, participants discussed the concept of “high standards” and local context.

6.3.2.1 High Standards

Participants (n=33) described their perspectives on the definition of “high standards,” any concerns they have about their institutions’ ability to implement high standards, and the processes for and strengths and weaknesses of providing and receiving local context.

Participants mentioned the following topics when defining “high standards”:

- Protection of human subjects (n=15)
- Accreditation (n=8)
- Quality of review (n=7)

- Rigor of review (n=6)
- Monitoring of review (n=5)
- Compliance of reviewers (n=4)
- Study context incorporated into review (n=3)
- Personal gauge of participants (would they or would they not participate in the study) (n=2)
- Community response to the proposed research (n=2)
- Integrity of the reviewing institution (n=2)
- Quality of informed consent (n=1)

Participants described "**protection of human subjects**" as the most important measure of high standards. These protections, as outlined by some participants, include protection of patients' safety, rights, data, and privacy:

> The high standard is the role of the IRB is to protect human subjects from unreasonable harm due to research. — Investigator
>
> I think number one is patient safety, right? — Study Coordinator
>
> I'd say that the substantive scientific rigor and the way that that rigor is managed in the context of treating all human subjects with dignity and respect and beneficence and autonomy. — Institutional/Other IRB Representative

For **"accreditation**," participants discussed that institutions that are accredited are accepted as understanding and implementing high standards for review. A number of participants also discussed how the use of accreditation is one measurable way to determine the use of high standards. Participants said:

> I think many academic institutions like to measure high standards, IRB review standards, by whether people are certified. — Investigator
>
> We're an accredited IRB, so the accreditation process sets standards that are above, in many cases, the regulatory minimums and include like requiring accredited organizations to have systematically implemented best practices into the processes for IRB review. — Research Administration Leadership Representative
>
> If you're an accredited IRB, I would assume that you're going a little above and beyond what [the Office of Human Research Protections and the Food and Drug Administration] require. — Research Administration Leadership Representative

For "**quality of review**," participants talked about the extra steps their institutions take to ensure quality, such as additional administrative reviews and specialty committees related to the topics of research being covered in specific projects. Participants also commented on the speed of review as a proxy for the quality of review. Participants described:

> Of course, they have to have approval as well, and we do an administrative review, but all those things like [clinical research units], specialty committees, [institutional department review], research contracts, all that still has to happen. So, I don't feel like anything falls through the crack, because those things happen, plus we get the approval from the external IRB. — Research Administration Leadership Representative

> I guess I would be concerned if the reviews were going faster than they usually should by a particular IRB. Obviously the whole process itself is faster in my opinion, but if all of a sudden I was turning around reviews much faster or significantly slower that would worry me. — Investigator

> High standards would be good ethical and regulatory review, so you have the quality protocol, and you know that all of the sites are able to implement that protocol, as approved. — Research Administration Leadership Representative

For "**rigor**," participants said specific groups or boards that meet to review particularly complicated or difficult protocols are needed to ensure that the review is rigorous and appropriate based on the content of the protocol. A research administration leadership representative explained:

> Our board has expertise meetings for particular protocols that would require it so a lot of issues come up in terms of appropriate science, safety, things like that that we probably do less of now with, when we are the relying institution than we did before.

Participants said that "**monitoring**" at their institution leads to high standards, while other participants discussed lack of monitoring as an indicator of a lack of high standards. Two research administration leadership representatives explained:

> That's a place that they really need to have a much more robust monitoring effort for their studies and they don't really. As opposed to the industry studies, which are monitored to death, the [organization name] studies are hardly monitored at all.

> There's sort of an inherent belief that if you have one group overseeing the research and the consenting process for the entire project, that you will get a more consistent delivery of the protections of the subjects.

Research administration leadership representatives, investigators, study/regulatory coordinators, and other IRB and institutional representatives (n=23) described the following concerns with maintaining high standards using a sIRB process:

- Concerns about monitoring and reporting (n=14)
- Quality of review (n=7)
- A lack of experience of the reviewing institution (n=4)
- Trust in the reviewing site (n=3)
- Site-specific concerns vs concerns for the entire study (n=3)
- Reporting of adverse events vs deviations in the protocol (n=2)

- Legal protections (i.e., Food and Drug Administration regulations and HIPAA requirements) (n=2)
- Workload (n=1)
- Protection of human subjects (n=1)
- Use of a scientific review (n=1)
- Compliance issues (n=1)

For "**monitoring and reporting**," participants said that the extensive monitoring and reporting that is necessary with the new sIRB process—or lack of monitoring or systems—could lead to issues with maintaining high standards. Participants said:

> Because if there's not a portal that you can go to to see your approved protocol, your approved consents, and that's not available to everyone, then that would open up easily to mistakes of, "I used last year's version of the consent," or some other issue like that. — Study Coordinator

> I think we do have some nervousness about this, how well studies are monitored remotely. — Research Administration Leadership Representative

> But again, I go back to the issue of post-approval monitoring that needs to be very carefully fleshed out. — Institutional/Other IRB Representative

For "**quality of review**," participants said different institutions had different levels of quality in their processes and, therefore, may maintain high standards to lesser levels than the local IRB. Some participants also described that, with the new policy, they have less voice in identifying the reviewing IRB, which can affect the overall quality of the review. Participants explained:

> When we're the relying IRB, the way I think about it is there are definitely efficiencies to be gained by having a single IRB. But there are also situations when one IRB out of the 14 that are looking at a study will say, oh, gosh, this risk is missing. Nobody thought of it, but it's missing. And then, it will percolate throughout all the other sites. So that's something you're giving up with the single IRB review. Less eyes can mean less opportunities to catch something. —Institutional/Other IRB Representative

> I'd say, when we rely on another institution, I think number one is, particularly now with the mandate to do this, what is the quality of the IRB review? I think, again, in the old days, we could kind of pick and choose. You kind of knew who you're dealing with. Now it's more, you've got to do it or else you don't get the money. —Research Administration Leadership Representative

Participants also discussed that, because the NIH sIRB policy is new, reviewing institutions "**lack experience"** with these reviews, which could lead to issues maintaining high standards. Participants said:

> …often times the relying site doesn't really know where and what they need to communicate. —Research Administration Leadership Representative

> I think there are some inconsistency problems when we're the relying institution. And I think it's an education problem. —Institutional/Other IRB Representative

Eight participants said that they have **no concerns** about maintaining high standards when using a sIRB process. An investigator elaborated:

> No, not at all. For me there's been no difference. If anything, I think, because we are the IRB of record …I have been extraordinarily cautious because it's my first multi-site trial and I'm working with a vulnerable population. So, things that I'm pretty 99% sure are not questions for the IRB, or are not ethical human subject related questions, I still ask, and I still make sure that I've at least phoned my IRB contact or emailed when I have questions about things, and whether something requires reviews or doesn't…I think in some ways, being the IRB of record, sort of makes you on your toes even more because you feel responsible for all these other people, institutions, and their reputations, and their relationships with the community.

6.3.2.2 Local Context

Questions about local context were asked only of research administration leadership representatives, investigators, and study/regulatory coordinators.

Participants (n=21) discussed methods for providing and receiving local context information. Methods described were:

- Using forms and templates (n=14)
- Communicating directly with site (n=7)
- Providing information during reliance agreement discussions (n=5)
- Obtaining and incorporating information as part of administrative reviews (n=4)
- Using local context experts (n=4)
- Engaging in ongoing communication between the reviewing IRB and relying institution (n=4)
- Incorporating information about local context as part of the formal IRB review process (n=3)
- Including contacts and local context information as part of the institutional profile (n=3)
- Trusting that sites are providing accurate local context and that reviewing IRBs are incorporating it appropriately (n=3)
- Following Food and Drug Administration (FDA) guidelines for vulnerable populations (n=2)
- Documenting that each relying site has their own FWA (n=1)
- Having legal counsel reviews local context (n=1)

For "**forms and templates**," participants, mostly from a reviewing perspective, said these forms include local context sheets, consent forms in which Health Insurance Portability and Accountability Act (HIPAA) language can be adjusted, and site information sheets. Participants said:

> We will do that in terms of the local context sheets, the document that we have to provide when we sign onto the master agreement. — Research Administration Leadership Representative

> I have a site information sheet. It collects local contacts. I get that along with the reliance agreement itself. — Research Administration Leadership Representative

Participants, mostly from a reviewing perspective, said they use "**direct site communication"** to give and receive local context information. A regulatory coordinator said:

> If there's other stuff, you just have to communicate it directly to them. They usually have some forms or a contact, but it's a little strange.

Participants discussed that local context information is shared during the initial development of the "**reliance agreements"** between sites. Participants indicated:

> That's especially done at the time when the agreement is signed. There are templates through SMART IRB for local context. — Regulatory Coordinator

> [The incorporation of local context] ends up mostly being part of the IRB review. So, the general output ends up being on our IRB submission form or the researcher's submission form to the IRB and we ask them questions about it. And then, in our workflows from the IRB staff perspective, we have points where we remind the staff of this is happening in California, make sure that you look at XYZ. If this is happening in Texas, or Nevada then the age of majority's different in Nevada and in Alabama. So, we kind of have some prompts in our workflow. We ask the question in our application, but the researchers don't always answer them correctly and it's not always the best thing. So, you have to do it protocol by protocol but you also want to know if there's any at the reliance stage, you want to know if the institution has specific rules about things or it wants to make you aware of state law things that they interpret a special way because then you can build – what we do is we build it into our internal process checklist— Research Administration Leadership Representative

Participants discussed the use of "**additional administrative reviews"** to ensure that local context has been gathered and incorporated appropriately. A research administration leadership representative explained:

> That's what happens when you do the administrative review, and all the approved documents come in to you. You look for those things. And you're so well trained to it, because you live it every time you review any study, that it's automatic to check.

For "**local context experts**," participants explained, from the reviewing perspective, that experts are used to address local context related to specific ethnic groups or the social context of particular populations. In addition, local context experts are requested when there is a need for people available with expertise in specific areas. Research administration leadership representatives indicated:

> We're using it to assess—it could be something where our concern from a subject safety standpoint was that you had a person with sufficient expertise and discipline. So, we might ask as part of that local context questionnaire, "Please confirm that you have somebody who has expertise in X," right? So, part of it might be in our assessment of whether the site is even capable or resourced enough to perform the study as planned.

> When we have to go to other places, for instance, an American Indian reservation, we would try to bring

> in a consultant to look at that. The most obvious example is when we're called upon for prisoner research, when we're a central IRB, and then we have a number of people that we can call on as prisoner representatives.

For "**ongoing communications**," participants explained, mostly from the reviewing perspective, that they work with relying sites and communicate back and forth during multiple steps in the process to ensure that the local context is accurate and being incorporated correctly. A research administration leadership representative said:

> We kind of do it in two parts. There's some questions on our protocol submission form that ask for the local context like specific state laws that might affect the conduct of the study, and then there's some local context things that we ask about at the institutional level during the reliance agreement part. For example, even though this is legal, does your institution have a reason that you don't permit it? There are some organizations that do have those kinds of things.

Two participants said that a reviewing IRB that they partnered with did not incorporate the local context that they provided.

Participants (n=8) described positive experiences with communicating local context information. These experiences focused on:

- Using consistent and automated forms and templates (n=4)
- Monitoring and reporting by individuals who understand the new policy and can oversee the success of multiple sites (n=4)
- Using a SMART IRB form for all participating sites to explain local context to the reviewing site (n=1)
- Having a liaison who can review local context information and serve as a local point of contact (n=1)

Participants explained that keeping "**forms and templates"** standard and consistent helps to communicate local context effectively. A regulatory coordinator explained:

> I think the fact that they're overseeing five or six different studies under one umbrella, we know the form is standard. We know there's consistency and they're not changing their form. There is consistency in that form, and knowing what they're going ask, and what they need to report back and get it done, so that's been quick to turn it around.

Participants described that "**monitoring and reporting**" includes having staff who sign off on reviewing the applications and keep track of who can be contacted at each site if there are questions. A research administration leadership representative said:

> We make sure that we have sign-off by the local IRB or the relying IRB so that we know the IRB has reviewed it and has either completed parts of that or it has agreed to the information that's been provided. So, that's a good thing.

Participants (n=7) described negative experiences with communicating local context information. These experiences focused on:

- Lack of necessary infrastructure (n=2)
- Not tracking changes and or requiring periodic updates from relying sites about local context (n=2)
- Lack of standard forms and templates to ensure consistent local context is submitted by each site (n=2)
- Lack of a liaison who can serve as the point-person and can oversee the entire study (n=1)
- Limited incorporation of local context because local concerns outside of privacy language are rarely incorporated (n=1)

For "**lack of infrastructure**," participants explained that the infrastructure and staff time needed to address institutional considerations, and to ensure local context is communicated and incorporated accurately, is limited. A research administration leadership representative said:

> It's unclear sometimes who to provide it to or who is requesting it. Different institutions go about it differently of having either the IRB communicate directly with another IRB or for the study team to the IRB or the study team, the lead study team. So, what hasn't worked well is just not having a standard for how to communicate.

6.3.3 NIH sIRB Goals 3 through 5

Goals 3 through 5 are to allow research to proceed effectively and expeditiously, to eliminate unnecessary duplicative IRB review, and to reduce administrative burden.

These three NIH sIRB goals were explored simultaneously during the interviews. Participants in each group were asked questions about these goals; however, questions were tailored to the participants' roles or participation in the sIRB process.

6.3.3.1 Communications

Research administration leadership representatives, investigators, and study/regulatory coordinators (n=20) were asked questions about communication mechanisms when they relied on another IRB. Participants identified the following modes of communication between the reviewing IRB and study teams:

- IRB software (n=9)
- Email (n=8)
- Phone (n=6)
- In-person communication (n=4)
- Call center (n=1)
- Letter (n=1)

Some participants also identified various points of contact when describing how messages were relayed between the reviewing IRB and study teams. These are:

- Designated liaison (n=3)
- Study coordinator (n=2)
- Site PI (n=2)
- Direct communication with the lead PI (n=1)
- Local site IRB (n=1)
- Lead study team (n=1)
- Representative of the sponsor (n=1)

Research administration leadership representatives (n=8) listed modes of communication between the reviewing IRB and relying institution. These are:

- Email (n=3)
- IRB software (n=3)
- Forms and templates (n=2)
- Phone (n=1)
- Letter (n=1)

Some participants also described points of contact between reviewing IRBs and relying institutions, which are:

- Liaison (n=1)
- Site investigator (n=1)
- Lead investigator (n=1)
- IRB administrator (n=1)
- Lead study team (n=1)

A research administration leadership representative elaborated on relying on IRB software:

> There are these systems that I have actually found those to be, at least right now, extremely inefficient to communicating this information. I think they have some promise, and so I'm looking forward to where they go.

Research administration leadership representatives, investigators, and study/regulatory coordinators (n=14) described efficiencies of communication between the reviewing IRB and study teams, and between the reviewing IRBs and relying institutions; therefore, we combined the responses here. They are:

- Having a single point of contact (n=3)
- Minimizing touchpoints at the IRB office by training lead investigators (and having them train sites) (n=2)
- Working with competent study teams (n=2)

- Having a better protocol or quality of review in the end because of frequent communication (n=2)
- Having a call center (n=1)
- Having IRB software that assisted in organizing and tracking communications (n=1)
- Having support staff accessible due to an “open-door policy” (n=1)

Regarding “**a single point of contact**,” a research administration leadership representative said:

> It's efficient for us, in that, obviously, there's a single point person, and you also are guaranteed that the lead PI is aware of everything that's happening. I think when you do it one by each with the sites, not that you mean to do it, but it's easy to not keep the lead PI in the loop.

A range of responses were also given by research administration leadership representatives, investigators, and study/regulatory coordinators (n=13) on factors they found challenging or burdensome with their communication systems. Responses about communication between the reviewing IRB and study teams and between the reviewing IRB and relying institutions are combined. These factors include:

- Increased workload (n=5)
- IRB software not fulfilling potential (n=4)
- Unknowledgeable staff (n=4)
- Having the lead study PI communicate with the relying sites (n=3)
- Having to rely on a point person for communication (n=2)
- The cost of maintaining the “open-door” communication policy (n=1)
- Security features that make email difficult (n=1)
- Managing documents in an accurate and standardized manner (n=1)

For “**increased workload**,” participants described the burden of having to manage and be responsible for all of the relying sites. Research administration leadership representatives said:

> It’s definitely a lot more work for the lead team and it can be very cumbersome to manage multiple sites in our systems and to manage the documents and requirements that go along with that.

> I think that the burden might be a bit heightened when we serve as sIRB, because there’s just that underlying knowledge that we’re responsible for all of these sites and we need to make sure they’re all in order.

For “**IRB software systems**,” participants spoke about the systems not having functionality that would support their needs, particularly the ability to allow outside institutions to have access to exchange study documents with reviewing IRBs using the IRB portals. A study coordinator described:

> I think that it has not been overly efficient. You know there is an online portal where we can go in and download some of our stuff. But, for instance, there was recently a protocol amendment approved by the sIRB of record and that was not automatically distributed to everyone…I feel like if you have the universal portal, that’s what it should do.

For "**unknowledgeable staff**," participants described interacting with institutional or study staff who lack either the knowledge or the engagement to make communications more efficient. Participants also described challenges that arose when an unskilled study team served as go-between because of the potential for communication breakdowns, delays in sharing information, and potential confusion on the behalf of study teams. A research administration leadership representative stated:

> We had another experience with an NIH funded multi-site study where they had a program manager who was very knowledgeable and very engaged, and very good at facilitating communication amongst the stakeholders involved at all the sites and the IRB. And she was just so knowledgeable and so good that it just – it was the easiest thing for everybody was to have the communication between her and the IRB and then she disseminated it out. She knew who to call to get things moving and to get action. She, I would say, would be the exception – I don't commonly come across somebody who is so knowledgeable and engaged in the management of multi-site study at the lead PI site.

For "**having the lead PI communicate with the sites**," participants mentioned that this mode was inefficient and that they preferred direct contact with the sites. A research administration leadership representative said:

> It's like playing telephone, like when you were a kid. You don't speak IRB speak. You're communicating it to the local investigator. They're coming back to you. You're communicating back to me. It's not great.

For "**relying on a point person**," participants described difficulties when the point person is overburdened, out of the office, or when staff turnover happens. A research administration leadership representative said:

> The history of the whole file is gone, you know. They have to go back and piece it all back together. It's hard for them. It's just like jumping into anything that's halfway started.

6.3.3.2 Roles and Responsibilities

Research administration leadership representatives and other IRB and institutional representatives (n=16) described numerous activities they continue to engage in as relying institutions. The most frequently mentioned roles included:

- Adhering to privacy practices, including documentation (n=7)
- Conducting ancillary reviews (n=6)
- Conducting compliance and oversight responsibilities (n=5)
- Conducting "shadow reviews" (n=4)
- Completing auditing and monitoring tasks (n=3)
- Providing administrative support from IRBs to local study teams (n=2)
- Making determinations of whether reliance is permitted (n=1)
- Reviewing consent forms (n=1)
- Conducting continuing reviews and reviewing study amendments (n=1)
- Reviewing data usage/transfer agreements (n=1)
- Tracking progress of any given protocol (n=1)

For “**adhering to privacy practices**,” a research administration leadership representative explained:

> Largely, HIPAA is staying with us, at least right now, because I can’t rely on these IRBs to actually carry it out, so that would be issuing HIPAA waivers. Assessing our HIPAA authorization form has been a regulatory compliance thing that sticks with us. We’re happy to do that though, because we have some weird state laws that only we really know how to do, and we’re set up to do that.

For “**conducting ancillary reviews**,” participants specifically mentioned verifying trainings for research personnel, and also completing the conflict of interest reviews. A research administration leadership representative described the activities involved with the conflict of interest reviews:

> We still have to do the conflict of interest and make sure we communicate that to the overall big body. They might ask the conflict of interest questions too with regards to that specific study, but they might not know the history, right? We do still have a responsibility in some of those aspects.

For “**conducting compliance and oversight responsibilities**,” participants mentioned ensuring that institutional policies and state laws are followed, and also monitoring and reporting if any misconduct and/or adverse events occur throughout the life of a trial. A research administration leadership representative described the rationale for remaining involved in these types of oversight duties:

> While we may not be the reporting entity for something like a series of continuing noncompliance, we can be and may need to evaluate independently on our own, especially if it involves local resources.

For “**conducting shadow reviews**,” participants said that, although the ethical review was performed elsewhere, all or some portion of the review that considers ethical issues still occurred at the relying institutions. Such reviews have included separate scientific reviews and extensive administrative reviews. A research administration leadership representative elaborated:

> We’re insuring that the IRB of record’s review is consistent with our policies and procedures. So, there’s an ethics review that figures into that, along with a scientific review.

For “**completing auditing and monitoring responsibilities**,” a research administration leadership representative characterized this as the “ongoing responsibility for oversight of the safety of subjects on site.”

Four participants said most responsibilities remain at the relying institutions but did not list specific activities.

Research administration leadership representatives and other IRB and institutional representatives (n=14) described activities that shifted from their institution to the reviewing IRB. The most frequently mentioned activities are:

- Ethical review of the study protocol (n=7)
- HIPAA determinations (n=3)
- Ancillary reviews (n=2)

- Reporting requirements (n=2)
- Compliance with federal requirements (n=1)

For "**ethical review**," an institutional/other IRB representative described what this entailed, including the review of consent forms:

> It [becomes] their job to technically do this ethical review. And that goes along with reviewing the informed consent for things like, you know, comprehensiveness and whether or not people can understand it and things like that. So, reviewing like language actually on the informed consent, and how that reads, readability of the consent becomes their problem. And then, you know, protocol questions, whether or not the protocol is appropriately designed.

For "**HIPAA determinations**," a research administration leadership representative said:

> We served as a privacy board or an arm of the privacy board. So, we make HIPAA determinations for our own studies. But when we have a reviewing IRB, we say it's all or none. We either make the determination or you do. We've gotten agreements back that say oh, well. If you want to make the determination or we'll make it together or whatever like that, we don't accept that.

Some participants were less descriptive and simply explained that **few or no activities shifted**, maintaining that they still did everything they would do if they were the IRB of record.

Research administration leadership representatives and institutional and other IRB representatives (n=7) described the following success with how they have divided responsibilities. Areas of success are:

- Efficiencies gained with the shifting of responsibilities, including having fewer research staff involved (n=2)
- Allowing reviewers to use their time for other important matters (n=2)
- Having only one entity, the IRB of record, responsible for reporting (n=1)
- More room for collaboration and interaction between IRBs (n=1)
- Being able to create the terms to be a fully reliant IRB (n=1)

For "**having fewer research staff involved**," participants reflected that fewer studies require full board review and that fewer staff are needed overall because multiple IRBs are not reviewing the same modifications.

For "**focusing time on other issues**," participants talked about how the division of responsibilities allowed them to either tend to other important local issues or spend more time reviewing other types of trials (e.g., commercial studies).

Four participants reported no issues, stating that their role was "not very complicated when it comes to relying," and they have encountered "a pretty smooth work flow" overall.

Research administration leadership representatives and institutional and other IRB representatives (n=10) described the following challenges with how they have divided roles and responsibilities:

- Little to no gain in efficiencies (n=2)
- Lack of established systems or processes (n=2)
- Still having to assess consent forms for institution-specific language (n=1),
- Still having to verify trainings of staff involved in research (n=1)
- Confusion among study teams about the array of varying policies and procedures (n=1)
- Being subject to another institution's unfamiliar policies when auditing (n=1)
- Experiencing a loss of knowledge of current research trends due to having to review more commercial studies (n=1)

For "**little to no gain in efficiencies**," participants described a lack of efficiency in general terms and the amount of effort spent gathering information. A research administration leadership representative said:

> I would love to get rid of these regulatory responsibilities. I'd be happy for them to take it. What's the challenge is that if they don't take it, the review I have to undertake in order to do that takes almost just in that same amount of information in order to issue those waivers as it would for us to gather the information in order to make the determinations under the Common Rule, if that makes sense. So we had based those into our review to the Common Rule, and they were kind of overlapped and seamless, and so we didn't have to collect additional information. I now have to collect almost the same amount of information as I would if I were reviewing to the Common Rule.

Participants described the "**lack of established systems or processes**" for supporting the sIRB model. An institutional/other IRB representative said:

> I think it's just that we don't have a national system around this. So, everybody's doing it a little differently. I think the policies are…so variable across institutions, which is good in some ways. You know, everybody needs their policies to work for their people and align with their institutional priorities. It's not realistic that everybody could have identical policies. But that's going to be the biggest difficulty over time is variability.

6.3.3.3 Duplicative Reviews

Participants (n=28) spoke about activities they found to be duplicative between the reviewing IRB and the relying institutions. These activities are:

- Conducting "shadow reviews" at relying institutions (n=9)
- Completing multiple documents and forms (n=7)
- Conducting ancillary reviews (n=6)
- Reporting of adverse events and noncompliance (n=3)
- Verifying training requirements of research staff (n=2)
- Reviewing the risk profile of the study (n=2)
- Submitting documents to sponsors (n=1)

- Processing amendments and continuing reviews (n=1)

For "**conducting shadow reviews**," participants described having an ethics review conducted by both the reviewing IRB and the relying institution's IRB. Representatives from one institution interviewed said they conduct an ethics review of protocols that are also reviewed by a sIRB. While quicker than a full board review, these types of reviews still closely scrutinize the ethics as they relate to risk and liability and are similar to what happens during an expedited review process. A research administration leadership representative explained how frustrating this can be for investigators:

> [Investigators are] always disappointed when they hear that [further reviews are required beyond the IRB of Record], because they think they got out of it – but that's the only platform right now for which all of [name of institution] research is entered and described. There's really nowhere else… And the sequence is a bit frustrating and ineffective for them, because they submit the study, once it's been approved by the central IRB they submit it in [name of institution] system. The [clinical entity at institution] review still takes place, and they invariably want changes that can't be made… And then when they get to the point of [clinical entity at institution] review complete, they have to stop, and if it hasn't already been reviewed by the central IRB, they have to send all of their documents to the central IRB. Then it comes back approved, and then it comes to us for our administrative review. And that's very frustrating to have to stop, take all of your documents, load it into the central IRB software, and get their review back.

All other participants who discussed shadow reviews described experiences they have had, when their institution served as the sIRB, in which relying institutions' IRBs also provided ethics reviews. These participants clarified that their own institution did not provide a duplicate ethics review when they relied on another institution. A study coordinator explained that these shadow reviews sometimes occur due to a lack of understanding or lack of trust:

> I think that [duplication] was on the relying IRB for not understanding and not trusting the process. So, that's when I would talk with the site coordinators, and they're like, "Oh, yeah, my study is going to go to the board on this day," and I'm like, "It should not go to a board, what are you doing?" And then because we were trying to get people up and going, then I'd call [Name], and I'm like, "[Name], would you reach out to this person?" because each of the relying institutions were supposed to have an administrative person who's responsible for helping facilitate this.

For "**completing multiple documents**," participants' expressed concern with having to provide the same information to multiple institutions in slightly different formats. This requirement applied especially to local context forms and reliance applications. However, the back-and-forth nature of wordsmithing consent form language was also mentioned as being duplicative. A research administration leadership representative explained:

> There are some relying institutions that still undertake a review of the consent form, according to their own standards, which, arguably, is duplicative.

Investigators also described their frustration with the extra effort taken to submit an entire application to two IRBs—or being tasked with uploading all the approved documents from the IRB of record into the relying institution's IRB software. Investigators also spoke about delay in the review process and getting their study up and running due to approvals being required from both institutions. A study coordinator said:

> We had our sIRB approval to be a participating site and then had to submit everything through all of our review processes at [the reviewing institution], and then a couple months later we got IRB approval for the study here at [home institution]. So, it took just as long as if we would have submitted it normally. And there was still just as much information that we needed to supply to our [home institution's] IRB system as there would have been if it was the IRB of record.

For "**conducting ancillary reviews**," participants pointed out that these types of reviews sometimes happen at both the IRB of record and the relying sites. Participants spoke of reviews for radiation safety, HIPAA requirements, and conflict of interest specifically. A research administration leadership representative said:

> A lot of reviewing IRBs that are like independent IRBs will just say, "Hey PI, you tell me whether you or anybody has a conflict of and if there's a management plan." We don't do that. We ask everybody to fill out a report form and tell us about conflicts of interest and then we go back to the organization and say, "Oh, by the way we got this report from this PI, did you have this report? Did you want to look at it? You need to tell us what to do with it." So, there's a little bit of duplication there. They might already have it and then sometimes they'll say, "Oh no, we didn't know that so and so had this." So, now they have to go back to the investigator and follow-up on that conflict of interest review. So, those are some of the duplicative processes.

Several participants said that a certain level of duplication was necessary, and that duplication did not equate with a flaw in the sIRB model. These participants explained that it was essential for an institution to embark on some reviews to maintain a level of knowledge about the types of activities their institution would be involved in. A research administration leadership representative said:

> You have duplicative documents, and it's needed, because we need to know what's going on—the reviewing IRB is the IRB of record, so they of course have to have those documents. And some people would be like, "why does that relying site have to have it?" And it's, like, because it's happening here, we need to have some pulse of what's going on.

Four participants reported they did not consider any activities to be duplicative.

6.3.3.4 Administrative Burdens

Participants (n=32) described numerous administrative burdens both when serving as a reviewing IRB and when relying on another IRB.

Research administration leadership representatives, investigators and study/regulatory coordinators, and institutional and other IRB representatives (n=18) described the following administrative burdens when relying on an external IRB:

- Information gathering (n=5)
- Communication (n=4)
- Entering protocol information into the local IRB software by local site teams (n=4)
- Monitoring and reporting (n=3)
- Compliance (n=2)
- Shadow reviews (n=2)
- Reviewing consent forms to make sure they are following institutional policies (n=1)
- Negotiating reliance agreements (n=1)
- Verifying that training requirements of staff have been met (n=1)
- Conducting ancillary reviews (n=1)
- Having to repeatedly provide redundant information (n=1)
- Preparing for unforeseen events (n=1)
- Having to decline to give advice to local study teams that are relying on an external IRB (n=1)

For "**information gathering**," participants described obtaining updates on the status of the study as a challenge, because that information was not readily available or regularly provided. Participants also mentioned the difficulty of obtaining finalized forms and approvals from the IRB of record to file in-house, the challenge of conducting an audit on a study even when the site IRB was not the IRB of record, and how tedious it can be to collect information from an external institution about "someone else's systems, logistics, technology, rules, policies, all of that." An institutional/other IRB representative explained:

> Understanding the status of a study. Yeah, I think local context but I think we have a decent process for that. But I think, bigger picture, if our administration wants to know what studies are being conducted, what's the status, they've historically been able to rely on the IRB for that information. They can't anymore.

For "**communication**," participants described challenges with communicating with lead institutions to nudge them for updates, the burden of being notified only after reportable events that occurred at their site had been reported to sponsors and federal agencies, and the inherent challenges of communicating with individuals outside their institutions, especially when they were in different time zones. A regulatory coordinator elaborated:

> When we're the relying institution, the administrative burden is just insuring communication happens. A lot of times the reviewing institution doesn't push out documentation in a timely manner and you discover, oh, we're a protocol behind. Oh, I didn't know this change happened. So, that tends to be the issue and you realize, well, crap, we're working off old stuff and can you update us?

For "**entering information into the IRB software**," participants described the burden placed on study teams at relying sites in the context of having to serve as a liaison with the site IRB to ensure that all information communicated from the IRB of record was appropriately relayed and entered into local IRB software.

For "**monitoring and reporting**," participants described the task of monitoring the IRB of record to ensure they are following the procedures they agreed to as burdensome, having to problem-solve about a reportable event after the event was reported, and the challenge of monitoring other sites without being familiar with their policies and procedures. An institutional/other IRB representative said:

> [Relying on another institution] doesn't take any weight off me. It actually increases my burden in the sense that we're doing the exact same things as the study team is but we're struggling with somebody else's system. How are we going to pull all that information out?

Two participants said there were **no administrative burdens** when they were relying on another IRB.

Research administration leadership representatives, investigators and study/regulatory coordinators, and institutional and other IRB representatives (n=28) described the following administrative burdens when <u>serving as the reviewing IRB</u>:

- Document handling and organizing (n=8)
- Communication with relying sites and sponsors (n=8)
- Information gathering (n=6)
- Issues related to deficiencies in IRB software systems (n=6)
- Document review (n=3)
- Human resources needed (n=3)
- Monitoring and reporting (n=2)
- Creating and getting sign-off on reliance agreements (n=2)
- Ultimately being in charge of the entire study (n=2)
- Managing participating sites (n=2)
- Providing advice and education to those who are unfamiliar with the process (n=2)
- Billing for services (n=1)
- Burden on the lead study team to interface with other institutions that have different policies and requirements (n=1)
- Making determinations about the capacity to serve as the reviewing IRB (n=1)
- Volume of reviews to manage (n=1)

For "**document handling and organization**," an institutional/other IRB representative provided context to the issue:

> The main administrative burdens would be all of the document handling. If it weren't for the coordinating center, someone at the lead site would have to create all of the documents. Even if there's a template, we're reviewing all of the documents from all of the other sites. It's the creation, maintenance, and distribution of documents, of protocols, of procedure manuals.

A research administration leadership representative said:

> I think we had one that was a minimal-risk study, but had 50 different sites, and they all wanted their own approval letters and they all want their own consent form templates. So it's up to that reviewing IRB to keep track of all of those. So, that could be, you know, every time there is an amendment, you might have to change 50 consent forms. And that's a lot of work for one IRB to do.

For "**communication with relying sites and sponsors**," participants described that there was a lot of back and forth to get up and running every time a site was added when they were first implementing the sIRB model, and the burden of time lost due to communication bottlenecks for staff assigned to review certain aspects of the protocol when they were overburdened or away from work. A research administration leadership representative described the burden of managing the bulk of email communication:

> All of the email communication with the lead investigative team—they know what they typically do, but now they've got a site asking the questions and they don't know how to answer it. So, we're getting lots of those sorts of things.

For "**information gathering**," participants mentioned the burden of obtaining complete information on initial requests from relying IRBs, and the challenge of having to be persistent about obtaining local context information from participating sites. An institutional/other IRB representative said:

> When we're the reviewing IRB, it's not getting information from the study team, it's getting information from the other IRB. It's getting all of the local context information, like, complete. It's getting the right information from them the first time. I can't tell you how many times we'll, like, they'll say, "Okay, here's the language I want in my consent form." And we'll get their consent form ready, and then they'll come back, and they'll be, like, "Oh, by the way, I also want you to put these five things in there." Well, you already, I'm already half, I'm almost done. So, I think it's a matter of getting the right information from them the first time, the local context information. And then the other big piece, when you're the reviewing IRB, is that a lot of times you can't get that information from the relying institution's IRB, because the relying study team hasn't provided the right information to their IRB.

For "**IRB software**," participants described how their software systems were not designed for a high volume of document processing and storage. The combined investigator/study coordinator interview said:

> We use [IRB software] here at [name of institution]. And it is not designed to support so many documents. It is very, very slow and cumbersome. So, if you need to submit multiple documents, each one takes a long time. On a scale from 1 to 100, right about five. It's bad. It's bad. People really struggle to just, to get from one screen to the next can take five minutes sometimes. And you have 40 documents you upload. You can just imagine the frustration. You can spend the whole day there while this thing is doing nothing. It's horrible.

Other participants described the extra time and effort required to build these software systems, and the systems still not functioning to a level that was adequate for the job. A study coordinator also mentioned the shortcomings of the notification feature that was built into their software platform:

> When you make a notification inside of our system, like, if we list all the principal investigators, all the relying institution principal investigators as site personnel within our IRB, every single notification—whether it's a submission or approval—gets sent to everybody and whether it applies to that site or not. And so, that was one thing that we were, like, "Well, we're oversaturating the system to where people are not going to pay attention. They're, like, 'Here's another random message from [name of university] that doesn't apply to me.'" So, when would somebody know when it does apply to them? And that was some problems we had with system functionality.

6.3.3.5 Burden Comparison: Local IRB Model vs sIRB Model

Research administration leadership representatives, investigators, study/regulatory coordinators, and institutional and other IRB representatives (n=23) described whether the sIRB model, in comparison with the local IRB model, was associated with more burden, less burden, comparable burden, or a different type of burden.

6.3.3.5.1 From the Perspective of a Relying Institution

Participants (n=3) who stated that the **burden was more** reasoned that reliance agreements were infrequently used before the policy, that figuring out how to manage the repository of information was previously more straightforward, and that they had to solicit information from fewer sources before the sIRB policy.

Participants who believed there was **less burden** (n=2) mentioned the efficiencies in terms of time that were gained with reliance agreements, once established. One participant spoke about the effectiveness of having a single standard consent form that allowed for minimal changes.

Of the participants (n=4) who said that the **level of burden was comparable**, reasons were that obtaining accurate information from researchers remains an issue. Participants also said that the standardization of the process currently leads to the same level of burden but could eventually lead to more efficiencies over time.

Participants who commented on the **burden being different** (n=2) said that the burden had merely been shifted. A research administration leadership representative said:

> In terms of the third goal, reducing administrative burden, I completely disagree. This is a completely different type of work. And the work has been shifted onto the IRB administration process. And yes, it's true, the committee itself is relieved of work. The local site investigator is relieved of work. But the IRB administrative burden is significant.

6.3.3.5.2 From the Perspective of a Reviewing IRB

Participants who considered the sIRB model to be **more of a burden** (n=11) cited the lack of established relationships and/or processes, the hurdle of incorporating local policies and regulations when using the sIRB model, the growing complexity of reliance agreements, the learning curve associated with using a new model, and the resources needed for the administrative work that comes with using the new model. An institutional/other IRB representative described the lack of familiarity when working with new IRBs:

> Prior to the single IRB policy, I only had to know my own institution's policies. I had to know how my IRB wanted to see my consent form structured. I needed to put things in a format that my IRB was going to review, and I think because you have some common framework, I understood what the IRB was asking me if they had a question. Now, I feel like there's a little collective unease, a little uneasiness for the relying sites. When something's going to the IRB, it's definitely much more closed off and separated. There isn't a relationship there.

The participant who felt the sIRB process was **less burdensome** (n=1) cited time to approval as the main factor, stating that approvals with the local IRB model took longer:

> [Prior to the sIRB model] you had to get your IRB all the way done and signed, sealed, delivered and send it off to somebody else. And then they were ripping it apart and sending it on. Do your IRB again. It was just a very long process. So, [the sIRB model is] still better.

Participants who stated the **burden was comparable** (n=4) focused on their institution not yet having enough experience to see additional burden, with one specifying that it certainly has not grown any easier, but is not harder either.

The single participant who said it was a **different type of burden** described the greatest burden as communication and stated that there were now more staff to assist in that process, which came with a new set of benefits and challenges.

6.3.3.6 Time Comparison: Local IRB Model vs sIRB Model

Participants (n=27) were asked how, if at all, the amount of time needed for providing IRB and other reviews and activities had changed under the sIRB model compared with the local IRB model.

6.3.3.6.1 From the Perspective of a Relying Institution

Investigators, study/regulatory coordinators, and other IRB and institutional representatives (n=3) said that the sIRB model required <u>more time</u>. Participants said more time was needed because the sIRB met less frequently than their own institutional IRB, which made the process take longer; because no processes were in place for establishing reliance agreements; and because more involvement was required from institutional officials to make determinations about whether to cede review to another institution. An institutional/other IRB representative said:

> One thing that I touched on but I haven't really talked about is the leadership or management time that has to go towards this. It's a lot heavier and needing higher level input. I can have my average study screen reviewed by what most people call IRB analysts, and everything can just go through that process without much management touch. This requires a lot of management touch. It's an institutional decision whether or not to rely. And that can't be made by one of my IRB analysts or my screeners is what we call them. I don't think that will change over time. I think that needs to live at a high level. It is an institutional decision.

Investigators, study/regulatory coordinators, and research administration leadership representatives (n=3) said the sIRB model required <u>less time</u>. Reasons included not having to conduct the ethics review as a relying institution, not having to conduct a full board institutional review as a relying institution, and having an IRB of record that met more frequently than the institutional IRB of the relying institution.

Research administration leadership representatives, investigators, and study/regulatory coordinators (n=3) said the sIRB model required the <u>same amount of time</u> as the local IRB model. Participants explained that time was still spent obtaining institutional approval when relying on another institution and to prepare submissions. Overall, participants felt that any time they may save from relying on another institution was spent when serving as the sIRB. A research administration leadership representative said:

> I think it's a wash. I would say we probably rely as much as we review.

6.3.3.6.2 From the Perspective of a Reviewing Institution

Research administration leadership representatives, investigators, study/regulatory coordinators, and other IRB and institutional representatives (n=10) described the following ways in which the sIRB model requires <u>more time</u>:

- Gathering information and coordinating responses to sites (n=5)
- More amendments (n=2)
- Learning curve (n=1)
- New job positions (n=1)
- Establishing new relationships (n=1)
- Lack of established systems (n=1)
- Assisting sites with audits (n=1)
- Responding to reportable events (n=1)

For "**gathering information and coordinating responses to sites**," participants said the sIRB model requires more time to collect and process information and potentially respond to it. An institutional/other IRB representative said:

> There's more back and forth and more complexity and it takes more time to get the information that we need, I think. Or it's harder to get the information we need.

For "**more amendments**," participants spoke about the added time required for processing amendments to add new study sites and for reviewing general protocol amendments for any approved sites. A research administration leadership representative said:

> It's really the process of adding multiple sites [via amendments]. And you know I think it gets exponentially more complicated when you have greater than five sites or greater than ten sites because then you're just wading through so much information.

Research administration leadership representatives, investigators, and study/regulatory coordinators (n=4) also described situations in which the sIRB model requires <u>less time</u>.

Participants described that less time is needed with the sIRB model when reliance agreements do not need to be negotiated or had been previously established. In addition, less time is needed when there is less communication overall, when standardized documents are used, or after their IRB has established a sIRB workflow. A research administration leadership representative said:

> Our time for reviews have decreased. So, we've been able to open trials, all trials, sooner than we were before because our whole IRB is operating on a more efficient level.

Other research administration leadership representatives, investigators, study/regulatory coordinators, and other IRB and institutional representatives (n=7) reported the amount of <u>time did not change</u>. The following reasons were given:

- Time shifted to different entities (n=2)
- Reliance terms must be negotiated (n=1)
- Continued need to conduct amendments and negotiate consent language (n=1)
- Continued need to conduct ethics review (n=1)
- Having good processes in place (n=1)
- Necessary time for collecting and submitting materials (n=1)
- No net difference when your institution both relies and reviews (n=1)

Two participants said <u>the amount of time did not increase or decrease, but was different</u> or had shifted from the participating sites to the reviewing IRB. An investigator said:

> There are two questions. One thing was, does it change the actual amount of work? And then the other one is about moving the work. So, it did – even when it was the first time, and there was this learning curve, and there was the right agreement that had to be signed, it did lessen the work for the sites. It just moved it to here [sIRB], so our sort of gestalt about it was that it wasn't that it saved absolute time, but that it definitely moved who's responsible – you know, it shifted the work.

6.3.3.7 Study Startup, Recruitment, and Conducting Research Efficiently: Local IRB Model vs sIRB Model

Three probes were asked of investigators and study/regulatory coordinators: (1) whether the sIRB process had affected study startup time, (2) their ability to recruit research participants, and (3) their ability to conduct research efficiently.

6.3.3.7.1 Study Startup

Participants (n=5) provided their perspectives on study startup time, with three participants saying the sIRB process had improved study startup time (one said gradually, over time), one saying it had slowed it down, and one mentioning there were too many confounding factors to be able to accurately assess the impact.

6.3.3.7.2 Recruitment

Participants (n=8) said the new sIRB policy had no impact on recruitment, while one participant maintained that the new model had slowed recruitment because of the longer approval process for social media recruitment posts.

6.3.3.7.3 Conducting Research Efficiently

Participants (n=7) discussed study conduct, with several stating that once the sites are up and running, the ability to realize some efficiencies had improved. Two participants noticed a trivial improvement, and two stated that the sIRB model had no impact on their ability to conduct research efficiently.

6.3.4 NIH sIRB Goal 6

Goal 6 is to prevent systemic inefficiencies.

Participants in all groups considered whether the sIRB process prevents systemic inefficiencies. Questions focused on perceptions of (1) inefficiencies with the local IRB model, (2) how the sIRB model addresses those inefficiencies, and (3) new inefficiencies associated with the sIRB model.

Participants (n=27) described the following inefficiencies with the local IRB model:

- Duplication (n=8)
- Heavy workload (n=6)
- Need for local control (n=4)
- Lack of consistency n=4)
- Varying language on consent forms (n=5)
- Different dates for submission required for different sites (n=3)
- Site differences in reviewing applications and different opinions on acceptable “cut-off points” and expiration dates (n=2)
- Variation in determinations made at each site (n=2)

- Adverse events that vary in severity based on the number of participants in total who have been involved in the study (n=1)

For "**duplication**," participants described having to complete the same IRB forms at every site and having the same protocol reviewed multiple times by multiple sites. Participants also said that duplication in IRB review led to a less efficient review process because study documents and protocols were reviewed independently by each site involved in the multi-site study. Participants said:

> Having to do your IRB 800 times…every IRB at each institution kind of putting their own stamp, which usually didn't have any big significant changes. — Investigator

> Just having the same study reviewed over and over again just doesn't really make good sense, so that's an inefficiency. — Investigator

Participants explained that "**heavy workloads**" included having to keep track of IRB reviews and multiple review times at multiple sites, having multiple boards reviewing the same protocol, and reviewing lengthy communications from the reviewing IRBs. A study coordinator said:

> I think with the local IRB model, from the coordinating center perspective, one of the big inefficiencies was having to keep track of everyone's IRBs and having to keep track of who is doing the submissions and what information you need back from them and all the different deadlines that they have. Continue to review deadlines and all that kind of stuff.

For "**need for local control**," participants said that the local IRBs' desire to exercise local control over reviewing the protocol and IRB documents led to inefficiencies. Participants also said that often IRBs were compelled to insert their own language into the documents being reviewed, which resulted in increased differences and inefficiencies. Participants elaborated:

> I think most people in IRB or regulatory are control freaks. It's hard, and we have to remember many ways to do the right thing. — Research Administration Leadership Representative

> Many of the IRBs will ask similar questions, and then the coordinators at all these different sites have to answer the same questions. And even if the central site provides answers, there is still this whole process of back and forth and back and forth. And then, also, once a site looks at, gets approval locally, we have to review and make sure that they actually didn't change something in the consent form that made a different study or is wrong; so that has to get reviewed again. Right, so you're just talking about reviews, and reviews, and reviews. — Investigator

"**Lack of consistency**" occurred, explained participants, when multiple IRBs reviewed the same protocol and provided different feedback or prioritized different components of the application. In addition, some of these inconsistencies included the different types of documentation required and the specifics included in the protocols being reviewed. Participants said:

> You've got 12 different IRBs that all want something different, and I'm not sure that it's all value added. — Research Administration Leadership Representative

> I think the local IRB model before was inefficient. I think there was just room for a lot more disparity between the sites in terms of their documentation before. So, one institution's IRB might've required rewriting of a whole section. — Institutional/Other IRB Representative

For "**varying language**," participants described how having multiple sites review the same consent forms results in minor language changes in the forms due to the subjective preferences of the various IRBs and multiple templates. Participants said:

> Each of those IRBs are you know, providing feedback that's a little bit different from the others, so I think that's what --- that's the biggest inefficiency in the single site model. Is that now you have IRBs you know, 15 different IRBs who all have slightly different revisions to the informed consent, or the protocol, or whatever. — Institutional/Other IRB Representative

> I think the biggest thing is consent forms. One institution will say, oh, this language needs to be updated in the consent. And then do we go through a process involving 14 different consents, or do we roll that consent back through every IRB to try to get them back on the same page? I think consent forms have been the biggest inefficiency. And that can happen to some extent with protocols. But IRBs generally lay off the protocol and go crazy on the consent. — Institutional/Other IRB Representative

Participants (n=19) provided the following examples of how the sIRB process addressed the inefficiencies with the local IRB model:

- Improved consistency (n=7)
- Decreased workload (n=6)
- Reduced duplication (n=4)
- Streamlined language and templates (n=2)
- Improved efficiency by making tracking and amendments move faster (n=2)
- Improved subject safety (n=1)

Of note, this question was not asked of all participants when it was clear to the interviewer at this point in the interview that the participant had several concerns about the sIRB process.

For "**improved consistency**," participants discussed the consistency of language in consent forms, which has helped to improve on inefficiencies of the overall review process. Some participants also mentioned the overall consistency of the review that occurs when one IRB is responsible for the entire review. An institutional/other IRB representative said:

> *When there is a single IRB model, we feel, at least most institutions feel a little less compelled to wordsmith. Which I think is good. I think it has helped some of those things.*

For "**decreased workload**," participants discussed the amount of time that becomes available for other jobs when the institution serves as the relying site for a study. Participants said:

> *And we can now throw more of our attention into the high-risk studies that present more liability to the institution, mainly the [name if institution] PI initiated single-site studies. Now we have more manpower to throw onto those.* — Research Administration Leadership Representative

> *I think for the relying sights, I think there is quite a bit of reduction. They get to say, "These are our policies. Make sure that the documents all meet our standards."* — Institutional/Other IRB Representative

For "**reduced duplication**," participants observed that tasks has been reduced. A research administration leadership representative said:

> *Well, it's certainly taken away the duplication in effort.*

Participants (n=29) described the following inefficiencies that were created with the introduction of the sIRB model:

- New roles and responsibilities (n=7)
- Lack of systems and processes (n=6)
- More reviewing responsibilities (n=5)
- More burden on researchers (n=5)
- More document handling (n=4)
- Duplicative activities (n=4)
- Lack of trust in external IRBs (n=3)
- Amendments leading to "double reviewing" by the central IRB and the local IRB (n=2)
- Cost to implement systems similar to commercial IRBs and lack of funding to support the development of these systems (n=1)

For "**new roles and responsibilities**," participants spoke about the amount of training and education required in preparing staff for their new sIRB roles and responsibilities. In addition, some participants said inefficiencies were created by having to determine what roles fall under the responsibility of the IRB vs what roles remain the responsibility of the institution. Participants said:

> [Inefficiencies were created] because of the training time it takes, either from the lead study team or from the IRB office, in training those external site personnel to the requirements of the [reviewing] IRB. — Research Administration Leadership Representative

> I think it's largely figuring out, getting the institution to understand what our institutional responsibilities versus IRB responsibilities, and determining how those are going to be handled and where those are going to live. — Institution/Other IRB Representative

For "**a lack of systems and processes**," participants explained that academic institutions do not have processes in place to serve as the sRB efficiently. In addition, some participants said no systems are in place for supporting the sharing of updates and changes of documents between sites. Participants said:

> And again, a lot of that is just because this process is still new, and the IRBs who are doing this don't have the right resources and the right processes in place to do this. If we had, frankly, if there were an NIH central IRB that everybody had to use for all of your NIH studies, all of this would be fine. Because that one, in theory, that one IRB would have processes in place, it would look like a commercial IRB. And if it had the resources and the systems of a commercial IRB, then a lot of these systemic inefficiencies would be solved. The real problem is that we just don't—academic IRBs are not in a place where they can act like that yet. — Institution/Other IRB Representative

> …the new inefficiencies would be the negotiation of separate agreements, lack of support for communications and sharing of updates and amendments, continuing approvals, [adverse event] reporting, things like that. —Research Administration Leadership Representative

For "**more reviewing responsibilities**," participants said the amount of personnel time required for reviewing sites with the sIRB model must be considered for staffing needs moving forward. Participants said:

> I think as the reviewing IRB, you just have a lot more responsibility, and not taking that lightly is really important, so I just don't think anybody who is the reviewing IRB is thinking, "Our work is going to be reduced." — Institution/Other IRB Representative

> I think just the time and the personnel that needs to be involved in the process to get it done in a reasonable amount of time. So I think the IRBs that are serving as the reviewing IRB are going have to think about their human resources to get it done. — Institution/Other IRB Representative

For "**more burden on the researchers**," participants said there is burden associated with having to keep track of which rules apply to which protocol, depending on who reviewed it, as well as the ins and outs of processes of the reviewing sites, especially for researchers who have multiple active protocols at multiple reviewing sites. Participants said:

> I think investigators are going to have a real hard time keeping track of which rules they're supposed to follow for which studies. I think they need some mechanism to know, or we as a community need to come to some consensus on the things that typically vary from IRB to IRB, and say, "Okay, everybody, let's agree that unanticipated problems are reported within 10 days. Everybody's going say 10 days and that's fine. Nobody's—you know, let's all change our policy to agree to that. Some say within 30 days and some say within 5 days. So, that's an inefficiency that I don't think we anticipated. How are people going to manage meeting the obligations of those reliances? — Research Administration Leadership Representative

> I think one of the other bigger inefficiencies is for our research teams. I'm increasingly concerned about them and where they're going to land in all of this. We can work out our IRB processes and work out something here eventually…the efficiency of one of our researchers having 20 studies and they all

> come to us is that they learn our processes. They learn our reporting requirements, they learn how to communicate with us, they learn who to call on the phone. They understand how to work with us, and they can come up with an efficient system of who to call, so where does this go, what's the step here. And now, a busy researcher with 20 studies, those 20 studies could be with any IRB in the nation, and every time they submit an application or do that, it's a difficult process of who does this go to, who do I talk to, are they going approve this. — Research Administration Leadership Representative

Four participants said that no new inefficiencies were introduced.

7. Other Findings

This section describes other findings related to the sIRB process.

7.1 Selecting a sIRB

Questions about selecting a sIRB (i.e., a reviewing IRB) were asked only of investigators and study/regulatory coordinators (10 transcripts[*]).

Investigators and study/regulatory coordinators (n=10) named numerous individuals and other entities who have been involved when they have selected a sIRB in the past:

- IRBs at lead sites (n=8)
- PIs (and their coordinators) (n=4)
- Local institutional administrators (n=4)
- Sponsors (n=3)
- Research networks (n=1)
- External relying sites (n=1)
- IRBs at sites other than lead sites in rare cases when capacity is an issue (n=1)

Investigators, study/regulatory coordinators, and one research administrator (unprompted) (n=7) described numerous factors they consider when determining whether to rely on a sIRB for multi-site studies:

- Whether they have an established working relationship with the selected institution (n=3)
- Keeping project funds at their own institution (n=2)
- Lowering their own operating costs (n=2)
- Avoiding duplicative reviews that occur with the local IRB model (n=2)
- Saving time by allowing their own institution to serve as the sIRB (n=2)
- Bolstering the reputation of their own institution (n=1)
- Whether the proposed reviewing IRB was accredited (n=1)

[*] A dyadic interview was conducted with an investigator and study coordinator. Therefore, a total of 11 investigators/study coordinators participated in the interviews; 10 transcripts represent those interviews.

Of those investigators who said having **"an established working relationship"** with the reviewing IRB was an important factor, all three had selected their own institution to serve as the reviewing IRB for a recent multi-site study because they were familiar with how their own institution operated. A study coordinator said:

> I feel that they actually work almost like collaborative partners with us…We have developed some personal relationships with multiple people at the IRB so if we ever have a question or we're thinking we want to head in a direction, we can run it by them to get their thoughts before we invest resources.

In most cases, investigators and study/regulatory coordinators said that the preference is for the IRB at the lead site to serve as the reviewing IRB. Some participants mentioned that the PI is a critical part of the process for choosing a reviewing IRB. However, the ultimate decision was a collective one, with much consideration given to the preferences of the PI. In some situations, the IRB at the lead site and/or institutional administrators decided whether their own institution would serve as the reviewing IRB or whether they would allow the study to be reviewed elsewhere. Several participants said this decision was based on the capacity available at the IRB at the lead site. A few participants noted that standardization of the process for selecting and becoming a reviewing IRB is needed, given that the NIH sIRB mandate is still new.

Investigators and study/regulatory coordinators (n=9) described factors that made the process of identifying a reviewing IRB <u>easy</u>:

- Having an established process for selecting a reviewing IRB (n=4)
- Lack of PI or study/regulatory coordinator involvement because others select the reviewing IRB (n=3)
- Familiarity with the reviewing IRB because they are using their own (n=2)
- Having forms and templates to use (n=2)
- Having dedicated resources for this purpose (n=2)
- Efficiency or speed of the selection process (n=1)
- Having clear and established roles and responsibilities for selecting a reviewing IRB (n=1)

For "**having an established process**," participants described using familiar process, such as using their own IRB, or working with a central IRB, as well as the convenience of tools provided via SMART IRB:

> SMART IRB, with the experience that I have, has been the easiest at this point because they all just agreed to use ours as the IRB of Record. And the paperwork is set up for you, but you still have to actually sign the letters and everything else.— A regulatory coordinator

For "**others selecting the sIRB**," participants described that individuals others than the PI can decide which sIRB to use, such as the network or sponsors, or when their institution has pre-determined sIRBs to use. A regulatory coordinator stated that they appreciated the sponsor choosing the reviewing IRB because the process required "a lot of time, and time is money, and we don't have time." An investigator elaborated:

> We have a liaison here [who helps facilitate the process] and that we have these pre-standing, predetermined, already agreed upon central IRBs that we "are allowed to use." I actually appreciate the experience and the detail that our university provides for [selecting those sIRBs].

Investigators and study/regulatory coordinators (n=6) also described <u>challenges</u> they faced with identifying a reviewing IRB:

- Lengthy selection process (n=4)
- Lack of infrastructure to facilitate the selection process (n=1)
- Having to establish reliance agreements (n=1)
- Not budgeting for the cost of the selection process and the selected IRB (n=1)

For "**a lengthy selection process**," a regulatory coordinator elaborated on how the sIRB paperwork and the sign-offs required for relying on an external IRB increased the overall time in selecting and establishing a reviewing IRB:

> It's very time-consuming to even, in the very beginning, to determine what IRB you're even using. To be honest, the last few industry-sponsored studies have said, "Well, we have a central, but you can use your local." And I mean hands down, we'll say local, because (1) we have a great local IRB and (2) it's much quicker in that regard because then you're not having to get paperwork signed and all the legal stuff signed to use the central IRB.

One participant said there were no challenges associated with selecting a reviewing IRB.

Investigators and study/regulatory coordinators (n=6) described the amount of time it takes to complete the sIRB selection and reliance process, from identifying the reviewing IRB to finalizing all agreements. Some said the time was nominal (i.e., 1 to 2 months for one participant, 6 months for another). Others said the process took more time than they would have liked, with one specifying that finalizing the reliance agreement caused delays. One participant explained that they use master agreements that have a two-week turnaround when a master reliance template was already on file for an institution.

Investigators and study/regulatory coordinators (n=8) described factors that they believed could be used as indicators that the selection and reliance process was a success, as well as factors that would indicate the process was ineffective.

<u>Successful</u> indicators are:

- Efficiency (n=8)
- Agreement from all parties on the terms of reliance (n=2)
- When sites truly rely on the reviewing IRB (i.e., trust and willingness) (n=2)
- Having an IRB approval process that is thorough (n=1)
- Having a reviewing IRB that supports and collaborates with the lead investigator(s) (n=1)
- Being able to secure needed resources to make the selection or reliance process work (n=1)
- Having clearly defined roles and responsibilities as a result of the reliance process (n=1)

"Efficiency" was defined by most participants as having an expedient selection or reliance process that resulted in quicker study startup. However, several participants offered further nuance to express specific aspects of efficiency, such as not having to alter or compromise study timelines. Participants also mentioned

that “not needing to file an extension” or efficiencies in the renewal process would be a measure of success. Another participant described efficiency as “indicated by a decline in the number of emails, questions, and objections to particular things.”

Investigators and study/regulatory coordinators (n=8) also described several factors that, to them, would signal an <u>unsuccessful</u> selection or reliance process:

- Lengthy process (n=6)
- Relying sites that are unwilling to truly cede to another IRB (n=1)
- Having no clearly identified point of contact (n=1)
- Being unable to come to agreement on the terms of reliance (n=1)
- Having no or minimal support from the reviewing IRB or institution (n=1)
- Being unable to get a site on-boarded for the study (n=1)

For **“lengthy process**,” participants focused on processes that resulted in a shift in timelines. An investigator said:

> [The indicator of nonsuccess] was just the time delays…If it was taking six months or so to get through, you’re going to find another way to do it. Especially with NIH funding, you’re kind of on a timeline. So, you never expect for just that aspect to take that long. You’re like, “I still have to do the whole study and get results and I want to stay funded.” So, there is a time crunch involved.

A few Investigators and study/regulatory coordinators (n=3) shared suggestions for improving the process of selecting a reviewing IRB:

- Having more clarity and guidance on the process after naturally becoming more acquainted with it over time (n=2)
- Relying more on the use of the SMART IRB platform, because it allows the reviewing institution to have more control (n=1)

7.2 Participant Experiences

Participants in all groups were asked to consider how the sIRB process might influence the experiences of study participants.

Twenty-two participants said they <u>did not</u> believe the sIRB process <u>affect</u> the study participant experience in any way. Many explained that changes in IRB processes happen behind the scenes and, therefore, do not affect participant-facing aspects of the study. In addition, a few participants explained that research staff do not typically speak to study participants about IRB-related issues.

A number of participants expressed that, if the sIRB process is implemented correctly, there should be no impact on the experience of study participants:

> If it's done the way that it should be, it shouldn't [have any impact]. If you've got a good IRB that's going to assure human subject protection, it shouldn't be any different than what I used to do, which is an IRB that's very protective of human subjects. So, it shouldn't be any different from that standpoint. — Investigator

Other participants shared the following perceived <u>improvements</u> in study participant experiences:

- Increased efficiency with study startup (n=7)
- Consistent risk profile (n=5)
- Consistent informed consent forms (n=4)

For "**increased efficiency**," participants explained that projects initiate much faster with the sIRB process, which allows participants to get involved in a study faster due to a faster review timeline. Some participants explained that the increase in efficiency could potentially lead to new therapies being available to participants faster, which could be a benefit to both research participants and the public overall. Participants said:

> If anything, maybe more research is offered faster to them through the timelines of the review process. So, by removing the administrative burden that's needed to get a study or site up and running for a potential therapy that could impact quality of life, sure. But I don't know that they would really see any other direct impact besides that. — Study Coordinator

> I think it helps studies get up and running more quickly. It gives them access to collaborative research that may have huge implications both therapeutically or quality-of-life–wise. — Research Administration Leadership Representative

For "**consistent risk profile**," participants mentioned that all study participants are being treated under the same protocol, ensuring that issues at one site are addressed at other sites. This also results in all participants' adverse event deviations being reviewed in the same way regardless of study site. Participants explained:

> I think probably one aspect that might be beneficial for them is that, since there is just one institution that's reviewing all sites, if there's problems at multiple sites that seem like it's kind of a theme, then that central IRB can address that problem at all sites. — Institutional/Other IRB Representative

> I think, if it goes perfectly, study participants are all being treated under the same protocol, and I think study participants are getting the value of all adverse events deviations, weird things that happened, being reviewed centrally. So, I think it's consistency of the research, I think would be the main thing. — Research Administration Leadership Representative

For "**consistent informed consent forms**," participants said that study participants receive the same information from the consent form regardless of the site, which could result in a higher-quality consent document and consistent experiences for participants at each site. A research administration leadership

representative said:

> Well, at a minimum, you won't have 10 different versions of a consent form for 10 different study sites. So, at a minimum, everybody's getting the same information in writing if there's a consent form for the study and participants are being asked about how to participate in the same way with the same language or the same requirements are applying to that. So, at a minimum, they're getting the same protection regardless of what site the study's happening in, in terms of how the IRB viewed the study.

Participants also shared the following areas where the sIRB process may <u>complicate</u> the study participant experience:

- Confusing contact information (n=4)
- sIRB not understanding and/or incorporating local context issues into the consent form (n=1)
- Having consent forms that look very different from forms participants are used to if they participate in numerous studies at their own institution (e.g., formatting, phrasing) (n=1)

For "**confusing contact information**," participants explained that questions might arise if a participant gives consent at one site but then is told that, if they have questions or concerns, they are to contact an investigator from a different site. Some participants implied this might create a slightly negative or more difficult experience for participants.

> The only thing I can think of is, for those people who need somebody to talk to or have a subject complaint, that might feel a little different to them. I'm participating here at [university] in a study, but now I have to call [another university], because I haven't gotten my payment, because that's what we always get calls about. So, that's the only subject-basing impact. It might be a little bit worse for them. — Institutional Official/IRB Other

7.3 Top Benefits of the sIRB Process

Participants (n=33) described the following benefits of using a sIRB process:

- Increased consistency (n=15)
- Increased efficiency (n=14)
- Improved collaboration between study staff at multiple sites (n=10)
- Ease of amendments and renewals for relying sites (n=4)
- Improved participant protections (n=4)
- Enhanced quality of science (n=4)
- Fewer protocols being reviewed by full boards (n=2)
- Increased support for higher-liability studies (n=2)
- Sites all have the same study schedule and begin screening and enrollment at similar times (n=1)
- Fewer errors because documents are handled by one site (n=1)
- Reduced cost due to full reviews by a single site (n=1)
- Centralized documents and repository to track changes to and most recent versions of documents (n=1)

- Reliance agreements used to increase the acceptability of sites relying on the sIRB (n=1)

For "**increased consistency**," participants mentioned improved consistency between study sites in consent forms, ethical considerations, data collected by the different sites, timelines and renewal dates, and processes. Some participants also explained that having a sIRB led to consistent changes across sites, which resulted in sites making fewer errors in terms of using the wrong version of a protocol or the wrong consent form. Participants said:

> The number two [benefit] I think would be consistency that, in theory, having one IRB review the protocol and subjected to the scrutiny that's required and going back and forth with the sponsor or the PI should result in a very good process that gains consistency throughout the various locations where the study will be conducted. — Institutional or Other IRB Representative

> Homogeneity of the data. Everybody is under the same determinations. Everybody is under the same protocol. — Research Administration Leadership Representative

> And I do maintain that I think my staff is less likely to make mistakes, or use the wrong form, or something because when we make a change, it's made across all sites at the same time. We sent out the same memos. There's no potential for us to miss a site or forget about something. I think it's less error-prone in the end. — Investigator

For "**increased efficiency**," participants said efficiencies included faster turnaround of documents, faster approval, faster participant enrollment, and faster assessments of adverse events. Some participants linked increased efficiency to more cost-effective studies. A study coordinator said:

> I think overall and long-term, there would be the benefit of kind of overarching insight into how the patients are doing at the trial. It's going be a lot faster to be able to assess things like adverse events, right? I think that the NIH will start to see trials being conducted faster and a little bit more in line with industry standards. That's an overall benefit, and I think it will come down to cost as well. Time is money!

For "**improved collaboration**," participants spoke about increased opportunities for learning from one another during the review process, because they are now communicating with other IRBs more regularly. Participants also discussed how the sIRB process allows staff to learn how other institutions implement the new process and gives staff an opportunity to build on existing relationships in a meaningful way due to the increased collaboration required under the new policy. A research administration leadership representative said:

> I think the other part is learning from each other, because you're talking more amongst each other, like the IRBs themselves. We've barely talked to each other, I'd say, in the past, unless we had to. But now we talk to each other a lot, because we have to. You know? So, I think that is nice. I think we probably learn from each other. I know I have purposely asked people, so, how do you do this in this case? And we learn, you know, we just have, it's more collaboration, I guess you would say.

For “**ease of amendments and renewals**,” participants spoke about the benefit of having single continuing review dates and how relying sites have much less work to do for renewals and continuing reviews. For “**improved participant protections**,” participants mentioned higher-quality consent forms and having central review of safety events. For “**enhanced quality of science**,” participants spoke about the IRB becoming more efficient in analyzing large samples of patients because the reviewing IRB will become more comfortable with being responsible for adverse event reports from all sites rather than just their local sites. Participants also described that IRBs will “get better at approving patient-facing things,” because they will have more exposure to different types of patients, develop expertise in more areas, and become more proficient in subsequent reviews of similar protocols.

7.4 Top Burdens of the sIRB Process

Participants (n=32) described the following burdens of using a sIRB process:

- Processes and systems (n=17)
- Communication (n=8)
- Duplicative activities—submission of documents at both the reviewing and local IRB (n=6)
- Sites having a hard time releasing local control (n=5)
- Lack of support for investigators in helping them understand how to apply to different IRBs (n=5)
- Variation among participating sites in what needs to be submitted to varying reviewing IRBs (n=5)
- Lack of uniformity of documents (n=5)
- Longer time to review based on risk profile of protocol (n=4)
- Educating sites and site staff on the requirements of the sIRB policy (n=4)

For **“processes and systems**,” participants described a lack of training for staff on the processes associated with the sIRB policy, lack of an electronic system that is accessible to external investigators, and the need for guidelines to limit variation in how IRBs approach the sIRB process each time. A regulatory coordinator said:

> Each IRB is changing their opinion on how it’s supposed to be done and what they actually need to review and whether they're going approve or just acknowledge. And so every time you submit a new central IRB study, our IRB has different thoughts on how it should be done.

For **“communication**,” issues include communicating information related to local context, coordinating communications between sites, and overall confusion about communicating information to the IRBs through the submission process. An institutional/other IRB representative said:

> And then the communication and coordination across sites, making sure that all sites understand what that communication flow process is going be.

For “**duplicative activities**,” participants explained that duplicative activities result in documents and protocols that have to be submitted to both the reviewing IRB and to the site IRBs. Participants explained:

> Other burdens would be the relying site has to submit to two places and get institutional approval from their home institution and ethics approval from whoever the IRB of record is. — Research

Administration Leadership Representative

> Study teams are surprised when I say to them, even if you rely on external IRB, a lot of the other things still need to be in place. So, for them, it's extra because they have to deal with now this other system, this other IRB that they have to submit with them, and then they also have to submit with us.
> —Research Administration Leadership Representative

7.5 Additional Information About SMART IRB and the IRB Reliance Exchange (IREx)

Participants mentioned two tools—SMART IRB and the IRB Reliance Exchange (IREx)—that they use as part of the sIRB process. We describe below participants' experiences with using the tools as well as their perceptions of the benefits and limitations of each tool. We did not specifically ask participants during the interviews to discuss their experiences with these tools. Rather, at the request of the NIH working group, we conducted a secondary analysis of the data to identify the benefits and limitations of the tools.

7.5.1 SMART IRB

7.5.1.1 Typical uses

Typical uses of the SMART IRB platform include:

- Templates for facilitating reliance agreements (including master agreements)
- Forms for collecting local context information
- Communicating with participating sites
- Document repository and distribution
- Documenting institution responsible for auditing
- Documenting institution responsible for ancillary reviews
- Using the "acceptance and flexibility" form
- Using language to inform the creation of local reliance agreements
- Using as a database for managing studies
- Serves as a form of credential or accreditation of higher standards
- Potential use as an evaluation metric: time to get enrolled and use SMART IRB for reliance agreements

7.5.1.2 Benefits

Participants reported several benefits of using the SMART IRB platform:

- Makes the negotiation of reliance agreements much more efficient
- Saves time with the provision of forms and templates
- Facilitates communication with participating sites
- Limits the number of revisions sites can make to documents
- Provides a means for sites to enter local context information
- Gives reviewing sites more control
- Helps manage and track various studies

7.5.1.3 Limitations

Participants also noted several limitations of the SMART IRB platform:

- Limited functionality for collecting local context information
- Not user-friendly
- Not well suited for nonclinical studies (e.g., low-risk socio-behavioral research)
- Inefficient for communicating information to participating sites
- Limited functionality for updating forms
- Unnecessarily lengthy reliance template

7.5.2 IREX

7.5.2.1 Typical uses

Typical uses of IREx include:

- Document repository and distribution
- Facilitating reliance agreements (including incorporation of the SMART IRB template)
- Capturing local context information
- Communication with participating sites
- Creating study-specific research plans
- Potential use of IREx as a database for local context information

7.5.2.2 Benefits

Participants reported several benefits of using IREx:

- Can customize notifications to be sent to select participating sites only
- Able to identify the most current documents
- Serves as a central repository for storing all documents in one location
- Better than SMART IRB
- Participating sites can access and upload documents

7.5.2.3 Limitations

Participants also noted limitations of IREx:

- Could lead to site delays if the system breaks down or goes offline, because it serves as a repository of current documents (e.g., consent forms)
- Not user-friendly
- Inefficient for communicating information to participating sites

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Appendix A

SIRB Question Guide
IRB chairs and administrators only (360° interviews) and IRB leadership (PRIM&R interviews)
Version 2.0
February 19, 2019

1. Interviewer Name	
2. Participant ID#	
3. Interview Date (mm/dd/yyyy)	|___|___|/|___|___|/|___|___|___|___|
4. Participant agrees for interview to be digitally recorded	Yes ..... ☐ No ..... ☐
5. Time Interview Began (hh:mm)	|___|___ | : |___|___| am/pm
6. Time Interview Ended (hh:mm)	|___|___| : |___|___| am/pm

Step 1: Complete Q1-3 above before starting the interview.
Step 2: Introduce yourself at the beginning of the interview. Thank participant for taking part in the interview.
Step 3: Read "Introduction and overview" below to participant.
Step 4: Ask for the participant's permission to record interview. Tick appropriate box in Q4 above.
Step 5: Turn on audio recorder if permitted. Document time interview begins in Q5 above, and conduct interview.
Step 6: At the end of the interview, thank the participant and ask if she/he has any further questions. Document time interview ended in Q6 above.
Step 7: Provide reimbursement and document appropriately.

Section 1: Introduction and overview

- Hello, thank you for taking time out of your busy schedule to speak with me today. My name is [Name], and I am a _____ with Duke University. (For telephone interviews: Is now still a good time to talk?)
- Before we begin, I'd like to tell you more about this interview and the research we're conducting.
- The Clinical Trials Transformation Initiative at Duke University– known as CTTI – is partnering with NIH to develop a framework for evaluating the implementation of NIH's single IRB policy.
- We are conducting interviews with IRB representatives, investigators and study coordinators to learn about their experiences with using the single IRB review process when their institutions serve the reviewing IRB or when they are a relying institution or both. We're also interested in hearing people's suggestions on realistic metrics on how the single IRB process can be evaluated

- The interview will take roughly 1 hour.

- With your permission, I would like to audio-record the interview. The audio-recording will be stored on a secure server and destroyed after the findings of this research are published. If you do not want the interview audio recorded, I will take detailed notes throughout the interview instead.

- Before I start asking questions, I'd like to highlight some terminology that I'll reference throughout the interview, as often different terms are used to describe the same idea. I know you are quite familiar with these terms but I want to make sure we're thinking of these terms in the same way.

    - When I refer to a Reviewing IRB, which is also known as the single IRB, I mean the IRB of record for a particular multi-site study for the duration of the study.

    - When I refer to a Relying institution, I mean the IRB or institution that will rely on an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying IRB's institution. The NIH's single IRB policy refers to these institutions as "participating sites."

Are these the same terms you use—or do you use different terms?

- **Lastly, for all questions, we are only referring to NIH-funded, multi-site research.**

- Do you have any questions for me at this point?

[If yes, answer the participant's questions.]

Is it okay if I turn on the audio recorder now?

[If yes, begin audio recording now.]

[If no] That's okay, I'll take detailed notes as we talk.

Section 2: Development of the sIRB process map

Overview: A template sIRB process map has been developed by the CTTI team. This template process map will be modified as follows:

360° interviews: The template process map will be first reviewed by an IRB chair and an IRB administrator as part of the 360° interviews. Based on their feedback, the template will be modified so it depicts the process followed at each 360°university. Each university's modified sIRB process map will then be used in the subsequent interviews with IRB representatives at the university in order to gather details on the specific roles and responsibilities, input, and output of each representative, as it relates to the sIRB process. Additional modifications can be made to the process map during these interviews.

PRIM&R interviews: Modifications will be made to the template sIRB process map during the interviews so we can learn about the variety of sIRB processes followed across institutions of multiple sizes.

Interviewer instructions:

- Explain the purpose of the sIRB process map exercise to the participant:
  - *We are interested in learning about the flow of activities when your institution serves as a reviewing IRB and when it is the relying institution.*
  - *The CTTI team will use the process map to identify areas in which to focus metrics in the evaluation framework.*

- Show the template sIRB process map.
  - *This is a sample sIRB process map of how activities may occur when institutions implement the sIRB process at their university. Explain flow.*

- Ask questions below.
- Write any modifications directly on the process map.

Questions

1. Let's talk about when your institution serves as the *reviewing IRB.* How is the flow of activities at your university **different** from what is presented in this template map? *[Interviewer: Show the reviewing IRB map. Start at the beginning of the map and finish with the last step.)]*

2. Now let's talk the flow when your institution *relies on outside IRB* for ethics review. How is the flow of activities at your university, when it was the *relying institution*, **different** from what is presented in this template map? [*Interviewer: Show the relying institution map. Start at the beginning of the map and finish with the last step.]*

Section 3: Current and baseline metrics

Now I'd like to speak with you about IRB-related metrics.

1. What IRB-related metrics does your IRB currently collect? *[Probe about when these metrics were initiated—before or after the initiation of the NIH's sIRB process; any metrics related to time; IRB-related metrics planning to collect; quality, form, and completeness of the data]*
    a. What IRB procedures and tools were used before the new policy or used concurrently with the new policy? If SMART is used, when was it started? What was the workload prior?

2. *[If have metrics]* In thinking about how to evaluate the sIRB process, how could those metrics be used as baseline metrics, if at all?
    a. How could those metrics be improved upon so they could measure the sIRB process moving forward?

3. What suggestions do you have for the type of information that could be used as baseline metrics for evaluating the sIRB process?

Section 4: NIH sIRB goals

Now I'd like to speak with you about the NIH's goals for the sIRB process and learn about your institution's experiences as they relate to these goals.

Goal #1:

The first goal of NIH's sIRB policy is to "enhance and streamline IRB review for multi-site research."

In a moment, I'd like to hear your thoughts on whether or not this policy has enhanced and streamlined the IRB process for the review of NIH funded multi-site research at your university.

Let us first start with your thoughts on how this policy may have streamlined review—and then I'll ask you for your thoughts on how they may have not.

1. Based on your institution's experience, how has the implementation of NIH's sIRB policy *streamlined* your university's ethics review of the study protocol for NIH-funded, multi-site research? *[Probe about the specific areas that have been streamlined and exactly how those areas have been streamlined compared to the local IRB review model]*.
    a. What suggestions do you have on how these areas can be realistically measured to appropriately reflect the efficiencies of this new policy? *[Probe about each topic mentioned]*

2. How has the implementation of the sIRB policy fallen short of streamlining or simplifying your university's ethics review of the study protocol? *[Probe about the specific areas that have NOT been streamlined and exactly how those areas have NOT been streamlined compared to the local IRB review process]*.
    a. What suggestions do you have on how these areas can be measured to appropriately reflect the burden of this new policy? *[Probe about each topic mentioned]*

Now let's talk about the other activities that must take place at your university in order for research to proceed.

3. Based on your institution's experience, how has the implementation of NIH's sIRB policy *streamlined* your university's overall process for reviewing of NIH-funded, multi-site research, <u>beyond the ethics review</u>? This includes activities beyond the ethics review of the protocol, such as ancillary reviews and conflict of interest. *[Probe about the specific areas that have been streamlined and exactly how those areas have been streamlined compared to the local IRB review model]*.
    a. What suggestions do you have on how these areas can be realistically measured to appropriately reflect the efficiencies of this new policy? *[Probe about each topic mentioned]*

4. How has the implementation of the sIRB policy fallen short of streamlining or simplifying your university's overall review process <u>beyond the ethics review</u>? *[Probe about the specific areas that have NOT been streamlined and exactly how those areas have NOT been streamlined compared to the local IRB review process]*.
    a. What suggestions do you have on how these areas can be measured to appropriately reflect the burden of this new policy? *[Probe about each topic mentioned]*

Goal #2:

The second goal of NIH's sIRB policy is to "maintain high standard for human subjects protections." My next questions will be about this goal.

1. How would you define "high standards?"

2. Based on your institution's experience, I'd like to hear about any concerns you may have had regarding your institution's ability to maintain a high standard for human subject projections when using a sIRB process when you rely on another institution.

3. When your institution has served as the *reviewing IRB*, how did you gather local information relevant to the study from other institutions or sites particularly information related to vulnerable populations?
    a. How did your institution use the local information?
    b. What has worked well with this process?
        - What has not?

4. When your institution has been the *relying institution*, how did you gather local information relevant to the study, particularly information related to vulnerable populations?
    a. How was that information communicated to the reviewing IRB?
    b. To the best of your knowledge, how was that information incorporated into the IRB review?
    c. What has worked well with this process?
        - What has not?

5. What suggestions do you have for evaluating the collection and incorporation of local knowledge into the sIRB process for multi-site studies?

Goals #3 – #5:

Three other goals of NIH's sIRB policy are to allow "research to proceed effectively and expeditiously," "eliminate unnecessary duplicative IRB review," and "reduce administrative burdens."
We will now discuss topics related to these goals, specifically focusing on what has worked well, what hasn't, and how these items can be evaluated.

1. When your institution serves as *reviewing IRB*, how do you interact with the study PI and local investigators? *[Probe about direct communication or through the local IRB]*
    a. What has been efficient about this process, if anything?
    b. What has been burdensome about this process, if anything?
    c. How could this process be evaluated?

2. This question is similar to the last question, but now let's focus on when your institution has been the *relying institution*. How do you communicate information beyond local contextual information with the reviewing IRB?
    a. What has been efficient about this process, if anything?
    b. What has been burdensome about this process, if anything?
    c. How could this process be evaluated?

3. What, if any, regulatory responsibilities have remained with your institution when your institution has been the *relying institution*? (e.g., informed consent)
    a. Beyond ethics review, what regulatory responsibilities have shifted to the reviewing IRB when your institution has been the relying institution?
    b. What has worked well with this division of responsibilities?
    c. What has not?
    d. How could these divisions of responsibilities be evaluated?

4. When your institution has been the *relying institution*, what ethics reviews, if any, still take place?
    a. Why?

5. What (other) activities have you found to be duplicative between the reviewing IRB and relying institution?

6. What have you found to be the main administrative burdens when you have been the *relying institution*?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could administrative burdens be evaluated?

7. What have you found to be the main administrative burdens when serving as the *reviewing IRB*?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could administrative burdens be evaluated?

8. How, if at all, has the amount of time needed for providing IRB and other reviews and activities changed under the sIRB model compared to the local IRB model? *[Probe about specific aspects that have increased time and decreased time, and how this time investment may have changed over time]*.
    a. How could we evaluate the time necessary for using the sIRB model in comparison to the local IRB model?

Goal #6:

The remaining NIH sIRB goal we'll discuss is to "prevent systemic inefficiencies."

1. Beyond what you have already shared, what systemic inefficiencies previously existed with the local IRB model, if any?
    a. How has the sIRB model improved upon these inefficiencies, if at all?
        - How has it not?
    b. How has the sIRB model created new inefficiencies, if at all?

Concluding Section

I have few remaining questions to wrap up our conversation today.

1. How, if at all, does using a sIRB process improve the research experience for study participants? *[Probe to 1) identify the specific part of the sIRB process that is most impactful and why, and 2) the specific part of the participant experience that is most impacted by the use of a sIRB process]*
    a. *[If identified participant improvements]* How could this be measured?

2. Based on your experience, what do you think have been the top three benefits of using a sIRB process for multi-site studies? *[Probe about why these benefits were selected, if the benefit was not previously discussed, as well as how to measure them, if not previously discussed.]*

3. What do you think have been the top three burdens? *[Probe about why these burdens were selected, if the burden was not previously discussed, as well as how to measure them, if not previously discussed.]*

For the last two questions, please focus your answers on what you think your institution could reasonably do.

4. What are your top three suggestions for how to evaluate the day-to-day work that your institution does to implement the sIRB process—often referred to as process evaluation?

5. What are your top three suggestions for how to evaluate the impact of using a sIRB process for multi-site studies—meaning, how to evaluate whether the sIRB process is achieving NIH's sIRB goals?

6. Is there any topic that we haven't discuss yet that you'd like to mention?

Thank you for your time. May we contact you if we have any additional questions?

SIRB Question Guide
IRB representatives other than IRB chairs and administrators only (360° interviews)
Version 2.0
February 19, 2019

1. Interviewer Name	
2. Participant ID#	
3. Interview Date (mm/dd/yyyy)	|___|___|/|___|___|/|___|___|___|___|
4. Participant agrees for interview to be digitally recorded	Yes ..... ☐ No ..... ☐
5. Time Interview Began (hh:mm)	|___|___ | : |___|___| am/pm
6. Time Interview Ended (hh:mm)	|___|___| : |___|___| am/pm

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Step 5: Turn on audio recorder if permitted. Document time interview begins in Q5 above, and conduct interview.
Step 6: At the end of the interview, thank the participant and ask if she/he has any further questions. Document time interview ended in Q6 above.
Step 7: Provide reimbursement and document appropriately.

Section 1: Introduction and overview

- Hello, thank you for taking time out of your busy schedule to speak with me today. My name is [Name], and I am a _____ with Duke University. (For telephone interviews: Is now still a good time to talk?)

- Before we begin, I'd like to tell you more about this interview and the research we're conducting.

- The Clinical Trials Transformation Initiative at Duke University– known as CTTI – is partnering with NIH to develop a framework for evaluating the implementation of NIH's single IRB policy.

- We are conducting interviews with IRB representatives, investigators and study coordinators to learn about their experiences with using the single IRB review process when their institutions serve as the reviewing IRB or as a relying institution or both. We're also interested in hearing people's suggestions on realistic metrics on how the single IRB process can be evaluated.

- The interview will take roughly 1 hour.

- With your permission, I would like to audio-record the interview. The audio-recording will be stored on a secure server and destroyed after the findings of this research are published. If you do not want the interview audio recorded, I will take detailed notes throughout the interview instead.

- Before I start asking questions, I'd like to highlight some terminology that I'll reference throughout the interview, as often different terms are used to describe the same idea. I know you are quite familiar with these terms but I want to make sure we're thinking of these terms in the same way.

    - When I refer to a Reviewing IRB, which is also known as the single IRB, I mean the IRB of record for a particular multi-site study for the duration of the study.

    - When I refer to a Relying institution, I mean the IRB or institution that will rely on an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying IRB's institution. The NIH's single IRB policy refers to these institutions as "participating sites."

Are these the same terms you use—or do you use different terms?

- **Lastly, for all questions, we are only referring to NIH-funded, multi-site research.**

- Do you have any questions for me at this point?

[If yes, answer the participant's questions.]

Is it okay if I turn on the audio recorder now?

[If yes, begin audio recording now.]

[If no] That's okay, I'll take detailed notes as we talk.

Section 2: Development of the sIRB process map

Overview: A template sIRB process map has been developed by the CTTI team. This template process map will be modified as follows:

360° interviews: The template process map will be first reviewed by an IRB chair and an IRB administrator as part of the 360° interviews. Based on their feedback, the template will be modified so it depicts the process followed at each 360°university. Each university's modified sIRB process map will then be used in the subsequent interviews with IRB representatives at the university in order to gather details on the specific roles and responsibilities, input, and output of each representative, as it relates to the sIRB process. Additional modifications can be made to the process map during these interviews.

PRIM&R interviews: Modifications will be made to the template process map during the interviews so we can learn about the variety of sIRB process followed across institutions of multiple sizes.

Interviewer instructions:

- Explain the purpose of the sIRB process map exercise to the participant:
  - *We are creating a sIRB process map for each of the 360° case study universities so we can have a pictorial representation of the sIRB process followed at that university.*
  - *The map displays the flow of the position-specific roles and activities as they relate to the sIRB process.*
  - *The IRB chair and administrator at each university will start the process by modify the template specifically for their university.*
  - *The details of each role will then be gathered at the subsequent interviews with IRB representatives at each university.*
  - *The completed sIRB process maps will give insight to the CTTI team on the processes universities follow to implement the sIRB process.*
  - *The CTTI team will use the process map to identify areas in which to focus metrics in the evaluation framework.*

- Show the template sIRB process map.
  - *This is a sample sIRB process map of how activities may occur when institutions implement the sIRB process at their university.*
  - *I'll now ask you questions about how your specific IRB role fits within this map from two perspectives: 1) when your intuition is the reviewing IRB and 2) when your institution is the relying institution. Then I'll ask you questions about how these process might change based on the type of protocol.*

- Ask questions below.
- Write any modifications directly on the process map.

Questions

Let us first start with the process when your IRB serves as the reviewing IRB.

1. Where is your role on this sIRB process map?

2. What specific activities do you do that relate to the sIRB process when your iRB serves as the reviewing IRB?
   a. What do you need from others so you can do your role? *(Probe from whom/type of position).*
   b. What is the outcome of your activities?
      - What is the next step after you fulfill your role?

Now let us talk about the process when your institution is the relying institution.

3. What specific activities do you do that relate to the sIRB process when your institution is relying on another IRB for the ethics review?
   a. What do you need from others so you can do your role? *(Probe from whom/type of position).*
   b. What is the outcome of your activities?
      - What is the next step after you fulfill your role?

4. How does your role differ, if at all, based on the type of research—for example a drug trial versus a low risk behavioral intervention versus a biospecimen study? *(Probe for any differences between when serving a s reviewing IRB or as a relying institution).*

Section 3: NIH sIRB goals

Now I'd like to speak with you about the NIH's goals for the sIRB process and learn about your institution's experiences as they relate to these goals.

Goal #1:

One goal of NIH's sIRB policy is to "enhance and streamline IRB review for multi-site research."

I'd like to hear your thoughts on whether or not this policy has enhanced and streamlined your role with reviewing multi-site research.

Let us first start with your thoughts on how this policy may have streamlined review—and then I'll ask you for your thoughts on how they may have not.

1. Based on your experience, how has the implementation of NIH's sIRB policy *streamlined* your roles and responsibilities for reviewing or facilitating NIH-funded, multi-site research—as it relates to the ethics review of the research? *[Probe about the specific areas that have been streamlined and exactly how those areas have been streamlined compared to the local IRB review process]*.
    a. What suggestions do you have on how these areas can be realistically measured to appropriately reflect the efficiencies of this new policy? *[Probe about each topic mentioned]*

2. How has the implementation of the sIRB policy fallen short of streamlining your role and responsibilities in reviewing or facilitating NIH-funded, multi-site studies—as it relates to the ethics review of the research? *[Probe about the specific areas that have NOT been streamlined and exactly how those areas have NOT been streamlined compared to the local IRB review process]*.
    a. What suggestions do you have on how these areas can be measured to appropriately reflect the burden of this new policy?

Now let's talk about the other activities that must take place at your university in order for research to proceed.

3. Based on your experience, how has the implementation of NIH's sIRB policy *streamlined* the role you play in the overall review process, <u>beyond the ethics review</u>? *[Probe about the specific areas that have been streamlined and exactly how those areas have been streamlined compared to the local IRB review model]*.
    a. What suggestions do you have on how these areas can be measured to appropriately reflect the efficiencies of this new policy? *[Probe about each topic mentioned]*

4. Based on your experience, how has the implementation of the sIRB policy fallen short of streamlining or simplifying the role you play in the overall review process, <u>beyond the ethics review</u>? *[Probe about the specific areas that have NOT been streamlined and exactly how those areas have NOT been streamlined compared to the local IRB review process]*.

a. What suggestions do you have on how these areas can be realistically measured to appropriately reflect the burden of this new policy? *[Probe about each topic mentioned]*

Goal #2:

The second goal of NIH's sIRB policy is to "maintain high standard for human subjects protections." My next questions will be about this goal.

1. How would you define "high standards?"

2. Based on your experience in your role, I'd like to hear about the any concerns you may have had regarding your institution's ability to maintain a high standard for human subject projections when using a single IRB process.
    a. Let's first start when your university has served as the *reviewing IRB* for multi-site research. What concerns, if any, related to maintaining a high standard for human subject projects have you had?
    b. What about as the *relying institution*?

Goals #3 – #5:

Three other goals of NIH's sIRB policy are to allow "research to proceed effectively and expeditiously," "eliminate unnecessary duplicative IRB review," and "reduce administrative burdens."
We will now discuss topics related to these goals.

1. What responsibilities have remained with your role when your institution has been the *relying institution*?
    a. Which of your previous responsibilities, if any, have shifted to the reviewing IRB when your institution has been the relying institution?
    b. What has worked well with this division of responsibilities?
    c. What has not?
    d. How could these divisions of responsibilities be evaluated?

2. What (other) activities related to your role are duplicative between the reviewing IRB and the relying institution?

3. What have you found to be the main administrative burdens, if any, in your role when your institutions has been the *relying institution*?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could administrative burdens be evaluated?

4. What have you found to be the main administrative burdens, if any, in your role when serving as the *reviewing IRB*?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could administrative burdens be evaluated?

5. How, if at all, has the amount of time changed for your role and responsibilities for providing IRB and other reviews and activities under the sIRB model compared to the local IRB model? *[Probe about specific*

aspects that have increased time and decreased time, how this time investment may have changed over time].

6. How do you think we could evaluate the time necessary for using the sIRB model in comparison time spent implementing the local IRB model?

Goal #6:

The remaining NIH sIRB goal we'll discuss is preventing systemic inefficiencies.

1. Beyond what you have already shared, with your role and responsibilities, what systemic inefficiencies have existed with the local IRB model, if any?
    a. How has the sIRB model improved upon these inefficiencies, if at all?
        - How has it not?
    b. How has the sIRB model created new inefficiencies with your role, if at all?

Concluding Section

I have few remaining questions to wrap up our conversation today.

1. How, if at all, does using a sIRB process improve the research experience for study participants? *[Probe to 1) identify the specific part of the sIRB process that is most impactful and why, and 2) the specific part of the participant experience that is most impacted by the use of a sIRB process]*
    a. *[If identified participant improvements]* How could this be measured?

2. Based on your experience, what do you think have been the top three benefits of using a sIRB process for multi-site studies? *[Probe about why these benefits were selected, if the benefit was not previously discussed]*

3. What do you think have been the top three burdens? *[Probe about why these burdens were selected, if the burden was not previously discussed]*

For the last two questions, please focus your answers on what you think your institution could reasonably do.

4. What are your top three suggestions for how to evaluate the day-to-day work that you do to implement the sIRB process—often referred to as process evaluation?

5. What are your top three suggestions for how to evaluate the impact of using a sIRB process for multi-site studies—meaning, how to evaluate whether the sIRB process is achieving NIH's sIRB goals?

Thank you for your time. May we contact you if we have any additional questions?

SIRB Question Guide
Investigators and Study Coordinators
Version 2.0
February 19, 2019

1. Interviewer Name	
2. Participant ID#	
3. Interview Date (mm/dd/yyyy)	|___|___|/|___|___|/|___|___|___|___|
4. Participant agrees for interview to be digitally recorded	Yes ..... ☐ No ..... ☐
5. Time Interview Began (hh:mm)	|___|___ | : |___|___| am/pm
6. Time Interview Ended (hh:mm)	|___|___| : |___|___| am/pm

Step 1: Complete Q1-3 above before starting the interview.
Step 2: Introduce yourself at the beginning of the interview. Thank participant for taking part in the interview.
Step 3: Read "Introduction and overview" below to participant.
Step 4: Ask for the participant's permission to record interview. Tick appropriate box in Q4 above.
Step 5: Turn on audio recorder if permitted. Document time interview begins in Q5 above, and conduct interview.
Step 6: At the end of the interview, thank the participant and ask if she/he has any further questions. Document time interview ended in Q6 above.
Step 7: Provide reimbursement and document appropriately.

Section 1: Introduction and overview

- Hello, thank you for taking time out of your busy schedule to speak with me today. My name is [Name], and I am a _____ with Duke University. (For telephone interviews: Is now still a good time to talk?)

- Before we begin, I'd like to tell you more about this interview and the research we're conducting.

- The Clinical Trials Transformation Initiative at Duke University– known as CTTI – is partnering with NIH to develop a framework for evaluating the implementation of NIH's single IRB policy.

- We are conducting interviews with IRB representatives, investigators and study coordinators to learn about their experiences with using the single IRB review process when their institutions serve the reviewing IRB or when they are a relying institution or both. We're also interested in hearing people's suggestions on realistic metrics on how the single IRB process can be evaluated.

- The interview will take roughly 1 hour.

- With your permission, I would like to audio-record the interview. The audio-recording will be stored on a secure server and destroyed after the findings of this research are published. If you do not want the interview audio recorded, I will take detailed notes throughout the interview instead.

- Before I start asking questions, I'd like to highlight some terminology that I'll reference throughout the interview, as often different terms are used to describe the same idea. I know you are quite familiar with these terms but I want to make sure we're thinking of these terms in the same way.

    - When I refer to a Reviewing IRB, which is also known as the single IRB, I mean the IRB of record for a particular multi-site study for the duration of the study.

    - When I refer to a Relying institution, I mean the IRB or institution that will rely on an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying IRB's institution. The NIH's single IRB policy refers to these institutions as "participating sites."

Are these the same terms you use—or do you use different terms?

- **Lastly, for all questions, we are only referring to NIH-funded, multi-site research.**

- Do you have any questions for me at this point?

[If yes, answer the participant's questions.]

Is it okay if I turn on the audio recorder now?

[If yes, begin audio recording now.]

[If no] That's okay, I'll take detailed notes as we talk.

Section 2: Selecting a reviewing IRB

To start, I'd like to speak with you about your institution's sIRB selection and reliance process, specifically.

1. Please describe the process you have followed to identify a sIRB for your multi-site studies.
    a. Who was involved in that process? We are interested in the type of personal and not personal names.
    b. What roles did each person play?
    c. Who made the final decision about which IRB to use as the reviewing IRB?

2. What did you find to be easy about the process?
    a. What did you think was difficult about the process?

3. About how much time and effort did it take to complete the sIRB selection and reliance process, from identifying the reviewing IRB and finalizing agreements between your institution and the reviewing IRB?

4. What would be indicators that would suggest that the sIRB selection and reliance process is a success?

a. What indicators would suggest that this process was not a success?
b. Is there anything that you would do differently NEXT time?

Section 3: NIH goals

Now I'd like to speak with you about the NIH's goals for the sIRB process and learn about your experiences with the sIRB process as they relate to these goals.

Goal #1:

The first goal of NIH's sIRB policy is to "enhance and streamline IRB review for multi-site research."

I'd like to hear your thoughts on whether or not the sIRB has enhanced and streamlined the IRB process for the review of your multi-site research.

Let us first start with your thoughts on how this policy may have streamlined review—and then I'll ask you for your thoughts on how they may have not.

1. Based on your experience, how has the implementation of the sIRB policy *streamlined* the entire review process for your multi-site research? This includes the IRB review of your protocol as well as other reviews and activities needed to be completed for your protocol to be approved to start data collection. *[Probe about the specific areas that have been streamlined and exactly how those areas have been streamlined compared to the local IRB review model]*.
    a. What suggestions do you have on how these areas can be realistically measured to appropriately reflect the efficiencies of this new policy? *[Probe about each topic mentioned]*

2. How has the implementation of the sIRB policy fallen short of streamlining or simplifying the entire review process for your multi-site research? This includes the IRB review of your protocol as well as other reviews and activities needed to be completed for your protocol to be approved to start data collection. *[Probe about the specific areas that have NOT been streamlined and exactly how those areas have NOT been streamlined compared to the local IRB review process]*.
    a. What suggestions do you have on how these areas can be measured to appropriately reflect the burden of this new policy? *[Probe about each topic mentioned]*

Goal #2:

The second goal of NIH's sIRB policy is to "maintain high standard for human subjects protections." My next questions will be about this goal.

1. How would you define "high standards?"

2. Based on your experience, what concerns have you had regarding your institution's ability to maintain a high standard for human subject projections when using a single IRB process?
    a. How could those concerns be evaluated?

3. When your institution was the *relying institution*, how did you communicate local information relevant to the study population to the reviewing IRB, particularly about vulnerable populations?
    a. What has worked well with this process? [Probe: how sufficiently local information was incorporated into review]
        - What has not?

4. What suggestions do you have for evaluating the collection and incorporation of local knowledge into the sIRB process for multi-site studies?

Goals 3 – 5:

Three other goals of NIH's sIRB policy are to allow "research to proceed effectively and expeditiously," "eliminate unnecessary duplicative IRB review," and "reduce administrative burdens."
We will now discuss topics related to these goals.

1. When your institution has been the *relying institution*, how has the *reviewing IRB* communicated with you?
    a. What has been efficient about this process, if anything?
    b. What has been burdensome about this process, if anything?
    c. How could this process be evaluated?

2. What activities, if any, have you found to be duplicative between the relying institution and reviewing IRB?

3. What have you found to be the main administrative burdens, if any, when your institution has been the *relying institution*?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could these administrative burdens be evaluated?

4. What have you found to be the main administrative burdens for you, if any, when your institution serves as the *reviewing IRB* for your multi-site studies?
    a. How are these burdens different, if at all, from administrative burdens prior to the sIRB policy?
    b. How could these administrative burdens be evaluated?

5. How, if at all, has the amount of time taken from point of submission to point of approval changed under the sIRB model compared to the local IRB model? *[Probe about specific aspects that have increased time and decreased time, and how this time investment may have changed over time]*.
    a. How could we evaluate the time required for using the sIRB model in comparison to the local IRB model?

6. How has the sIRB process, if at all, impacted study start up time?
    a. How can this be evaluated?

7. How has the sIRB policy impacted your ability to conduct research efficiently? *[Probe about benefits, burdens, initial review, ongoing review, adverse event reporting]*
    a. [If not addressed above] How, if at all, has the sIRB process impacted your ability to recruit participants?

8. How, if at all, does using a sIRB process improve the research experience for study participants? *[Probe to 1) identify the specific part of the sIRB process that is most impactful and why, and 2) the specific part of the participant experience that is most impacted by the use of a sIRB process]*
    a. *[If identified participant improvements]* How could this be measured?

Goal 6:

The remaining NIH sIRB goal we'll discuss is to "prevent systemic inefficiencies."

1. In your opinion, what systemic inefficiencies have previously existed with the local IRB model, if any?
    a. How has the sIRB model improved upon these inefficiencies, if at all?
        - How has it not?
    b. How has the sIRB model created new inefficiencies, if at all?

Concluding Section

I have few remaining questions to wrap up our conversation today.

1. Based on your experience, what do you think have been the top three benefits of using a sIRB process for multi-site studies? *[Probe about why these benefits were selected, if the benefit was not previously discussed, as well as how to measure them, if not previously discussed, as well as how to measure them, if not previously discussed.*]

2. What do you think have been the top three burdens that did not existing with the local IRB review model? *[Probe about why these burdens were selected, if the burden was not previously discussed, as well as how to measure them, if not previously discussed, as well as how to measure them, if not previously discussed..]*

For the last two questions, please focus your answers on what you think your institution could reasonably do.

3. What are your top three suggestions for how to evaluate the day-to-day work that your institution does to implement the sIRB process—often referred to as process evaluation?

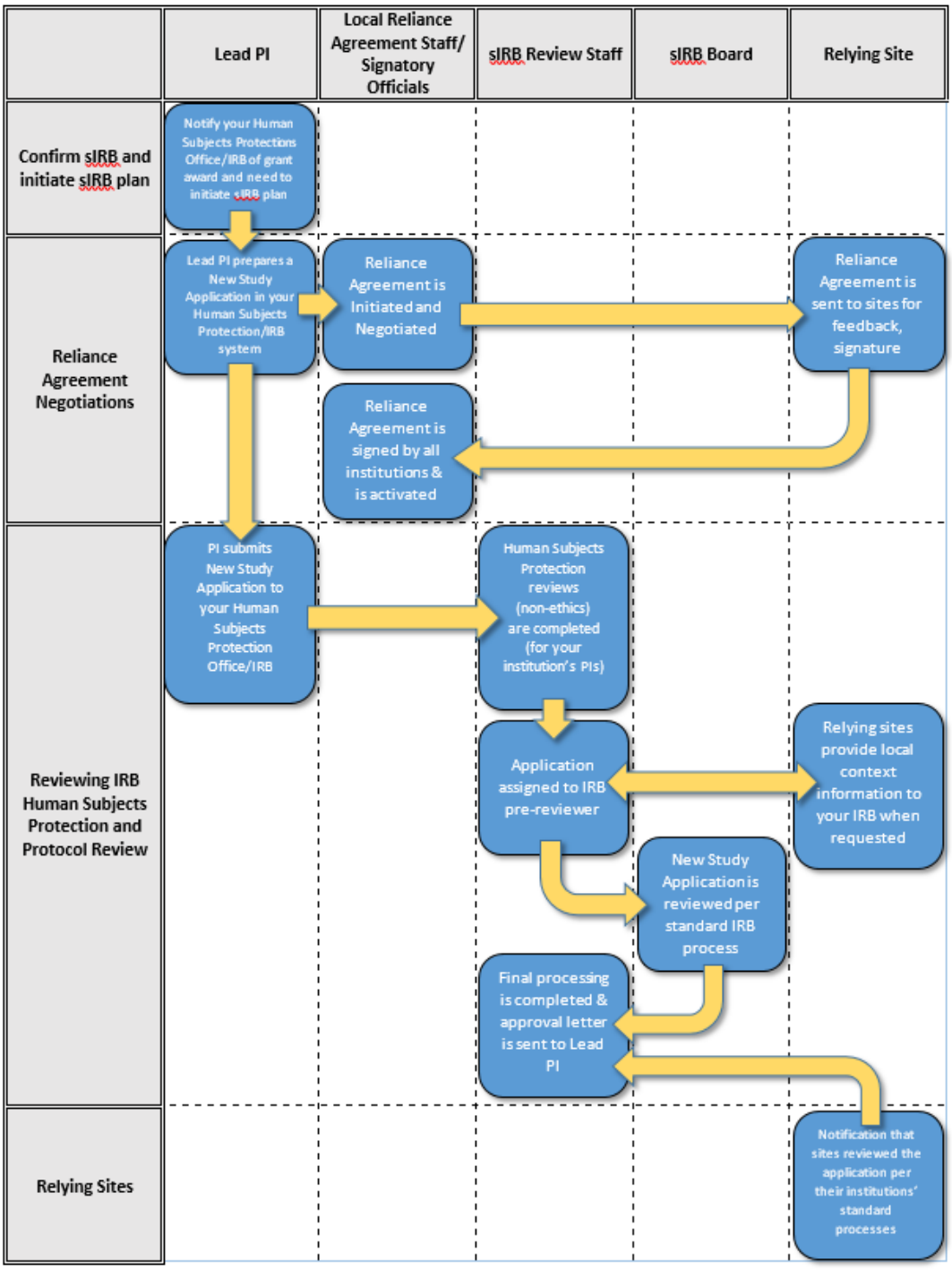
4. What are your top three suggestions for how to evaluate the impact of using a sIRB process for multi-site studies—meaning, how to evaluate whether the sIRB process is achieving NIH's sIRB goals?

Thank you for your time. May we contact you if we have any additional questions?

Appendix B

CLINICAL TRIALS TRANSFORMATION INITIATIVE

Single IRB Process Map: Reviewing IRB



Currently Available IRB Metrics – Results of Desk Review

This document contains a list of metrics currently collected at institutional review boards (IRBs) or coordinating centers to evaluate IRB performance. The items were collected from publications, publicly available presentations, listings on websites, and correspondence with institutions and NIH funded central IRBs. Time from submission to IRB approval is the most routinely tracked metric. Metrics about single IRB use are becoming more common. Data collected outside the IRB, such as site preparation time, are less consistently tracked by/less available to IRBs and are more likely stored by coordinating centers.

The table below includes five metric categories: Volume, Review Time, Staffing, Costs, and Quality

Category	Metric	Definition/Addition Information	Source
Volume	Total applications	Total applications to the central IRB (per year, per network, by review type)	8, 10, 11, 12, 19, 20, 27, 28, 30, 31
	Total parent applications	Total parent submissions to the sIRB (per consortium, overall)	8, 12
	Total # of amendments	Total number of amendments includes protocol/ICF changes, addition of "child" sites, staff amendments, protocol amendments, recruitment materials, etc.	8, 12, 19
	Total # of continuing reviews	Number of continuing review submissions per year	8, 12, 19
	Total # of other submissions/events	Number of protocol deviations/safety events/Data Safety Monitoring Board (DSMB) meeting summaries	8, 12, 19
	Number of studies relying on an external IRB	Number of studies relying on an external IRB	1, 11, 20, 30
	Number of studies using internal IRB review	Number of studies using institution's IRB(s)	1, 11, 20
	Number of requests to use outside IRB	Number of studies requesting to rely on outside IRB	1, 6, 20
	Number of active (open) projects	Open - A project that has obtained IRB review and approval. Research related activities can begin or are underway. Total and by type of review - exempt, expedited, full review.	3, 11
	Number of pending projects	Pending – A project has been submitted to the Human Subjects Office (HSO) and is currently under review by the HSO and/or the IRB. It has not received a formal IRB determination or IRB approval.	3
	Total number of forms submitted to IRB	Definition of Form = Any form type submitted to the IRB. This includes new projects, modifications, modification + continuing review, continuing review, HSRD (Human Subject Research Determination). Reportable Event Forms are not included in these figures.	3
	Total number of new sites reviewed	Total number of new sites reviewed per year	27
	Number of studies disapproved	Number of studies disapproved in last calendar year	27
	Number of reliance agreements executed	Number of reliance agreement and reliance agreement supplemental documents	20
	Total number of reliance consultation meetings	Number of meetings with investigators wishing to use sIRB for their studies. Determinations from meetings tracked - use institution as sIRB, agree to serve as sIRB pending award, decline reliance relationship.	20

Category	Metric	Definition/Addition Information	Source
Pre-award time	Time HRPP staff spend assisting with sIRB plan in grant proposals	Time HRPP staff spend assisting investigators in selecting sIRB for study, determining reliance agreements and platforms, developing communication plan, estimating sIRB budget, and writing sIRB plan for grant proposal.	7, 20
Reliance Time	Time to approve use of external IRB	Time from investigator submission to HRPP/request to rely on external IRB to time HRPP send email granting permission to use external IRB (does not include institutional approval time)	1, 13, 32, 33
	Time to execute IRB Authorization Agreement (IAA)	Time from request to rely on IRB to execution of IAA	8, 9, 18, 22, 32
	Time to sign-up/execute non study specific reliance arrangements	Time to join SMART IRB and IRB Reliance Exchange (IREX), and sign CIRB indemnification letter	9, 32
Pre-Review Time	Site time to submit materials to reviewing IRB	Time (in days) from when single IRB startup package sent to sites until all required information from the PI/research site is submitted to the single IRB. Includes time for information exchange time between coordinating center, investigators, local HRPP/institutional reviews, and sIRB.	2, 4, 8, 10, 15, 16, 17, 18, 25, 28, 32, 33
	Time spent pre-screening protocols	Time HRPP staff spend reviewing protocols prior to submission to IRB	6, 19
	Time spent educating and supporting study team	Time HRPP staff spend educating and assisting study teams to submit for IRB approval	6

Category	Metric	Definition/Addition Information	Source
Review Time	Total Human Research Protection Program (HRPP) Review Time for Studies Using External IRB Review	Number of days from receipt in HRPP office until "institutional approval" is granted	1, 2, 9, 12, 18, 24, 31, 33
	Total Human Research Protection Program (HRPP) Review Time for Studies Utilizing Own Institution's IRB(s)	Number of days from receipt in HRPP office until IRB approval letter is issued	1, 2, 5, 24
	IRB Submission to Review Time	Time (in days) from submission to review by convened IRB. This can be divided into time in pre-review (IRB Ops) and time with PI (during pre-review).	11, 12, 19, 31, 33
	Time with IRB	Time for board review or designated review	12
	IRB Review Time - Review of protocol (parent) submission	Time (in days) from IRB submission (PI sign-off) to IRB approval, with no contingencies	1-5, 8-25, 28-30, 33
	IRB Review Time - Site additions	Time (in days) of IRB approval of child sites (from submission of child site to approval of child sites)	2, 3, 4, 8, 9, 18, 20, 22, 24, 28, 32, 33
	Total IRB review time	Time (in days) from date initial protocol is submitted to sIRB to time all initial sites are approved and can start enrollment	4, 5, 9, 20, 24, 28, 31
	Protocol to IRB Approved Time	Total time in calendar days from protocol receipt by sites to IRB approval	17, 18, 25, 33
Other Reviews Time	Time required for continuing review	Date continuing review application is submitted to reviewing IRB until date of re-approval, Time (in days) for sIRB annual renewal (time from meeting date to approval)	4, 6, 8, 19
	Time for amendment approval	Time (in days) from date changes (to protocol or informed consent) are submitted to IRB to date approved to be changed at all sites	4, 6
Post-IRB approval	Site activation time	Time (in days) from sIRB approval to site activation	8, 18, 21, 25, 32
	Activation to enrollment	Time (in days) between activation and 1st consent	8, 32

Category	Metric	Definition/Addition Information	Source
Staffing	Full time employees (FTEs):Number of new studies	FTEs in HRPP office vs number of new submissions	1, 10, 12, 19, 26, 27
	Staff changes	Increases or decreases in FTEs related to single IRB process	13
	Staff time on institutional reviews when relying on outside IRB	Time tracking of HRPP staff to assist study team with submission for institutional reviews when using outside IRB	6, 32
	Staff time on all reviews when serving as sIRB	Time tracking of HRPP staff on all required reviews (institutional + IRB)	6, 32
	Staff time on training to facilitate sIRB review	Time spent training IRB staff on single IRB procedures	2
	Staff time to train study teams	Time spent training investigators, coordinators, coordinating centers	2, 6
	Number of employees dedicated to sIRB activities	Number of staffing positions performing activities required for sIRB - including reliance on outside IRBs and serving as sIRB	6, 13
Costs	Cost to upgrade or change information systems	Costs required to properly store information about multi-site review. For example to allow non-affiliated individuals to enter information. To accept training from outside personnel. To allow for approval of all internal reviews without IRB review. Etc.	2
	Costs of new staff	Salary/benefits of new employees hired for sIRB process	2, 6
	Costs of training IRB and other institutional staff		2, 32
	Costs of sIRB coordination	Costs for personnel at coordinating centers to communicate between sIRB and sites	2, 6, 32
	Calculated time of sIRB personnel executing sIRB tasks	Time spent multiplied by salary of employees completing tasks	6, 32
	Total IRB Expenditures	Total budget of IRB	11, 26

Category	Metric	Definition/Addition Information	Source
Quality, Quality Improvement, Compliance	The IRB Researcher Assessment Tool (IRB-RAT)	Validated instrument, proxy measure of IRB quality, that assesses 45 distinct IRB activities and functions.	23
	Non-compliance reported to IRB	Number of reports per year of noncompliance reported to the IRB	11
	Number of complaints reported to IRB	Number of complaints per year reported to the IRB	11
	Number of audits	Number of audits conducted. Categorized by audits of researchers and of IRBs and for-cause and random.	11
	Number of Inspections	Number of FDA, OHRP, Other agency inspections in last 10 years	27
	Number of OHRP determination letters	Number of OHRP determination letters in the past 10 years	27
	Number of FDA 483 and Warning Letters received	Number of FDA 483 and Warning Letters in past 10 years	27
	Number of critical observations or findings from other agencies	Number of critical observations or findings from other agencies in past 10 years	27
	IRB Research Community Feedback Survey	Survey requesting feedback about their IRB experience at the time of final approval for a new study. Used to improve performance. IRB forms & process, turnaround time, service received, quality and consistency of review, and responsiveness.	30
	Helpdesk responses	Query receipt to complete response to query; satisfaction survey for those that contact the Helpdesk	31

#	Source
1	Correspondence with Hallie Kassan, Director of Human Research Protection Program Northwell Health October 12, 2018 Call with Trial Innovation Networks about sIRB metrics, metrics in IREx.
2	https://www.irbexchange.org/p/wp-content/uploads/2018/11/IREx_Overview-1pager_20181114.pdf
3	University of IOWA IRB website: https://hso.research.uiowa.edu/ui-irb-metrics
4	Cincinnati Children's Hospital Poster PRIM&R 2018: Jeanette Bailey (Poster #24) Success With a Single Reviewing IRB Serving a Federally Funded Consortium
5	CREST 2 study comparison of sIRB and local IRB. Poster at PRIM&R 2018: Mike Linke (Poster #37) Single IRB Review Improves Approval Times for a NIH-Funded Multi-Site Study
6	JHU Time tracking study: Poster at PRIM&R: Scott Hines (POSTER #34) Identifying Costs in the Evolving IRB World: Data-Tracking for Effective Costing in the Implementation of Single IRB Review
7	Indiana University Grant Submission Process: Poster at PRIM&R: Ryan Ballard (Poster #57) Erasing Silos: Enhancing HRPP Collaborations for NIH Single IRB Proposals
8	Correspondence with NeuroNEXT Sr. Project Manager, Daniela Grasso Walker. And Pearl O'Rourke Director of Human Research Affairs at Partners HealthCare Systems.
9	STRESS Trials Presentation: https://clic-ctsa.org/content/ctsa-spring-meeting-2018-presentations
10	Correspondence with Mike Linke, University of Cincinnati, StrokeNet Central IRB. And Catherine Dillon, StrokeNet Data Coordination Unit, Medical University of South Carolina.
11	AAHRPP 2017 & 2018 Metrics on Human Research Protection Program Performance. http://www.aahrpp.org/apply/resources/metrics-on-hrpp-performance
12	Correspondence with Helen Panageas, Director, Institutional Review Board Operations, Office of Science and Research, NYU Langone Health
13	Not Less Work, But Different: Re-Engineering for Single IRB Review. Presentation at PRIM&R AER 2018. Johns Hopkins, University of Wisconsin-Madison, and University of Texas-San Antonio.
14	Dziak K.https://doi.org/10.1111/j.1475-6773.2005.00353.x
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16	McWilliams R. https://doi.org/10.1001/jama.290.3.360
17	Neuman, MD. https://journals.sagepub.com/doi/10.1177/1740774517735536
18	Stoffel B. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5846487/
19	Adams P. https://doi.org/10.1371/journal.pone.0113356
20	Correspondence with Ann Johnson. Director, Institutional Review Board, University of Utah.
21	MDIC Early Feasibility Study (EFC) Metrics. http://mdic.org/wp-content/uploads/2018/05/EFS-Metrics_MDIC-Website-2018.pdf
22	Kaufmann P. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4859204/pdf/nihms-782111.pdf
23	Hall DE. https://doi.org/10.1177/1556264615612195
24	Diamond MP. https://journals.sagepub.com/doi/10.1177/1740774518807888
25	Abbott D. https://journals.sagepub.com/doi/pdf/10.1177/2168479012464371
26	Models for Institutions Serving as sIRB of Record, Washington University. https://osp.od.nih.gov/wp-content/uploads/Session_I_2_Washington_University_CTSA.pdf
27	Models for Assisting Institution Relying on sIRB – Partnership and Innovation Exploring Single IRB Models to Support Clinical and Translational Research, Yale University https://osp.od.nih.gov/wp-content/uploads/Session_II_1_Yale_University_CTSA.pdf
28	Facilitating Single IRB Review for Multi-site Research: The OneIRB IT Platform, University of Pennsylvania. https://osp.od.nih.gov/wp-content/uploads/Session_III_1_University_of_Pennslyvania_CTSA.pdf
29	CTSA Program Common Metrics Operational Guideline: IRB Duration https://clic-ctsa.org/sites/default/files/common_metrics/Common-Metrics-Operational-Guidelines-IRB-Duration_2.2.17.pdf
30	Metrics Dashboard University of Minnestota. https://research.umn.edu/units/irb/about-us/irb-performance-metrics#active
31	Correspondence with NCCIRB Laura Covington, NCI CIRB Director Local Operations, Emmes Project Leader. February 5, 2019.
32	Vardeny, O. Transitioning to the National Institutes of Health single institutional review board model: Piloting the use of the Streamlined, Multi-site, Accelerated Resources for Trials IRB Reliance https://doi.org/10.1177/1740774519832911
33	Nichols, C. Use of single IRBs for multi-site studies: A case report and commentary from a National Drug Abuse Treatment Clinical Trials Network study. https://doi.org/10.1016/j.conctc.2019.100319