Published in final edited form as:

Ethics Hum Res. 2022 November ; 44(6): 32–38. doi:10.1002/eahr.500149.

Demonstration Project: *Transitioning a Research Network to New Single IRB Platforms*

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Abstract

Since the 2016 National Institutes of Health (NIH) mandate to use a single IRB (sIRB) in multicenter research, institutions have struggled to operationalize the process. In this demonstration project, the University of Utah Trial Innovation Center assisted the Collaborative Pediatric Critical Care Research Network to transition from using individually negotiated reliance agreements and paper-based documentation to a new sIRB master agreement and an informatics platform to capture reliance documentation. Lessons learned that can guide other academic institutions and IRBs as they operationalize sIRBs included the need for sites to understand what type of engagement or reliance is required and their need to understand the difference between reliance and activation. Requirements around local review remain poorly understood. Further research is needed to determine approaches that can achieve the NIH vision of reviews becoming

more efficient and improving study start-up times, relieving administrative burden while advancing human research protections.

Keywords

institutional review board; single institutional review board; research ethics; SMART IRB; reliance agreement

In 2016, the National Institutes of Health (NIH) mandated a single-IRB (sIRB) approach for federally funded studies carried out at more than one site in the United States.[1] In response, the National Center for Advancing Translational Sciences (NCATS) funded three sIRBs in the Trial Innovation Network (TIN) to operationalize the sIRB process nationwide. The University of Utah, Vanderbilt University Medical Center, and Johns Hopkins University were charged with developing and harmonizing their sIRB processes and standard operating procedures, which could then serve as a model for other institutions serving as an sIRB. The University of Utah IRB was already the sIRB of record for the Collaborative Pediatric Critical Care Research Network (CPCCRN) supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). The University of Utah IRB assisted this network to proactively implement an sIRB-of-record model, then called a “central IRB” model, for reviewing all network studies prior to the NIH mandate requiring sIRB review.[2] CPCCRN studies were using individually negotiated reliance agreements and paper-based reliance documentation. This made CPCCRN an ideal candidate for transitioning to new sIRB resources such as a master agreement and a common informatics platform to capture reliance documentation.

The Utah Trial Innovation Center (TIC) engaged in a demonstration project with sophisticated network sites of the CPCCRN to implement the SMART IRB Reliance agreement[3] and document the sIRB process for each network study in the Vanderbilt IRB Reliance Exchange (IREx) platform.[4] Although it was assumed that the transition would be smooth and intuitive since the network had already been implementing an sIRB model for the past four years, the project ended up being quite labor intensive. It also yielded valuable lessons. In this paper, we describe lessons learned during this transition in hopes that our experience will guide other academic institutions and IRBs as they operationalize sIRB support for multicenter clinical research.

TRANSITION TO THE SMART IRB AGREEMENT

At the time of this demonstration project, the CPCCRN consisted of seven academic clinical sites across the United States and a data-coordinating center at the University of Utah. The network seeks to reduce morbidity and mortality in pediatric critical illness and injury and to establish a framework for developing the scientific basis for pediatric critical care practice. These goals cannot be achieved without the support of collaborative clinical trials otherwise impractical at single institutions.[5] The data-coordinating center coordinates all aspects of network studies, including preparing the sIRB submissions on behalf of the network. When the TIN demonstration project started, there were seven sIRB-approved ongoing studies, and it was anticipated that new projects would be added at a rate of one to three per year.

The proposal was to transition immediately to the SMART IRB agreement and document reliance in the IREx platform as soon as it was available for early adopters. The SMART IRB agreement is a reliance agreement created in response to the NIH's mandate for sIRB review of multicenter research.[6] The reciprocal nature of this agreement allows its use for any study. Once it is signed, institutions can use it to serve as the sIRB for other parties to the agreement or to rely on an sIRB who is also party to the agreement. For institutions who have signed the agreement, there is no need to renegotiate any terms when starting a new study because it is a master agreement. The sIRB model described in the agreement includes two types of review. First, the IRB of record, also called the "reviewing IRB" or "sIRB," conducts the primary study review, focusing on the science and participant protections. Second, though local site institutions are expected to cede the review responsibility to the sIRB through a formal reliance agreement, they still retain authority and responsibility for their site local ancillary reviews by their human research protection program (HRPP). The goal of creating the SMART IRB agreement was to have an agreement with comprehensive terms that could be accepted by most research institutions to allow the sIRB model to be implemented. This would allow for a unified approach to reliance across the U.S. and eliminate the need to negotiate individual reliance agreements for every study.

CPCCRN INITIAL STATUS

Prior to the NIH mandate, seven out of eight sites within CPCCRN were already using an sIRB model with individually negotiated reliance agreements between each site and the University of Utah IRB. As the SMART IRB agreement became available and the NIH mandate came into effect, it was hypothesized that CPCCRN could benefit from using this standardized agreement for its reliance relationships between the sites and the sIRB. At the time, it was our hope as many institutions were already signing the SMART IRB agreement that switching CPCCRN sites to the SMART agreement would make the process of managing reliance relationships and terms more consistent for sIRB and institutions' HRPPs broadly, beyond CPCCRN. Additionally, switching reliance agreements and informatics platforms could ensure that processes and documentation were harmonized and in compliance with the new federal mandates. It was also an opportune moment to make the change, as the remaining sites that needed to enter into a reliance relationship with the sIRB could avoid beginning the process of establishing an individually negotiated agreement. Despite the benefits, there were a number of challenges encountered during the transition. Below, we discuss lessons learned during the transition to the SMART IRB reliance agreement for a national network.

CHALLENGES OF SMART IRB AGREEMENT ADOPTION DURING INITIAL STATUS

Education on reliance agreements was necessary.

Review by an sIRB is more streamlined if all sites agree to the same terms of reliance, with those terms managed by a single source—in this case, the nationally collaborative SMART IRB team and network. This prevents the sIRB from having to review multiple reliance agreements to determine if the terms were met for each study's review. The SMART IRB

agreement did not require individual negotiations between each site, and the sIRB agreement was instead a standard agreement that all sites could simply sign on to, meaning that the negotiation process would be streamlined for both the site and the sIRB. Understanding and educating relying sites on these key concepts was crucial. Education on the roles and responsibility of a reviewing IRB and a participating site was also critical, as outlined further below.

Sites were not initially motivated to make the switch.

Motivating investigators and research administration personnel at each site to make the transition proved difficult. When the CPCCRN sites were first approached to transition from individually negotiated reliance agreements to a nationally available agreement, the benefits were not obvious to site stakeholders, which likely was an important cause of delays in the transition period. Additionally, even though the decision to adopt the national agreement came from the NIH sponsor, the announcement to the network came from the centralized coordinating center. The initial perception that the coordinating center was adding to the sites' burden was difficult to correct. Because the sites already had approval using existing reliance agreements, research could continue during the transition, which meant that there was little immediate incentive to convert to a different type of reliance or review. There were few perceived short-term benefits to counteract the effort needed, and emphasis was placed on the long-term benefits. Unfortunately, these long-term benefits were not fully appreciated across the network at the beginning of the transition period.

The process took longer than anticipated.

Most CPCCRN institutions were not familiar with the SMART IRB agreement, and lengthy, careful review by institutional legal counsels was necessary before sites agreed to the transition.

Ceding review of individual studies was not well understood.

In addition to getting the SMART IRB agreement signed, institutions had to document study-specific cede or reliance decisions because the SMART IRB agreement is a master agreement, not specific to any one study. Thus, HRPPs that had already agreed to rely on the University of Utah IRB via a one-off agreement for all CPCCRN studies now had to document reliance for each study (n = 10) to finalize the transition to SMART IRB. While not a time-intensive task, it was an inconvenience.

Engagement in research determinations was not clear.

Another challenge was identifying which institutions were engaged in research due to multiple affiliations. At times, we experienced difficulties identifying which institutions were engaged in research and needed to execute the SMART IRB agreement because investigators had multiple medical-center or academic affiliations (e.g., children's hospitals). Without an intimate knowledge of a site's affiliation with or connection to other institutions, our sIRB had some difficulty discerning which HRPPs to contact regarding reliance. It became clear that each institution considered engagement differently, especially when it came to legal entities and academic affiliations with children's hospitals. Investigators and

study teams often did not have the working knowledge of what type of engagement or reliance their site required. We found ourselves casting a broad net for reliance to all connected sites but later determined that many of the affiliate institutions were not engaged in research and did not require reliance on the sIRB. Documentation of multiple institutions engaged in a single study required creative solutions. As described below, this sometimes led to new programmatic solutions in IREx.

Misunderstanding reliance and site activation was common.

Many sites were hesitant to quickly agree to rely on the sIRB even though they were planning to use the sIRB. The site HRPPs mistakenly believed that the sIRB approval decision would automatically activate their site, circumventing their institutional autonomy in authorizing an investigator to begin the research activities within their institution. This confusion is understandable and required education and outreach to correct.

Local review was not well understood.

During the CPCCRN transition to the SMART IRB agreement and IREx, it was apparent that not enough emphasis was put on local review of the relying site under the original existing reliance agreements. There was little consistency in how sites were conducting their local review, and there were no defined measures on what information should be relayed back to the reviewing IRB. Site HRPPs were unfamiliar with a local review process separated from formal IRB review, and site study teams were unfamiliar with HRPP requirements to activate their site research activities. In response, we devoted considerable effort to help distinguish sIRB approval from site activation, which always remains at the discretion of the institution and its HRPP. This clarification resulted in prompt agreement to rely on the sIRB, which is required before the sIRB can begin to review an individual site.

BENEFITS OF SMART IRB AGREEMENT ADOPTION DURING INITIAL STATUS

Transition could happen without disrupting active studies.

During the transition to the SMART IRB agreement, already-approved research at each CPCCRN site was allowed to continue under the previous reliance agreements until reliance under the SMART IRB agreement became effective. This ensured that research was not interrupted and that participants' rights were still protected during the transition, and obtaining new participant informed consent was not necessary.

Site agreements apply to multiple sIRBs.

CPCCRN sites worked more seamlessly with the other sIRBs within the TIN. Because the TIN sIRBs had also signed onto the SMART IRB agreement, if a need arose for these sIRBs to take part in the IRB review for any given study, it would not require negotiation of a new or additional agreement. This was a benefit to the network.

The SMART IRB reliance agreement can be used for future network studies.

Ultimately, all CPCCRN sites were operating under the SMART IRB agreement within 300 days of starting this project. This strengthened the ability of the network to use SMART IRB to streamline future projects involving up to 25 sites. The CPCCRN sites benefited from becoming familiar with a national model for reliance agreements and processes. The broadly shared understanding of its terms, expectations, and process makes it easier to initiate study-specific reliance decisions within CPCCRN and for other non-CPCCRN studies in which the same institutions participate.

Institutional acceptance of SMART IRB continues to improve.

After the initial resistance, institutional comfort with the SMART IRB agreement and its reliance process grew much faster than we had expected; the unfamiliar became quickly familiar. CPCCRN now also has the flexibility to work more seamlessly with many IRBs, not just the TIN SIRBs.

TRANSITION TO IREX

The next challenge was the adoption of IREx to capture reliance documentation—including study-specific cede decisions and local considerations—from participating institutions for all CPCCRN studies. IREx is a freely available, web-based platform maintained by Vanderbilt University Medical Center that supports sIRB review documentation and coordination for multicenter studies. The IREx platform has been in development for nearly a decade based on NIH support and connects institutional IRBs, HRPPs, and study teams and enables documentation of reliance relationships in a central location.[7]

During the transition to the SMART IRB agreement, IREx became the electronic repository for study teams and participating site HRPPs to communicate local considerations to the sIRB and coordinating team. TIN sIRBs developed the three core elements of local considerations, which include the institutional profile (IP), the human research protection survey, and an investigator survey. The IP captures overarching local and state laws and policies that apply to all studies at an institution. IREx served as a repository for this information and now offers universal access to the sites' IPs as a PDF downloadable from the public website. Information in these IPs does not change frequently, so site HRPPs can simply confirm their IP in IREx each time they rely on an sIRB for a study. However, the TIN sIRBs developed the human research protection and investigator surveys to capture study-specific local considerations, such as institutional policies, state laws, unique religious or social concerns, and community demographics relevant to a given study.

IREx provided the functionality to allow documentation of local considerations to be (1) provided by the appropriate parties (e.g., HRPP and the investigator) and (2) documented concurrently while also (3) ensuring that necessary communications were sent when information was completed or had been revised. This helped provide consistency in the information collected across all sites and streamlined the process for creating site-specific consent forms based on sites' responses. The local site HRPP will consider consent document language required by the institution (including contact information for

participants at their site), as well as review state-specific requirements (such as age of consent), institutional policies, the qualifications of and training records for local study teams, and similar considerations. Previously, the site HRPPs either did not fully weigh in when it came to local review, or there was not a standard process to submit local community data to the sIRB.

IREx also functions as a centralized hub where any authorized stakeholder, such as the lead study team or coordinating center, has access to the status of the reliance process and requirements necessary before a site can be moved forward for approval and subsequent site activation. The IREx portal has nearly replaced the overwhelmingly large number of unorganized email threads previously used to communicate these details.

CHALLENGES OF IREX ADOPTION DURING THE TRANSITION TO IREX

Clarifying expectations about study-specific reliance decisions.

One of the lessons learned about onboarding sites to use IREx was the value of using a metaphor to describe the study-specific reliance decision as a “handshake” or an agreement of intent, while reiterating that local site HRPPs still had jurisdiction of the project through its closure. This addressed the misconception that HRPPs mistakenly released their right to review a project and determine if local requirements were met appropriately when they made a reliance decision. It was important to reinforce that HRPPs still retained the ability to conduct local reviews and notify the sIRB if site requirements need to be adjusted, even after a reliance decision was initiated. This was not unique to the CPCCRN network; uncertainties and misunderstandings about roles of the sIRB and local HRPP programs are among the most common ongoing concerns about sIRB review.[8]

Communicating the value of standardization.

The need to standardize HRPP specific requirements is critical. The local review and site study teams were unfamiliar with requirements to activate the transition to the SMART IRB agreement. Some sites believed they needed to complete a full IRB review of a project—often overlapping heavily with sIRB review—prior to entering into a reliance agreement. Transition to IREx included standardization of HRPP reliance information, including clarification of what aspects require local review. Local review by site HRPPs may include local circumstances and preferences, variations in language, and economic and other contextual factors.[9]

Improving and enhancing new tools.

Many changes were made to IREx over the first few years and continue to be made. CPCCRN sites struggled with IREx early on because it lacked certain features that would make it a better system for communication, tracking, and accounting for nuanced differences between sites. However, based on the CPCCRN experience, many enhancements have been made to IREx, which can now do the following: (a) allow relying institutions to document whether their federal-wide assurance (FWA) components are engaged on studies, alone or in addition to the FWA; (b) facilitate documentation from multiple FWAs engaged by a single study team (e.g., combo sites); (c) provide special interfaces and dashboards for HRPP

liaisons that oversee FWAs at multiple institutions to better facilitate the capture of reliance documentation for multiple institutions; (d) accommodate studies where the lead site and the sIRB are not the same entity; (e) support sIRBs in the delegation of tasks, tracking, and follow-up to the lead study team or coordinating center, which plays a major role in sIRB coordination; and (f) allow lead study teams and coordinating centers to control when sites are notified about studies in IREx.

BENEFITS OF IREX ADOPTION DURING THE TRANSITION TO IREX

The ultimate benefit CPCCRN has experienced from using IREx has been standardization of the process and documentation for sIRB review. In addition, use of IREx has reduced duplicative data entry for study teams and the sIRB. Some site-specific HRPP data, such as institutional policies, state laws, unique religious or social concerns, and community demographics, were static and did not change based on the study. The ability to reuse this information could potentially reduce data entry burden. Therefore, a repository for this information was built into IREx, and future reliance agreements can use this existing IP without reentering the information for each agreement. If changes do occur, HRPPs can update this information when they confirm their IP in IREx with each subsequent study-specific site registration.

Changes in IREx, including standardization of the HRPP reliance requirements and IP, replaced unwieldy email threads and provided a centralized point of information for identifying the status of a reliance agreement for site approval. We acknowledge that IREx was built in response to the sIRB mandate and that it is an evolving system. The functionality has increased significantly during the time CPCCRN sites were transitioning, and as a result, it has become a useful tool.

DISCUSSION

Lessons learned include the importance of identifying long-term benefits of change prior to implementation of that change and using effective communication from the sponsor (NIH) to inform the stakeholders. Additionally, the coordinating center and sIRB learned the value of communicating the long-term benefits of using the SMART IRB agreement, better defining combo sites for pediatric studies, and identifying local review requirements that were not realized in the original central IRB model.

Once the transition was complete, the long-term benefits were apparent: using a national agreement streamlines IRB review within a network when multiple studies are conducted at once and allows institutions to use the agreement outside of CPCCRN. We demonstrated the difficulty of transitioning a research network that is using an existing sIRB model to new resources. Change is hard! Our project speaks to the challenges sIRBs face when changing their processes to align with federal mandates and leverage new tools.

Implementing a centrally accessible platform, such as IREx, has not only improved the transparency of what other local considerations the relying institution is required to address but has also improved the process of documenting the local considerations and

communicating them to the sIRB. As a result of this transition, CPCCRN sites have become well versed in nuances and the expansiveness of their local HRPP review process.

The creation of a new national policy mandating sIRB review for multicenter clinical studies has been confusing and disruptive to many study teams, IRBs, and research networks. The CPCCRN was no exception. This network was comfortable with the central IRB practices already proactively put in place, but the practices were not up to the standards of the new sIRB mandate. Transition to the SMART IRB agreement allowed a unified approach across institutions, effectually eliminating the need to negotiate individual reliance agreements for each site. Use of a mutually accessible platform, such as IREx, has made the process more transparent and eliminated confusion during the reliance process. It is clear that an effective communication plan is essential and obtaining stakeholder buy-in up front is critical before work begins. Further study is needed to determine whether this new sIRB approach provides more efficient study start-up and decreases the administrative burden of IRB review while still protecting human participants.

ACKNOWLEDGMENTS AND DISCLAIMER

We thank Valeriya Vasenina, MS, a project manager at the Utah Trial Innovation Center, for providing project-specific background and data and members of the Collaborative Pediatric Critical Care Research Network (CPCCRN) for their participation in this demonstration project.

Support has been provided by the Utah Trial Innovation Center, funded by the National Center for Advancing Translational Sciences under cooperative agreement U24TR001597. CPCCRN is funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development under agreement number U01HD049934. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

REFERENCES

1. “Final NIH Policy on the Use of a Single Institutional Review Board for Multi-site Research,” National Institutes of Health, released June 2016, effective January 25, 2018, https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html.
2. Burr JS, et al. , “Implementing a Central IRB Model in a Multicenter Research Network,” Ethics & Human Research 41, no. 3 (2019): 23–28.
3. “SMART IRB Agreement v2.0,” SMART IRB, October 2020, https://smartirb.org/agreement.
4. “IRB Reliance Exchange,” Vanderbilt University, accessed November 17, 2021, https://www.irbexchange.org.
5. Willson DF, et al. , “Collaborative Pediatric Critical Care Research Network (CPCCRN),” Pediatric Critical Care Medicine 7, no. 4 (2006): 301–7. [PubMed: 16738501]
6. “About Us,” SMART IRB, accessed November 17, 2021, https://smartirb.org/about-us.
7. “History of NIH Support for Vanderbilt’s Single IRB Platforms,” IRB Reliance Exchange, Vanderbilt University, https://www.irbexchange.org/p/history-2.
8. Corneli A, et al. , “Stakeholder Experiences with the Single IRB Review Process and Recommendations for Food and Drug Administration Guidance,” Ethics & Human Research 43, no. 3 (2021): 26–36.
9. Lidz CW, et al. , “Reliance Agreements and Single IRB Review of Multisite Research: Concerns of IRB Members and Staff,” AJOB Empirical Bioethics 9, no. 3 (2018): 164–72. [PubMed: 30285561]