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“You really do have to know the local context:” IRB administrators and researchers on the implications of the NIH single IRB mandate for multisite genomic studies

Nora B. Henrikson, PhD, MPH^{1,2}, Paula R. Blasi, MPH¹, Jeremy J. Corsmo, MPH³, Emily Sheffer Serdoz, MPA⁴, Aaron Scrol, MA¹, Sarah M. Greene, MPH⁵, Tanya L. Matthews, PhD¹, and James D. Ralston, MD, MPH²

¹Kaiser Permanente Washington Health Research Institute (USA);

²Kaiser Permanente Washington (USA);

³Cincinnati Children’s Hospital and University of Cincinnati, College of Medicine (USA);

⁴Vanderbilt University Medical Center (USA);

⁵Health Care Systems Research Network (USA)

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The institutional review board (IRB) is the bedrock for ethical and regulatory oversight of domestic research involving human participants in the United States. For research funded through the Department Health and Human Services, IRBs are minimally responsible for ensuring human subjects research is conducted in compliance with *45 CFR 46*, “the Common Rule;” which provides standards for ensuring that the rights and welfare of human study participants are protected (U.S. Department of Health and Human Services, 2018). However, IRB offices and Human Research Protection Offices or Programs (HRPPs, larger departments that may contain an IRB) also typically assume responsibilities for local oversight requirements for human subjects research, including Health Insurance Portability and Accountability Act (HIPAA) compliance; compliance with state laws and regulations; consistency with institutional culture; responsiveness to local study population sensitivities; and managing conflict of interest (COI) disclosures and required training. As a result, many local IRBs have become a de facto clearinghouse for centralizing and streamlining local study start-up processes and providing investigators with information on local considerations that often impact study design decisions. While this multi-function IRB model may decrease overall administrative burden on investigators,(Klitzman, Pivovarova, & Lidz, 2017) it can also result in wide variation in local practice between IRBs.

Corresponding author: Nora B. Henrikson, PhD MPH, Assistant Scientific Investigator, Kaiser Permanente Washington Health Research Institute, Kaiser Permanente Washington, 1730 Minor Avenue, Ste. 1600, Seattle, WA 98101, Office: 206-287-4675, Fax: 206-287-2871, Nora.B.Henrikson@kp.org.

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In 2016, the National Institutes of Health (NIH) announced the NIH Policy on the Use of a Single IRB for Multi-Site Research, a new policy requiring a single IRB (sIRB) to review multi-site studies that use the same protocol at all study sites. (National Institutes of Health, 2016) The new policy took effect on January 25, 2018. Multiple federally (NIH/FDA) supported efforts have been undertaken to develop national standards regarding the role of a relying institution (an institution that will rely on the review of an IRB that is not their own institution's IRB) and the role of a reviewing IRB (an IRB that will provide the sIRB review for multiple institutions). Examples of these efforts include the work of the NIH-funded SMART IRB Ambassadors and the Trial Innovation Network and the FDA funded Clinical Trials Transformation Initiative. In addition, several NIH-funded electronic systems have been developed to support sIRB review. Examples of these systems include the IRB Reliance Exchange (IREx), developed by Vanderbilt University Medical Center, and the SMART IRB Online Reliance System developed by the SMART IRB collaborative.

However, adherence with the new policy necessarily requires the separation of regulatory IRB work from other local compliance concerns. This requires concerted institutional effort for organizations who have evolved into a multi-function program, and there is little guidance for institutional IRBs for how best to support both assurance of compliance when relying on an external IRB and on rapid study start-up. In particular, genomic research involves unique local considerations that historically have been addressed through local IRB review programs. Differences in state laws regarding privacy and disclosure of genomic information, institutional policy or practice regarding the handling of genomic data, particularly return of results and incidental or secondary findings, and maintaining awareness of local cultural groups' views about genomic data and research have required significant local IRB knowledge and expertise. Our objective was to explore and identify the anticipated needs of both researchers and IRB administrators around implementing the new sIRB policy in the context of multi-site genomic research.

Methods

We conducted a qualitative study, conducting telephone-based semi-structured interviews with key informants involved in several NIH-funded genomics research networks. Networks included eMERGE (Electronic Medical Records and Genomics), CSER (Clinical Sequencing Exploratory Research) and IGNITE (Implementing Genomics in Practice).

Recruitment.

We used a purposive, convenience sampling strategy to identify potential key informants with expertise in either conducting multisite genomics research or with IRB/HRPP experience reviewing multisite genomics research studies. We selected IRB administrators, research leaders, and research administrators from health care institutions known to the investigator team to be engaged in NIH-funded multi-site genomics research. Participants were eligible if they had led genomics research studies as scientists or research administrators, or if they were IRB administrators who had reviewed genomics research studies. Where feasible, we sought participation from those exposure to studies involving genomic discovery and return of actionable genomic test results to research participants.

Potential participants were invited to participate by email invitations and up to two follow-up from one of the study investigators. If the person declined to participate, we asked them to identify another person from their institution.

Procedures

Between January and February 2018 (after the NIH sIRB policy was released, but before its widespread implementation), we conducted semi-structured phone interviews with individual participants. Each interview lasted approximately 45 minutes. The IRB at Kaiser Permanente Washington reviewed the study procedures and determined the study was exempt research. One to three study team members were present at each interview (PB, JR, SG, AS, NBH); one served as the interviewer and one took notes during the interview. Immediately after each interview, interviewers wrote summaries and impressions of each interview.

We used a sociotechnical framework of health informatics implementation in complex systems to guide development of our interview guide. Questions assessed needs of reviewing and relying IRBs across the institutional environment, including workflow and communication; clinical content; people; internal organizational policies, procedures, and culture; external rules, regulations and pressures; technical infrastructure; and system measurement and monitoring.(Sittig & Singh, 2010) Probes within the interview guide were informed by prior work on models for multisite IRB review(Greene, Braff, Nelson, & Reid, 2010) and elements of the sIRB policy, including potential context-specific variation in the interpretation of the Common Rule and HIPAA influenced by state law and local institutional policies. The interview guide was first vetted and refined based on feedback from members of the eMERGE study work group on return of results and ethical, legal and social issues. We further refined the guide through pilot interviews with a principal investigator, a research administrator, and an IRB administrator with experience in multisite genomics research.

Interviews began with questions about prior experiences in genomics and multisite research and future expectations for sIRB-supported genomics research. Interviews discussed the pre-award and active phases of studies. We then explained two use cases describing different types of genomics studies to elicit potential additional needs related to implementation of the sIRB policy to more fully understand anticipated actions and barriers. The first use case described a two-site study of genomic disease risk requiring collection of blood specimens from participants with linked electronic medical record (EMR) data for phenotypes. The sites were in different U.S. states and the study did not include return of results to participants. The second use case involved three study sites, each in different U.S. states, that were planning to return genomic testing results to adult study participants based on testing for the 59 variants determined clinically actionable by the American College of Medical Genetics and Genomics (ACMG).(Kalia et al., 2017) Each site planned to return results to participants and place the results in the participants' EMR. The interviewee's site would return positive actionable results through the clinical genetics department, while the other two sites would return these same results through primary care providers. For both use cases,

interviewees were asked to first take the perspective of the reviewing site and then the perspective of the relying site.

We sought a maximum sample size within resource constraints, and concluded the interviews after consensus that saturation of themes had been reached. We conducted all interviews during business hours, considering all participants in their professional capacity only. Participants did not receive any financial incentive for participating. The Kaiser Permanente Washington Human Subjects Review Office determined this project is exempt from IRB review according to federal regulations, per Category 2.

Analysis.

We used a template analysis approach to code and organize data for analysis. Template analysis involves developing an initial coding template or codebook based on an existing framework but with flexibility to modify the template based on the study's context and analysis. (Braun & Clarke, 2006; Brooks, McCluskey, Turley, & King, 2015; Crabtree & Miller, 1999) We developed an initial codebook based on our interview guide and the sociotechnical framework. Two investigators independently coded four transcripts (two from scientists/research administrators and two from IRB administrators). The team then compared coding to clarify and revise code definitions. Each transcript was then independently coded by two investigators using the revised codebook, with discrepancies resolved by consensus. All data were coded in Atlas.ti (version 7.5.2).

Investigators reviewed and summarized data from each code and identified novel and emergent themes. We then summarized the themes with supporting quotes in a coding memo structured around our research questions. Through iterative analysis meetings about the coding memo, we identified connections in the data and interpreted our findings.

Results

We invited 25 individuals to participate across 13 institutions. Seven individuals did not respond to our invitation; three declined to participate, and two were initially responsive but interviews were never scheduled due to logistic constraints. In total, we conducted 13 interviews across eight institutions. Participants included seven researchers serving as principal investigators and six people in administrative roles related to IRB administration.

Of the seven researchers, all but one reported spending 50% to 100% of their research full-time equivalency (FTE) on genomics studies, primarily from NIH-funded work. All reported spending more than half of their total FTE on research, except for one participant who reported 30%.

Researchers conducted a wide range of genomics-related research, from discovery science and genetic epidemiology, to biobank infrastructure development, to ethical, legal and social questions, including patient and family preferences and family history. Several organizations reported doing substantial research into best practices around return of results.

Of the six IRB-affiliated participants, all were in leadership roles in their institution's IRB or HRPP. One person reported a dual clinical and IRB role, and had specialized training in

genomics as part of that role, and one participant also reported a role in their institution's biobank. Participants reported a range of sizes of IRBs and case load (up to 1500 studies reviewed per year) and limited clinical trial experience. Two participants reported their institution refers clinical trial applications to external, commercial IRBs. Three participants commented on their institutional IRB's relationship with the institution's HRPP; two of these reported the IRB and HRPP were very closely aligned or under the same part of the organization.

Most participants (n=8) reported experience with multisite studies, including multisite genomics studies. A few participants (n=3) reported less experience with multisite studies, primarily limited to involvement in the eMERGE Network. Most participants reported previous experience either ceding to an external IRB or to a central IRB for multisite studies. Commercial IRBs were used infrequently by participants, and primarily used for industry-sponsored trials. Three participants reported that their institution has served as a reviewing IRB for multisite studies. Participants reported limited but varying IRB familiarity with genomics and genomic research.

Despite some differences in roles and genomics-related experience, common themes emerged across interviews with both researchers and IRB administrators. These themes centered around preparations for the sIRB policy and scientific decisions related to the implementation of the policy (Table 1).

Preparing for sIRB implementation

Theme 1. Most participants reported active preparation for the sIRB policy and reported anticipating some potential benefits to the policy.—Both researchers and IRB administrators reported active preparation measures in anticipation of the new policy. These included developing new guidance documents, processes, and forms, or repositories of documentation such as on a university intranet. Preparation activities reported by researchers included receiving internal communications or trainings related to the new policy, though several articulated unanswered questions about how the policy would work in practice. Anticipating the increasing costs related to the new policy, IRB administrators reported either hiring new staff or wanting to build capacity in the IRB for managing the division of responsibilities for the both the reviewing IRB and relying HRPP. Some IRB administrators mentioned adopting technical products that would ease the management of documents and applications across sites, such as the IRB Reliance Exchange (IREx).

When asked about how prepared they felt for the implementation of NIH's new sIRB policy, participants provided a range of responses ranging from feeling "quite prepared" to feeling "doubtful" about their institution's readiness. Most participants (n=9) reporting feeling prepared to at least be a relying site. Two institutions reported active planning to serve as a reviewing IRB for sIRB-reviewed projects.

Both researchers and administrators reported anticipated benefits of the new policy, including enhanced efficiency in IRB review and time to active study initiation; improved

standardization; maximum protection for human participants; and improved data quality across study sites.

Theme 2. Communication processes between sites, local IRBs and HRPPs, and the reviewing IRB during the active study period were unclear to participants—Both researchers and administrators expressed uncertainty about how to handle the communication of events during the active study period. These included communications about adverse events, protocol violations, noncompliance, safety monitoring and reporting, and local site modifications. Questions were raised about who from the relying site is responsible for communicating such events to the reviewing IRB; how these events are reported to the reviewing IRB or a study team member at the reviewing IRB site; through what channels events are communicated (via email, via submission to the reviewing IRB's electronic IRB system, etc.); and whether events must be communicated to the relying HRPP.

Further concern was expressed about how the reviewing IRB and local sites could be reassured that local study staff were adequately trained and carrying out the study protocol appropriately at all sites. As one researcher stated: *"when [some sites] cede authority to another IRB, they're assuming that that other IRB is taking responsibility for their staff at that other institution in terms of what that staff do: are they trained in human subjects? Are they following the protocol? And our IRB actually does not assume that."*

Theme 3. Participants lacked information and guidance to adequately select a reviewing IRB.—While the NIH policy states that the primary awardee selects the reviewing IRB, researchers reported using a combination of methods to identify the reviewing IRB, such as discussion with other participating PIs, discussions with their local IRB, and referring to the new sIRB policy.

Researchers were unclear about the extent to which a reviewing IRB would conduct scientific review of an application, rather than simply human subjects risk review. To select a reviewing IRB, researchers also mentioned using a reviewing IRB's experience serving as a reviewing IRB; their demonstrated ability and experience to assess local context issues at each site; and the overall quality or reputation of the reviewing IRB. However, researchers often noted this information was not typically readily available, particularly any sort of quality metrics for assessing IRB quality. Further, because of this noted lack of standardization and transparency between different IRBs, participants reported concern about IRB "shopping," in which a study group would select the least restrictive IRB to serve as the reviewing IRB. As one researcher stated: *"I would hate to be shopping for the least stringent IRB if we were trying to think about which site ... should be the IRB for all the project. But I could see those kind of shortcuts happening."*

Theme 4. Participants found it difficult to assess the genomics competency of reviewing IRBs.—Most participants reported that their IRB had at least some familiarity with genomics issues, though this ranged from "not that familiar" to extremely familiar, with one participant saying their IRB was the best in the country for genomics studies. Several participants also mentioned that their IRB's expertise had increased over time as their

familiarity had increased. Most participants emphasized the importance of having some sort of genomics expertise on the IRB.

Researchers also noted the importance of being able to assess an IRB's knowledge and experience related to genomic studies when choosing a reviewing IRB. Genomics expertise on the IRB itself was mentioned several times as a preferred option, as was a reviewing IRB's previous experience reviewing genomics studies. As one researcher noted: *"the reviewers think they're more comfortable with genetics -- or more knowledgeable about genetics than they really are."*

Participants reported potential ways of assessing or ensuring genomics competence of an IRB, including having a person on the IRB with genomics expertise, pre-application consultation with the IRB where the scientific team can provide education on the study and answer questions, and using other advisory groups (such as patients) who can provide other feedback to the IRB. The importance of a single IRB having current knowledge of local population views on genomics (eg tribal nations) was also mentioned, as one participant who stated: "Patient populations are very different....you're working with different communities in terms of research participation, because single IRB being sensitive to those variations may be complicated."

Theme 5. Participants expressed uncertainty about the roles and responsibilities of reviewing IRBs, relying HRPPs, and study teams for using standardized study materials and incorporating relevant local context information for genomic studies.—According to NIH's sIRB policy, local sites must provide the reviewing IRB with appropriate relevant information necessary for the reviewing IRB "to consider local context issues and state/local regulatory requirements during its deliberations;"(National Institutes of Health, 2016) sites then can modify the approved consent template to reflect their local context or regulations, such as around return of genomic test results. Then, as outlined in the policy and the SMART IRB Agreement (section 5.4),(2016) the reviewing IRB "will consider any local requirements communicated to the reviewing IRB" by the relying HRPP.

Several participants expressed uncertainty about a reviewing IRB's ability to apply state regulations, particularly around genetic privacy, for multiple sites, given the complexity of different regulations across states. Similarly, many participants expressed uncertainty about a reviewing IRB's ability to be attentive to local context issues at different sites.

Participants anticipated that any reviewing IRB would face challenges staying current on all the issues and regulations, or even knowing which ones needed to be considered, particularly around return of genomic testing results. Challenges cited by participants included the wide variety in norms and practices of each participating study site (e.g., which type of provider needs to return testing results to patients) and variation in state regulations on human subjects, special populations (e.g. tribal nations), and data and genomic privacy.

Participants noted that the unavoidable heterogeneity in local contexts across sites introduced a tension between the need for standardization in consent forms and protocols

between study sites, and addressing the local context needs of each site, particularly for genomic studies. As one IRB administrator stated: *“the whole issue of local context where we provide the other IRB with information about state laws and that kind of thing, everybody asks for that information differently.”*

Discussion

After the NIH sIRB policy was released, but before its widespread implementation, we conducted a qualitative study to explore the expectations and anticipated needs of scientists and IRB administrators affected by the policy, with specific emphasis on multisite genomics research. We found that while active preparations were underway, uncertainty remained about the logistics of communication, selection of a reviewing IRB, and reporting of events during the active study period. Specific to genomics studies, we identified needs related to reporting and integrating local context differences and state and institutional regulations that could hamper implementation of the sIRB policy, particularly for studies returning genomic results to participants. We identified several opportunities for guidance for relying and reviewing institutions, including communications plans, reporting of local context issues, study monitoring, and selection of a reviewing IRB. Tools that could assist institutions include information about quality and experience of candidate reviewing IRBs and a resource compiling all state laws relevant to genomics studies.

Largely, our results are consistent with previous research, including the NIH’s own summary of public comments, which convey a general sense of the potential benefits of efficiency and increased research integrity, with some concerns about attention to local context needs, the post-award role of the reviewing IRB, and practical and logistic concerns about implementation.(National Institutes of Health, 2016) Our study adds specific nuance with respect to genomics studies. Previous efforts at voluntary sIRB review found conceptual buy-in, but incomplete implementation from participating sites mainly due to uncertainty about how to handle local contextual differences.(Greene et al., 2010; Klitzman et al., 2017) Our study also found uncertainty around local context issues, indicating more education is needed for both IRBs and scientists. In addition, our interviews confirm that overall IRB review quality remains difficult to assess since there are no established IRB review quality metrics,(Wagner, Murray, Goldberg, Adler, & Abrams, 2010) and current efforts to assess IRB quality are primarily focused on efficiency and throughput metrics. The potential benefits of the sIRB model raised in our study echoed those predicted by the policy’s proponents: ultimately improved participant protections through increased transparency, oversight, and standardization.(Rahimzadeh, Dove, & Knoppers, 2017; Wolinetz & Collins, 2017)

Prior to the NIH mandate, sIRB review was associated with more efficient time to review completion,(Kaufmann & O’Rourke, 2015; Massett et al., 2018; Thornquist, Edelstein, Goodman, & Omenn, 2002) reduced staff time,(Wagner et al., 2010) and relatively high satisfaction from its users.(Massett et al., 2018) While our study did not evaluate efficiency or satisfaction, no participants in our study reported that their IRBs are anticipating short-term reduced staffing needs under the new mandate. Any impacts of the sIRB mandate on IRB staffing over time could be explored in future studies.

The National Cancer Institute's central IRB, implemented before NIH's sIRB policy, developed separate policies on the transparency and quality of reviews, consideration of local context, communications, and management of burden for reviewing and relying sites, (Massett et al., 2018) all of which were areas of uncertainty raised by participants in our interviews. Given the need for improved communication plans and guidance, NIH might benefit from generating similar resources. Of note, our research adds additional considerations for genomics studies, including the prominence of genomics-relevant state and local policies, local clinical contexts around returning research results, and a way to assess a reviewing IRB's experience reviewing genomics studies. Further, the need for sensitivity to local population differences has particular relevance for genomics studies given the shared nature of genomic information in many communities and regulations governing participants' rights to be involved in governance of their own genomic data.

We also, not surprisingly, found some uncertainties related to participants' views of roles and responsibilities of the reviewing IRB and relying HRPP. According to the policy and SMART IRB Agreement, the relying HRPP provides relevant local considerations for a specific study (e.g., local and state laws, ancillary reviews, standards, as well as institutional policies governing research at their institution), and the reviewing IRB then reviews and incorporates that information. However, confusion may arise in the thin line distinguishing each stakeholder's role. For example, the reviewing IRB can review only the information provided. It is not the reviewing IRB's responsibility to assess the completeness of the information provided by the relying HRPP or to assess the relying institution's compliance with laws that govern how they do research. This suggests a clear need for education on the roles and responsibilities of the reviewing IRB, relying HRPP, and local study sites in preparing and monitoring study activities and compliance.

Strengths of this study include in-depth interviews with stakeholders actively working on multisite genomic studies, the inclusion of both researchers and IRB administrators across the U.S., and the timing of the study after the policy was released but before its widespread implementation. Limitations include a lack of commercial IRB representation, limited sample size with a non-randomly selected group of stakeholders, and the cross-sectional nature of the study that limit longitudinal assessment. The timing of the study likely represents a unique moment in time and evolutions in experience and attitudes would very possibly be different as experience with the new policy increases, and by design provides only an initial qualitative characterization of the range of experiences.

Conclusion

Genomics researchers and IRB administrators are preparing for NIH's sIRB policy, but uncertainties remain about how the policy will be implemented in general and particularly for genomics studies. Optimal implementation of the NIH policy may require additional guidance for researchers and IRB administrators.

Best practices

Synthesis of the themes suggests several opportunities for guidance or resources that could assist researchers and administrators with implementing the sIRB policy (Table 2). First,

guidance for development of robust communication plans that include some detail about the roles and responsibilities of reviewing IRBs, relying HRPPs and study teams before, during, and after the active study period could help minimize uncertainty. Second, detailed communication plans also could ensure accurate and timely reporting of critical events and noncompliance issues. Third, a database with information on IRB quality, cultural and other local context differences, and disease or therapeutic area expertise could help study teams select a reviewing IRB. Fourth, a centralized repository of state regulations around genomic research and privacy could, if kept updated and used, improve the quality of IRB applications. Finally, critically important to genomics studies, guidance for collecting and resolving local context data at multiple relying sites would help local study teams and IRBs obtain consistent information for each local site.

These recommendations are applicable to academic IRBs or HRPPs, and the genomic scientists who partner with them, at institutions either serving as reviewing IRB or relying institutions. The applicability of these recommendations to other scientific disciplines beyond or to commercial IRBs is not known; but the general uncertainties identified in our study are consistent with prior reports.

Research Agenda

Our study was a cross-sectional study at a unique time point, before widespread implementation of the policy. Future studies should explore lived experiences of IRB staff and scientists after more widespread implementation, and include representatives of both reviewing and relying institutions. Evaluations of any guidance authored or adopted to support integration and adoption of the sIRB policy are also warranted. Future research with larger sample sizes and more survey-based designs could characterize more fully the distribution of experiences. Further research could also explore the decision-making processes of IRBs and scientists on when and how exceptions to the policy are selected or implemented.

Educational Implications

These results can be useful to institutions, scientists, and IRBs who are anticipating implementation of the sIRB policy. NIH also may find these results useful as they plan implementation guidance and explore resource allocations to facilitate optimal impact of the sIRB policy on review efficiency, data quality, and human study participant protections.

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Table 1.

Themes with supporting quotes

THEME 1. Most participants reported active preparation for the sIRB policy

"We feel quite prepared ... We have been communicating steadily to PIs since last spring ... We have all the external facing forms and documents that PIs need done. We have done some basic training with the sponsored programs office. We have a really detailed website that we started last spring and that's continued to evolve.... we did hire two additional positions and actually one of them is sort of an existing staff person that we redeployed into that position. And then we had to hire a new FTE." - IRB administrator

"They have stuff on their website ... they sort of have two sort of guidance documents for when [institution] is IRB of record versus when [institution] isn't and sort of the form that you fill out so, like, the reliance agreement, depending on what it is." - researcher

"Part of prepping for [the sIRB policy] was signing up for the SmartIRB ... we're starting to do some of the training now because of the change in the common rule, and this being one of them" - IRB administrator

"Well, I'm not sure I know, but since I haven't gotten any communication from them, I would have to say I'm doubtful about [our IRB's] readiness." - researcher

THEME 2. Communication processes between sites, local IRBs and HRPPs, and the reviewing IRB during the active study period were unclear to participants

"I hope that [my local IRB] will still be able to give me advice about things, because we're all working with the same guidance about human subjects research. So I'm assuming that I can still ask them questions, they can still provide some guidance on how to write things or how consents should look.... Does it shut down every site when one site has a problem? Or, you know, a small violation or you have to change procedures? So, yeah, I do worry about that. I don't know how much responsibility is shared between the sites and how much is still very independently looked at." - researcher

"How is the local IRB going to know about the adverse events? So if I report it to the single IRB, should my local IRB also know about it? And what's that chain of communication?" - researcher

"I think just going back to not knowing what pieces that the local IRB would have input on or control, like, I just don't know. I mean, I can't imagine them giving up complete control, right? Because they're still ultimately responsible for research that happens at [this institution]." - researcher

"Some of the IRBs want to be approached before the protocol is approved, and others don't want to be approached at all until you have an approved protocol. And so we're just trying to navigate that process with, you know, eight different sites that all have a different process for how they cede authority." - researcher

THEME 3. Participants lacked information and guidance to select a reviewing IRB.

"One of the fundamental issues and problems with IRB is there is no quality metrics or standards. And so the ability for me to know about the quality of another IRB and its practices is relatively opaque." — researcher

"I would hate to be shopping for the least stringent IRB if we were trying to think about which site should the IRB for all the project. But I could see those kind of shortcuts happening." - researcher

"In many cases, there isn't a scientific review committee, that the IRB serves as sort of an ersatz scientific review committee as well, outside of what their defined scope should be. And so that's what I would need to know from the single IRB, is are they also taking on the role of the scientific review committee or is that -how is that going to be handled?" - researcher

"So I think that's another potential problem with having a single IRB, is that if they are going to be responsible for ensuring that the consent form is consistent with state law and your study is a multi-state study, then that IRB needs to be able to make that assessment for multiple different states." - researcher

THEME 4. Participants found it difficult to assess the genomics competency of reviewing IRBs.

"I could see myself, especially early on in this new policy, wanting to have a discussion with our IRB representation from the other sites ... I would just want to know what their experience would be in [genomics or genetics] type of studies and then how comfortable they feel being the single IRB site." - IRB administrator

"[Our IRB is] becoming slightly more familiar with [genomics], especially in terms of regulatory issues and the new regulations that are out. I would argue that a lot of the panel members, the reviewers, probably think they're more comfortable with genetics — or more knowledgeable about genetics than they really are." -researcher

"Some of the board members get overly anxious when it comes to genomic studies and might have a different set of standards for approval than if it were a study that didn't have genomic investigation involved. And not that that's a bad thing, but I think it might lead to some bias against studies that might not be there otherwise." - IRB administrator

THEME 5. Participants expressed uncertainty about the roles and responsibilities of reviewing IRBs, relying HRPPs, and study teams for using standardized study materials and incorporating relevant local context information for genomic studies.

"The whole issue of returning results is a big challenge for us. What kind of results, which ones are they planning to return and when? How does that interact with the nature of the subject population? For example, what if the participants are kids but they're not actually going to have results for many years? Who is going to return the results? And what are they going to say to the participants? Is it going to be a certified genetics counselor? Those are the type of issues that we really wrestle with. It's primarily all about returned results." -researcher

“Everybody asks for [local context] information differently. ... The result of that lack of standardization is that that is a huge amount of extra work for us, and also gives us a little bit of concern about, from the national perspective, whether or not there are some inadvertent gaps and things that are being overlooked in various places.” - IRB administrator

“[Our state has] genetic and behavioral information privacy laws that are a bit more stringent for research data. And so I don’t know how that’s going to be managed and if the other IRB will also be acknowledging — you know, working with an outside state IRB.” - researcher

“And, you know, their population, patient populations are very different. And to the extent that they had different experiences, you’re working with different communities in terms of research participation, because single IRB being sensitive to those variations may be complicated.” - researcher

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Table 2.

Tools and resources that could help with sIRB implementation for genomic studies

Recommendation	Exemplar quote
Guidance on developing communications plans that outline roles and responsibilities for communication between investigators; between IRBs; and between IRBs and investigators	“I don’t know what my role is in this process. Am I involved? Or am I having the single IRB talk with my local IRB? I just don’t know that process ... I hope there would be something in writing that says, okay, here’s how you work with the single IRB, here’s how you work with your local IRB, here’s what my local IRB needs from me, here’s what the single IRB needs from me. I’m hopeful that that’s figured out ahead of time, or most of it anyway.” - researcher “My mental model would be that all of that communication and information is aggregated, because part of the goal would be to minimize the variation among the sites.” - researcher
Guidance about developing processes for reporting of active study phase information (safety, modifications, violations; staff training)	“What we expect is clear understanding of who is notifying who about noncompliance, about post-approval monitoring, audits, unanticipated problems. Suspensions, terminations, all those kinds of things.” -IRB administrator
Guidance about resolving competing local context issues at multiple relying sites, such as around standardizing consent forms	“When it gets to the return of results part, it can be a little more complicated because you really do have to know the local context.” IRB administrator
Information available to assess IRB quality, style differences, and genomics expertise between IRBs when selecting a reviewing IRB	“if there were public performance measures for IRBs, then you might know about, you know, how many protocols they reviewed and other markers to tell you about their knowledge and experience so you would hopefully at least have somebody who was used to reviewing similar protocols.” - researcher
Access to all state regulations around human subjects, data privacy, and protections around genomic data and privacy and special populations	“I feel like there could be some support, some body that supports the single IRBs that has access to regulatory information from all the states that the IRBs could confer with. Just some way of them readily accessing information to make sure that they’re not approving things that would not be acceptable in the jurisdiction that they’ve taken over. Something like that. Some way of providing more support.” - IRB administrator