Stakeholder Reflections on Implementing the National Institutes of Health's Policy on Single Institutional Review Boards

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Table S1.
Stakeholder Quotations for NIH sIRB Goal 1—Enhance and Streamline IRB Review for Multisite Research

Topic	*Stakeholder quotation*
Section 1: Overall review process	
Has streamlined	
Efficient review	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. —Investigator
Standardization of documents	But overall, with other changes, and it becomes 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
Familiarity	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. —Joint Investigator-Study Coordinator interview
Has not streamlined	
Lack of a standardized process	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 time frame 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

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Topic	Stakeholder quotation
Limited infrastructure	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 [principal investigator] and one coordinator, but in reality, there's a lot more people involved in the study than just those two people. — Study Coordinator
	The thing that needs to be worked on is defining the role of the local IRB or at least setting out guidelines for what the local IRB should do because I think that's the biggest potential hang-up. And I think local IRBs just don't know what their role is, so having some guidance from NIH "the local IRB should do this." —Investigator
Section 2: Ethics review	
Has streamlined	
Decreased workload	When we are the relying IRB, it certainly lessens our workload across the life of the study, because we have that one touchpoint. —IRB or Institutional Official
	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. —IRB or Institutional Official
No ethics review	[I]f you're relying on an external IRB for ethical and regulatory review, yeah, you streamlined your process because you're not doing it. —Research Administration Leader
	If we're relying on another IRB, we don't do an ethics review. So, it has streamlined it that way. —Research Administration Leadership Representative
	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 Leader
Has not streamlined	
Increased workload	If we're the reviewing IRB, though, it's absolutely more. —IRB or Institutional Official
	We've had three FTEs [full-time employees] 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 Leader
	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 Leader
Section 3: Beyond ethics review	
Has streamlined	
Efficiency	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. —IRB or Institutional Official
	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 to even send the study to you until it's clear to have an IRB review. We've done all our internal processes." —Research Administration Leader

Topic	*Stakeholder quotation*
Has not streamlined	
Lack of infrastructure, systems, and processes	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 [information technology] 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. —IRB or Institutional Official
	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 choke point 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 Administration Leader
Increased workload	The only way to 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. —Research Administration Leader
Ancillary review	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. —IRB or Institutional Official

Table S2.
Stakeholder Quotations for NIH sIRB Goal 2—Maintain a High Standard for Human Subjects Protection

Topic	*Stakeholder quotation*
Section 1: Defining "high standards"	
Protection of human subjects	The high standard is the role of the IRB, [which] 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. —IRB or Institutional Official
Accreditation	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 Leader
	If you're an accredited IRB, I would assume that you're going a little above and beyond what [the Office for Human Research Protections and the Food and Drug Administration] require. —Research Administration Leader
Quality review	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. —IRB or Institutional Official
	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 Leader
Section 2: Concerns about maintaining high standards	
Monitoring and reporting	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. —IRB or Institutional Official
	But again, I go back to the issue of postapproval monitoring that needs to be very carefully fleshed out. —IRB or Institutional Official
Differing quality of IRB review	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. —IRB or Institutional Official
	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 Leader

Topic	*Stakeholder quotation*
Section 3: Local context	
Positive experiences with sharing local context	
Consistent forms	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 to ask, and what they need to report back and get it done, so that's been quick to turn it around. -—Regulatory Coordinator
Monitoring and reporting	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. —Research Administration Leader
Negative experiences with sharing local context	
Lack of infrastructure	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. —Research Administration Leader

Table S3.
Stakeholder Quotations for NIH sIRB Goals 3 to 5—Allow Research to Proceed Effectively and Expeditiously, Eliminate Unnecessary Duplicative IRB Review, and Reduce Administrative Burden

Topic	*Stakeholder quotation*
Section 1: Roles that remain with the relying institution	
Adhering to privacy practices	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. —Research Administration Leader
Conducting ancillary 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. —Research Administration Leader
Conducting compliance and oversight responsibilities	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. —Research Administration Leader
Conducting shadow reviews	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. —IRB or Institutional Official
Section 2: Duplicate activities	
Conducting shadow reviews	[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. —IRB or Institutional Official
	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. —Study Coordinator
Completing duplicative documents and forms	There are some relying institutions that still undertake a review of the consent form, according to their own standards, which, arguably, is duplicative. —IRB or Institutional Official
Conducting ancillary reviews	A lot of reviewing IRBs that are like independent IRBs will just say, "Hey, PI [principal investigator], 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. —Research Administration Leader

Topic	*Stakeholder quotation*
Reasons to have duplicative reviews	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. —IRB or Institutional Official
Concerns for investigators	The PI has to enter all of the approved documents into our electronic system so that we can see everything. And here's the most disappointing fact for investigators. When they use an external central IRB, they still have to have all of their ancillary reviews and all of their CRU reviews done here. The only thing that's different is the IRB review. They're always disappointed when they hear that, 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 . . . . [T]he sequence is a bit frustrating and ineffective for them. —IRB or Institutional Official
Section 3: Administrative burdens—relying institutions	
Information gathering	Understanding the status of a study . . . . [I]f 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. —IRB or Institutional Official
Communication	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? —Regulatory Coordinator
Section 4: Administrative burdens—reviewing IRBs	
Document handling and organization	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. —IRB or Institutional Official
	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. —Research Administration Leader
Communications	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. —Research Administration Leader
Information gathering	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. —IRB or Institutional Official
IRB software	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 5. 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. —Joint Investigator-Study Coordinator interview

Table S4.
Stakeholder Quotations for NIH sIRB Goal 6—Prevent Systemic Inefficiencies

Topic	*Stakeholder quotation*
Section 1: Ameliorated existing inefficiencies	
Improved consistency	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. —IRB or Institutional Official
Decreased workload leads to availability for other activities	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- [principal investigator-] initiated single-site studies. Now we have more manpower to throw onto those. —IRB or Institutional Official
Section 2: Created new inefficiencies	
New roles and responsibilities	[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. —IRB or Institutional Official
	I think it's largely figuring out, getting the institution to understand what our institutional responsibilities versus IRB responsibilities [are], and determining how those are going to be handled and where those are going to live. —IRB or Institutional Official
Lack of systems and processes	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. —IRB or Institutional Official
	[T]he 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 Leader
More reviewing responsibilities	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." —IRB or Institutional Official
	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. —IRB or Institutional Official
More investigator burden	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. —IRB or Institutional Official