

Clinical Trials Transformation Initiative
The Single IRB Mandate: Identifying Benefits, Challenges, Solutions, and Informational Needs
Question guide for
IRB MEMBERS, Version 1.5

1. Interviewer Name	
2. Participant ID#	
3. Interview Date (dd/mm/yyyy)	_ _ _ / _ _ _ / _ _ _ _ _
4. Participant agrees for interview to be digitally recorded	Yes..... <input type="checkbox"/> No..... <input type="checkbox"/>
5. Time Interview Began (hhmm-24hr clock)	_ _ _ _ _
6. Time Interview Ended (hhmm-24hr clock)	_ _ _ _ _

- Step 1:** Complete Q1-3 above before the interview.
- Step 2:** At the beginning of the interview, introduce yourself; thank participant for taking part in the interview.
- Step 3:** Read Section A below to participant.
- Step 4:** Ask participant permission to record interview; tick appropriate box in Q4 above.
- Step 5:** Turn on audio recorder if acceptable, document time interview begins in Q5 above, and conduct interview.
- Step 6:** At the end of the interview, thank the participant and ask if she/he has any further questions; document time interview ended in Q6 above.
- Step 7:** Complete the IRB Personal Data Disclosure Form

Interviewer: Please read the following to participants at the beginning of the interview.

SECTION A: Information about this study
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- Hello, thank you for taking time out of your busy schedule to speak with me today. My name is [Name], and I am a _____ with the Clinical Trial Transformation Initiative. Is now still a good time to talk?
- Before we begin, I'd like to tell you more about this interview and the research we're conducting.
- The Clinical Trials Transformation Initiative – known as CTTI – wants to gather evidence on people's experiences with single IRB review, particularly for FDA-regulated studies. Findings will be used to develop recommendations on the use of a sIRB for FDA-regulated clinical trials. Recommendations will be submitted to FDA for consideration in accordance with Good Guidance Practice.
- As described in the informational sheet provided to you earlier, participating in this interview is voluntary. You can choose not to answer a question or you can stop the interview at any time.
- We do not think there will be any personal risks or benefits from the interview today. However, there is a risk of loss of confidentiality as with any study of this nature. Please avoid mentioning personal names during the interview.
- With your permission, I would like to audio-record the interview. The audio-recording will be stored on a secure server and destroyed after the findings of this research are published.
- If you do not want the interview audio recorded, I will take detailed notes throughout the interview instead.
- The interview will take roughly 1 hour. You will receive \$100.00 for taking part. In order to pay you through the Duke system, we will need your Social Security number. You are not required to share your Social Security number with us to participate in this interview, but we cannot pay you for taking part without it.
- Do you have any questions for me at this point? Information about who to contact if you have questions about the study after our time today, including the Duke IRB, can be found in the informational sheet.

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

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

[If yes, begin audio recording now.]

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

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

- When I refer to a Single IRB, I mean a review process in which one IRB is chosen—the reviewing IRB—to provide the ethics review for multi-site studies on behalf of all U.S.-based institutions that are involved in the study. This applies to domestic sites only within multi-site global research studies.
- When I refer to a Reviewing IRB, which is also known as a single IRB, I mean the IRB of record for a particular multi-site study for the duration of the study. Reviewing IRBs are often selected on a study-by-study basis, and act on behalf of relying institutions that cede authority and ethics oversight of the study to them.
- When I refer to a Relying IRB or institution, I mean the IRB or institution that will rely on an IRB from another institution to conduct the ethics review of a study that will be conducted at the relying IRB's institution.

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

[If participant asks about central IRB vs. single IRB, use this general distinction:

Both are designed to help streamline IRB review, and the terms are sometimes used interchangeably. In general:

- *A **Central IRB** is the IRB of record that provides the ethical review for multiple studies within a research network, consortium or particular program.*
- *A **Single IRB** is the IRB of record that provides a single ethics review on behalf of all sites in a multi-site study, and is chosen on a study-by-study basis.]*

Also, the majority of these questions will focus on FDA-regulated research. By FDA-regulated research, we mean research involving an FDA-regulated product such as a drug or device.

Do you have any questions before we begin?

[If yes, answer the participant's questions then proceed with the interview questions.]

[If no, proceed with asking the interview questions.]

Ok, let's get started!

SECTION B: BENEFITS OF USING A SINGLE IRB

First, let's talk about the benefits of using a single IRB for FDA-regulated, multi-site studies.

[Ask only to participants with planning sIRB experience]

1. To begin, what do you see as the main benefits of using a single IRB to review your multi-site studies?
 - a. Are there any additional benefits of using a single IRB to review your research that is FDA-regulated? [If yes] What are those benefits?

[Ask only to IRB members with sIRB experience]

[FOR ACADEMIC IRBs]

2. *[Ask question if participant has experience as a relying institution, from demographic questionnaire.]* In your experience, what have been the benefits of relying on another IRB for review of FDA-regulated multi-site studies?
3. *[Ask question if participant has experience as a reviewing institution, from demographic questionnaire.]* In your experience, what have been the benefits of serving as a reviewing IRB—meaning serving a single IRB—for FDA-regulated multi-site studies?

[FOR INDEPENDENT IRBs]

4. In your experience, what have been the benefits of serving as the single IRB for FDA-regulated multi-site studies?

[FOR BOTH ACADEMIC AND INDEPENDENT IRBs]

[After exhausting all answers to the question(s) above, probe about whether they experienced the following benefits of single IRB review, if not previously mentioned; ask participants to elaborate on reasons why they did or did not experience these anticipated benefits]

- a. Decreased administrative burden among local IRBs
- b. Reduced duplication of effort across site IRBs
- c. Eliminated disparities/subjective variations in IRB review between site IRBs [follow-up probe: improve quality of IRB review?]
- d. Improved cost-effectiveness of IRB review
- e. Enhanced human subjects' protections [follow-up probe: how so?]
- f. Improved ease of analyzing adverse events occurring at multiple sites
- g. Improved ability to select an IRB with the necessary expertise to review the trial
- h. Reduced time of initial review
- i. Increased efficiency in submitting protocol amendments/continuing reviews [follow-up probe: how so?]
- j. Improved ability to maintain version control due to centralized regulatory documents
- k. Enhanced ability to share research data between sites

SECTION C: CHALLENGES OF USING A SINGLE IRB

Now let's turn our attention to discussing the challenges of using a single IRB.

[Ask only to participants with planning sIRB experience]

5. As you plan for single IRB review at your institution, what factors have you or others identified that likely will be challenging in selecting a single IRB for FDA regulated multi-site studies? (Probe for greatest anticipated challenges)
 - a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
 - b. In general, what criteria do you think are most important to consider when selecting a single IRB?
6. What factors have you or others identified that will be challenging when relying on another institution's IRB for review of FDA regulated multi-site studies? (Probe for greatest anticipated challenges)
 - a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
7. What factors have you or others identified that will be challenging when your IRB will serve as the reviewing IRB for FDA regulated multi-site studies? (Probe for greatest anticipated challenges)
 - a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
8. Do you think the challenges would be the same or different for FDA regulated multi-site studies compared to non-FDA regulated multi-site studies? Please explain.
9. Under what circumstances would single IRB review be difficult and/or not appropriate for FDA-regulated studies?
 - a. What factors contribute to the difficulty (e.g., drug versus device studies, number of sites, others)?

[Ask only to participants with sIRB experience]

10. **[FOR ACADEMIC IRBs]** *[Ask question if participant has experience as a **relying institution**, from demographic questionnaire.]* In your experience, what have been the challenges in selecting a single IRB for FDA regulated multi-site studies? (Probe for greatest challenges)

- a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 - 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
 - b. Based on your experience, what criteria do you think are most important to consider when selecting a single IRB?
11. **[FOR ACADEMIC IRBs]** *[Ask question if participant has experience as a **relying institution**, from demographic questionnaire.]* What additional challenges have you faced when relying on another institution's IRB for review of FDA regulated multi-site studies? (Probe for greatest anticipated challenges)
- a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 - 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
12. *[Ask question if participant has experience as a **reviewing institution**, from demographic questionnaire.]* What challenges have you faced when your IRB has served as the reviewing/single IRB for FDA regulated multi-site studies? (Probe for greatest anticipated challenges)
- a. What solutions, if any, have you or others identified to overcome these challenges?
 - i. What factors remain without solutions?
 - 1. What makes these factors difficult to overcome?
 - ii. What type of information from federal regulations and guidance would be helpful in thinking through these challenges?
13. Are the challenges you mention the same or different for FDA regulated compared to non-FDA regulated multi-site studies? Please explain. *[explore for all challenges mentioned]*
14. **[If pressed for time, simply solicit general feedback on anything they would add or change about the table after they review it.]**
- Now let us talk about the division of responsibilities between single IRBs and relying institutions. Please take a look at the table called "Responsibilities of Institutions and Single IRBs for Multicenter Clinical Trial Protocols" that we previously sent you via email (at end of questionnaire). Take a moment to read through it.
- a. Considering all 4 columns listed in the table, and based on your experience, are the responsibilities listed here generally assigned to the correct institution or have you seen a different division of these tasks?
 - i. What responsibilities are missing from in this table, if any?
 - ii. *[If participant mentions additional responsibilities]* Who would be primarily responsible for these additional tasks?
 - b. How would these divisions change, if at all, if you were to make these responsibilities specific to FDA-regulated multi-site studies?
15. What difficulties, if any, have you faced when incorporating the local context into the single IRB review model?

- a. What concerns, if any, have you had related to regulatory liability in the event of noncompliance? If so, please describe.
 - b. What complications, if any, have you had with collecting and distributing information/communications across research sites?
 - c. *[FOR ACADEMICS -- Only ask question if participant has experience as a reviewing institution]* **[FOR ALL INDEPENDENT IRB MEMBERS]** What issues, if any, have you experienced when evaluating the consent process for populations across study sites?
 - d. What are potential ways to overcome these challenges? (Probe about each challenge)
16. Under what circumstances would single IRB review be difficult and/or not appropriate for FDA-regulated studies?
- a. What factors contribute to the difficulty (e.g., drug versus device studies, number of sites, others)?

SECTION D: INFORMATIONAL NEEDS FOR COMPLIANCE WITH sIRB MANDATE

Now I'll ask about informational needs for complying with the single IRB mandate.

[Ask of all participants]

17. **[FOR ACADEMIC IRBs]** What informational needs remain with regard to using a single IRB?
- a. **[FOR ACADEMIC IRBs]** What additional guidance or resources may be needed from your institution?

SECTION E: EXCEPTIONS

[Ask of all participants]

Now I'd like to talk about when there should be exceptions to the single IRB policy for U.S.-based FDA-regulated drug and device clinical trials. Both the NIH and the common rule have described exceptions. These exceptions can be found in the packet of materials we emailed you prior to the interview—with the header "Exceptions" on top.

For the common rule, multi-site research can be exempt from the single IRB policy for:

- Cooperative research for which more than single IRB review is required by law, including tribal law passed by the official governing body of an American Indian or Alaska Native tribe, and for
- Research for which any federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context

For NIH, exceptions to their policy are for:

- Foreign sites
- Career development (K), institutional training (T), and fellowship (F) awards
- Federal, state, tribal or local laws, regulations, or policies require local review

- Ancillary studies that are part of ongoing studies or parent studies that were not required to use a single IRB

NIH also allows exception requests to be submitted, but compelling justification for local IRB review is required.

18. What, if anything, is unclear about these exceptions?
19. With these exceptions in mind, do you think they suffice for FDA-regulated drug and device clinical trials or are there other exceptions that should be specified?
 - a. *[If suffice]* Why are these exceptions sufficient?
 - b. *[If need other exceptions]* What factors might influence the need for an exception to single IRB review for FDA-regulated DRUG trials? *[Probe until all factors/exceptions are described.]*
 - i. What about for DEVICES trials? *[Probe until all factors/exceptions are described.]*
20. What types of FDA-regulated studies, if any, do you feel should not be exempted from the single IRB review mandate?

SECTION F: REVIEW OF THE 2006 FDA GUIDANCE DOCUMENT
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Let us now talk about the FDA’s 2006 Guidance for Industry document that provides recommendations on using a centralized IRB review process in multicenter clinical trials. I’d like to hear your thoughts on what you think FDA should do to revise this document, so it can be helpful when you must use a single IRB for FDA-regulated clinical trials.

We’ll go through each section separately. As we do, I will ask you to reflect on each section in terms of what, if anything, you find to be unclear, how to make those things more clear, what you think should be added in a revision, and what you think could be left out of a revision.

I. Roles in Ensuring IRB Review: [Ask of all participants]

Let’s start with the section on “Roles in Ensuring IRB Review” on pages 9 and 10. Are you familiar with it or do you need time to read through it?

21. What information about the roles in ensuring IRB review is unclear, if any?
 - a. What could make it clearer?
22. What information, if any, should be *added* in a revision?
 - a. Why this information?
23. What information, if any, should be *left out* of a revision?
 - a. Why this information?

II. Addressing Local Aspects of Review: [Ask of all participants]

Next we’ll continue with the section on “Addressing Local Aspects of IRB Review” on pages 10 and 11.

[Give time to review if needed].

24. What information about addressing local aspects of IRB review is unclear, if any?
 - a. What could make it clearer?
25. What information, if any, should be *added* in a revision?
 - a. Why this information?
26. What information, if any, should be *left out* of a revision?
 - a. Why this information?
27. *[If not addressed above]* Are the possible mechanisms for meaningful consideration of local factors (bulleted information) helpful or unhelpful?
 - a. How so?
28. What additional information about local factors may be necessary?

III. IRB Records and Using a Central IRB at Unaffiliated Sites: [Ask of all participants]

Now let's talk about the section on "Documenting Agreements and Procedures" and "Using a Central IRB at Unaffiliated Sites" on pages 11-12. *[Give time to review if needed.]*

29. What information about documenting agreements and procedures in IRB records is unclear, if any?
 - a. What could make it clearer?
30. What information about using a central IRB at unaffiliated sites is unclear, if any?
 - a. What could make it clearer?
31. What information, if any, should be *added for either of these sections* in a revision?
 - a. Why this information?
 - b. What type of agreements or written procedures such as reliance agreements, Memoranda of Understanding, and communication plans are you currently using or creating?
 - i. Based on your experience, what information, if anything, from those documents do you think would be necessary to include in future FDA guidance?
32. What information, if any, should be *left out* of a revision?
 - a. Why this information?

IV. Cooperative IRB Review Models: [Ask of all participants]

And lastly we'll read the section that touches on Examples of Cooperative IRB Review Models on page 13.

33. What information about cooperative IRB review models is unclear, if any?
 - a. What could make it clearer?
34. What information, if any, should be *added or further clarified* in a revision?
 - a. Why this information?

35. What information, if any, should be *left out* of a revision?
a. Why this information?

V. Concluding remarks: [Ask of all participants, except when noted]

We just have a few more wrap-up questions and then we're done.

36. What additional sections or topics, if any, should to be added to a revision of the FDA guidance document?
a. What specific information should be provided in that section?
37. [*Ask of IRB members with single IRB experience only*] Based on your experience, what are your top three recommendations for other institutions to help them prepare to implement the single IRB mandate for FDA-regulated clinical trials?
38. Do you have any concluding thoughts on information that can help to develop recommendations on the use of single IRBs for FDA-regulated drug and device trials?

I want to sincerely thank you for your time and for the helpful information that you provided.

Responsibilities of Institutions and Single IRBs for Multicenter Clinical Trial Protocols*

Responsibility	Single IRB	Relying Institution	Both	Either
Execute IRB authorization			X	
Assess investigator qualifications			X	
Research education and training of IRB personnel	X			
Register with FDA and OHRP	X			
Notify sites of accreditation changes	X			
Ensure ethical standards and regulations	X			
Collate site specific information	X			
Approve informed consent forms	X			
Provide copies of IRB decisions, rosters, & minutes	X			
Notify sites of non-compliance concerns	X			
Education and training of investigators and study coordinators		X		
Credentialing of staff		X		
Maintain FWAs		X		
Conduct security and privacy review for HIPAA		X		
Ensure investigator compliance and conflict of interest		X		
Evaluate local context				X
Provide waiver of consent if indicated				X

Abbreviations: IRB, institutional review board; FDA, Food and Drug Administration; FWA, federalwide assurance; HIPAA, Health Insurance Portability and Accountability Act; OHRP, Office of Human Research Protections.

*This table adapted from the article *Using Central IRBs for Multicenter Clinical Trials in the United States* by Flynn et al. (2013).