

Appendix D: Question Guide for Industry and Trade Organization Representatives

Clinical Trials Transformation Initiative
 The Single IRB Mandate: Identifying Benefits, Challenges, Solutions, and Informational Needs
Question guide for
INDUSTRY and TRADE ORGANIZATION REPRESENTATIVES, Version 1.4

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.

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. [for phone interviews] Is now still a good time to talk?
- Before we begin, I'd like to tell you more about this interview and the research we're conducting.
- The Clinical Trials Transformation Initiative – 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.
- [for phone interviews] 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.

- 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.

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

[After exhausting all answers to the questions 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]

- b. Decreased administrative burden among local IRBs
 - c. Reduced duplication of effort across site IRBs
 - d. Eliminated disparities/subjective variations in IRB review between site IRBs [follow-up probe: improve quality of IRB review?]
 - e. Improved cost-effectiveness of IRB review
 - f. Enhanced human subjects' protections [follow-up probe: how so?]
 - g. Improved ease of monitoring
 - h. Improved ease of analyzing adverse events occurring at multiple sites
 - i. Improved ability to select an IRB with the necessary expertise to review the trial
 - j. Reduced time of initial review
 - k. Increased efficiency in submitting protocol amendments/continuing reviews [follow-up probe: how so?]
 - l. Improved ability to maintain version control due to centralized regulatory documents
 - m. Enhanced ability to share research data between sites
2. Do you think the benefits of a single IRB review are the same or different for FDA-regulated multi-site studies compared to non-FDA-regulated studies? Please explain.
 3. In your opinion, what systems are necessary to maximize the benefits of using a single IRB for FDA regulated multi-site studies?
 - a. Whose support is needed to initiate or maintain those systems?

SECTION C: CHALLENGES OF USING A SINGLE IRB
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Now let's turn our attention to discussing the challenges of using a single IRB.

[Ask only to participants with planning sIRB experience]

4. As you plan for using a single IRB review process, what factors have you or others identified that likely will be challenging in selecting a single IRB for your 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?
5. What factors have you or others identified that will be challenging when using a single IRB for review of your 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?

6. 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.
7. 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]

8. In your experience, what have been the challenges in selecting a single IRB for your 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?
9. What additional challenges have you faced when using a single IRB for review of your 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?
10. Are the challenges the same or different for FDA regulated compared to non-FDA regulated multi-site studies? Please explain.
11. Under what circumstances would single IRB review be difficult and/or not appropriate for your 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
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Now I'll ask about informational needs for complying with the single IRB mandate.

12. When you first started planning for single IRB review, what information or guidance did you find most helpful? Why?
13. At this point, what informational needs remain with regard to using a single IRB?

- a. What additional guidance may be needed from FDA regarding the single IRB review mandate?

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.

14. What, if anything, is unclear about these exceptions?

15. 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.]*

16. 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

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?

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

II. Addressing Local Aspects of Review:

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].*

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

III. 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.

25. What information about cooperative IRB review models is unclear, if any?

- a. What could make it clearer?
26. What information, if any, should be *added* in a revision?
- a. Why this information?
27. What information, if any, should be *left out* of a revision?
- a. Why this information?

IV. Other sections

28. *[If participant read entire guidance document in advance]* Do you have comments about any of the other sections in the guidance document that we did not cover?

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

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

29. 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?
30. *[Ask of Industry and 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?
31. 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.