APPENDIX 2. DRAFT INTERVIEW GUIDE

Hello, my name is [X]. Thank you for agreeing to participate in our interview of DSMB members to learn more about the ethical issues DSMBs face. The interviews will be deidentified; no identifying information will be shared about you or the trials in which you've been involved. You will have the opportunity to review transcripts with the option to request part or all of your interview to be deleted up to 1 week after the interview and participant names will not be used in any publications. Do you have any questions?

Let's begin by talking about your experience on DSMBs.

1. Please tell me a little about your current and prior experience serving on a DSMB.
    a. *Are you currently on a DSMB?*
    b. *Approximately how many DSMBs have you served on?*
    c. *What types of trials/diseases have you overseen as a DSMB member?*
        i. *Prevention vs. treatment?*
        ii. *Infectious v. chronic disease?*
        iii. *Pragmatic v. conventional?*
    d. *Have you served on DSMBs overseeing international studies?*
        i. *If the DSMBs reviewed international studies, did you feel you had the relevant expertise?*
            1. *Were there members of the DSMB from all of the countries in which it was conducted?*
    e. *What is or was your role (e.g., ethicist, statistician, chair, clinician, Secretary)?*

2. Please tell me about your training that helps you in this role.
    a. *Have you received any training about how to serve on a DSMB? (Formal or informal)*
        i. *If yes--tell me about the training you've received.*
            1. *Did it include an ethics component?*
        ii. *If yes--how useful was it for your DSMB work? What was most useful about it?*
    b. *Have you ever had any ethics training?*
        i. *If yes--tell me about the training you've received.*
        ii. *If yes--how useful was it for your DSMB work? What was most useful about it?*
    c. *Have you ever had any statistics training?*
        i. *If yes--tell me about the training you've received.*
        ii. *If yes--how useful was it for your DSMB work? What was most useful about it?*

3. What do you see as the most important responsibilities of the DSMB?
    a. *Probe with the following functions if not mentioned:*
        i. *Safety monitoring?*
        ii. *Efficacy monitoring?*
        iii. *Stopping trials based on lack of feasibility*
        iv. *Ensuring continued informed consent*
        v. *Considering ramifications of trial results for other ongoing studies*
        vi. *Determining whether participants should cross-over to the other arm if results are positive*
        vii. *Monitoring recruitment strategies and successes or failures?*

viii. *Ensuring trials are enrolling participants representative of the target population?*
ix. *Overseeing integrity of the data?*
x. *Balancing individual v. population benefits and harms of research?*
xi. *Addressing what information/interventions participants should receive post-trial, if any*

b. *Why are these responsibilities you've identified the most important ones?Are there some functions DSMBs should not take on?*
    i. *If so, which ones and why?*
c. *Do sponsors or other DSMB members agree with you your views on DSMB responsibilities?*
d. *Have you been on trials that have monitored some, but not all, of these aspects of trials?*
    i. *Why did they do this?*
e. *Is there anything you've monitored on a DSMB that is not usually in the purview of a DSMB? Why was that?*

4. What kind of guidance do you think is helpful for serving on a DSMB?
    a. *Probe with the following if not mentioned:*
        i. *Stopping boundaries/rules,*
        ii. *Statistical analysis plans,*
        iii. *DSMB charter,*
        iv. *Ethical frameworks/guidance,*
        v. *Ad-hoc guidance from, for example, ethicists/research ethics consultation services*
    b. *What makes this type of guidance useful or not?*
    c. *Are you aware of any ethics guidance for DSMBs—whether from an external source or specific to a trial or sponsor?*
        i. *If so, have you relied on any ethics guidance for DSMBs—whether from an external source or trial-specific?*

5. Please tell me about the biggest challenges you have faced as a DSMB member **prior to** the COVID-19 pandemic.
    a. *In general?*
    b. *That you would consider ethical challenges?*
        i. *Probe with:*
            1. *Making sure participants are protected,*
            2. *Balancing participant protection with population benefits,*
            3. *Considering equity in distribution of research benefits,*
            4. *Sharing or accessing confidential information,*
            5. *Relationships with other parties (e.g. sponsor, trial steering committee, DSMBs for related trials)?*

6. Please tell me about the biggest challenges you have faced as a DSMB member during the COVID-19 pandemic.
    a. *In general?*
    b. *Were there trials you were monitoring that were stopped because of the COVID-19 pandemic?*
        i. *Why were they stopped?*
    c. *For trials that were stopped, was your DSMB consulted on how or whether to stop the trial, unblinding, or post-trial monitoring decisions?That you would consider ethical challenges?*
        i. *Probe with:*
            1. *Making sure participants are protected,*
            2. *Balancing participant protection with population benefits,*
            3. *Considering equity in distribution of research benefits,*
            4. *Sharing or accessing confidential information,*
            5. *Relationships with other parties (e.g. sponsor, trial steering committee, DSMBs for related trials)?*

d. *Have you participated in trials of interventions that were stopped early?*
    i. *Were they interventions for COVID-19 or other diseases?*
    ii. *Can you tell me more about this experience?*

7. In dealing with these challenges, how did the DSMBs consider ethical issues?
    a. *Ad-hoc as they arose?*
    b. *With reference to pre-specified stopping boundaries/SAPs, or other guidance?*
    c. *After reviewing the ethics literature?*
    d. *After discussing with ethicists?*

8. Now that we have been in the COVID-19 pandemic for some time, what has changed (if anything) in terms of DSMB review of clinical trials?
    a. *What is working well?*
    b. *What is not working well?*
    c. *What have you learned from the COVID-19 experience?*

9. Based on your experience, how specific should the DSMB's statistical analysis plan be?
    a. *General statistical analysis plan or prespecified stopping boundaries?*
    b. *If a DSMB has a statistical analysis plan or prespecified stopping boundaries, what should the DSMB consider when deciding whether to deviate from the planned approach?*
        i. *Data from other trials*
        ii. *Totality of the evidence (safety and efficacy)*
        iii. *Feasibility concerns*
        iv. *Knowledge that would be useful given context in which the intervention will ultimately be given: e.g., target population, length of time intervention would be given to patients, anticipated difficulty in convincing clinicians to change behavior, anticipated future epidemiology of the disease, etc.*
    c. *If a DSMB decides to deviate from a pre-specified plan, should they alert anyone about this?*
        i. *The sponsor?*
        ii. *IRBs?*
        iii. *Participants?*

10. What do you think about the role of an ethicist on a DSMB?
    a. *Have ethicists been included on DSMBs on which you've served?*
    b. *Should they always be included? If not, when are they most helpful?*
    c. *What have ethicists on DSMBs you've served on contributed to the team?*
    d. *Have there been downsides of including ethicists?*

11. What do you think about how IRBs/RECs and DSMBs work together?
    a. *Have you ever served on an IRB/REC?*
    b. *Have you experienced IRBs and DSMBs working together?*
        i. *How have they worked together well?*
        ii. *Are there ways they have NOT worked together well?*
    c. *Should IRBs and DSMBs have an open line of communication, or should it all go through the sponsor?*
        i. *Why or why not?*
    d. *Should an IRB member serve on the trial's DSMB?*
        i. *Why or why not?*
    e. *Should a DSMB member serve on the trial's IRB?*

i. *Why or why not?*

12. If you had the ability to start from scratch and set new policies, what would you change about DSMBs to improve their ability to address ethical issues? Probes if needed:
    a. *Should ethical issues be explicitly incorporated within statistical analysis plans and stopping boundaries?*
    b. *Should RECs/IRBs and DSMBs work more closely together? If so, how?*
    c. *Should all DSMBs be required to include ethicists?*
    d. *For international studies, should DSMBs include additional local representatives?*
    e. *Is there training that DSMB members should routinely have?*

13. Is there anything else you would like to share with us?

Thank you for taking the time to answer these questions. Now we have a few demographic questions for you.

14. What is your current professional role?
    a. *E.g., clinician, clinician-researcher, statistician, academic, policy officer, other*)
    b. How long have you been working in your profession?

15. Which country do you live in? Is this the same country as the DSMB/s on which you've served?

16. What is your gender?
    - Man
    - Non-binary
    - Woman
    - Not listed, please tell us:

17. What is your age?

18. How would you describe your race or ethnicity?

19. What discipline(s) did you study in your undergraduate or graduate training?

Thank you for your time and willingness to talk with us. We truly appreciate the information you have provided us and will work to disseminate this information to develop better practices and policies to ensure DSMBs are well-equipped to address ethical issues.