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Title

UC Comments on Draft OHRP Guidance on Use of a Single Institutional Review Board for Cooperative Research (Docket ID Number HHS-OASH-2022-0011, July 1, 2022)

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OFFICE OF THE PRESIDENT
1111 Franklin Street, 11th Floor
Oakland, California 94607-5200

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August 30, 2022

Jerry A. Menikoff, M.D., J.D.,
Director, Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

RE: Docket ID Number HHS-OASH-2022-0011: Use of a Single Institutional Review Board for Cooperative Research Draft Guidance (July 1, 2022)

Dear Dr. Menikoff:

I write on behalf of the University of California (UC) system in regards to the "Use of a Single Institutional Review Board for Cooperative Research Draft Guidance" (Draft Guidance) notice published in the Federal Register on July 1, 2022.

The UC system is comprised of ten research-intensive campuses, six medical schools, and three affiliated U.S. Department of Energy national laboratories. As a system, UC receives approximately $6 billion annually of extramural awards to support research conducted throughout all UC locations, and generally receives five to six percent of the NIH annual appropriations for research.[1]

We appreciate the work the Office for Human Research Protections (OHRP) in providing clear, practical guidance on the use of single Institutional Review Board (IRB) for cooperative research. UC has extensive experience in single IRB reviews and were among the first in the country to offer the option of single IRB for multi-site studies that ordinarily would require separate IRB reviews at each participating site. All ten UC campuses and the Lawrence Berkeley National Laboratory signed an MOU to facilitate multi-UC single IRB review in 2009. Based on our experience, we offer OHRP editorial suggestions on terminology and to FAQs # 1 and 7. Furthermore, for FAQs # 2, 3, 5, 6, 8, and 9, we provide substantive feedback and ask that OHRP take further steps to reduce burdens on the IRB, including by developing a state law compendium for multi-site research. Further information is provided below.

[1] University of California Accountability Report 2021: https://accountability.universityofcalifornia.edu/2021/chapters/chapter-9.html

I. Editorial Suggestions

General Terminology

We would like to note that there is a distinction between the Human Research Protection Program (HRPP), which is the coordinating office of the IRB, and the IRB itself. Particularly at university-based institutions, an HRPP may consist of various regulatory, compliance, or training functions (e.g., departmental units that monitor and audit ongoing research, services to assist researchers with preparing regulatory submissions, or institutional approval requirements for research that are in addition to IRB review). Although there are variations in each institution's HRPP, including in infrastructure and processes, the IRB review process is only a subset of activities within an institution's HRPP.

We agree with the recommendation of Secretary's Advisory Committee on Human Research Protections (SACHRP) that the Draft Guidance refrain from advising that institutions may conduct additional internal IRB review, but instead leave to the research institutions any decision about conducting any additional local IRB and/or HRPP review for a study with a single IRB.

FAQ #1. What is cooperative research?

We suggest including the example of 'analysis of identifiable data' in FAQ #1 as a growing number of single IRB reviews are for data analysis. For example, please see the edit below in bold and italics:

> For example, an institution could be an awardee institution or responsible for seeking consent from participants, another could be performing research procedures, and another could be conducting laboratory analyses ***or analysis of identifiable data only*** for a key study endpoint.

UC also recommends specifically linking to the mentioned OHRP guidance, such as:

> Note that only those institutions that are "engaged" in the cooperative research need to comply with the regulations (see ***OHRP's guidance*** and correspondence on engagement).

FAQ #7. What are some of the operational capacities an IRB should have in order to serve as a single IRB?

UC recommends that OHRP include a bullet in this section on the following activity that a single IRB may perform: timely review of participant complaints and unanticipated problems / adverse events.

II. Substantive Feedback

FAQ #2. When must an institution rely on a single IRB for approval of cooperative research?

UC appreciates the clarification OHRP provides that exceptions to the single IRB requirement may apply when more than one federal agency is involved. UC also values having the explanation that if an institution engaged in cooperative research has "checked the box" on their FWA this does not

obligate them to always use a single IRB for studies which are not funded by a Common Rule agency.

However, additional guidance would be helpful in the following scenarios:

1. When one collaborator is supported or funded by a federal agency while the other site(s) is not federally funded or unfunded. In this instance, would the single IRB review requirement apply only to the subset of collaborators that are funded or supported by a federal agency or to all of the sites?
2. Instances in which a site(s) is conducting exempt level research while other engaged sites will perform non-exempt research. It is unclear if the classification of "non-exempt human subjects research" should be applied on the study level or individual site level. It would be helpful to receive clarification as to whether sites conducting exempt research can be excluded from using a single IRB by obtaining its own local exempt determination.

Additionally, we ask that OHRP permit an exception from the single IRB requirement for research where only one site is *actively* conducting research procedures, (i.e., when a site is only engaged in research when it is due to being the Primary Awardee of a federal grant, and the active research is done at another site). This would alleviate administrative burdens institutions face in accommodating this requirement. Examples of such burdens include determining which institution will act as the single IRB, agreement execution, educating study teams on the single IRB review process, and the potential need for additional IRB submissions to add the relying site.

Moreover, it would be helpful if OHRP can describe the criteria it uses to make exception determinations and the process for requesting an exception from the single IRB exception. Specifically, we ask that OHRP provide additional guidance on:

1. The timepoint investigators should request this exception from their funding agency (e.g., time of grant submission or time of award)
2. What form of documentation from the funder is sufficient to meet the criteria (ii) exception.

A common source of project delay and administrative burden is created due to the variability in the timing and process of determining if a single IRB exception is appropriate and has been granted. This has a particularly high impact on Just in Time (JIT) applications where funding can quickly become jeopardized.

Lastly, we ask that OHRP directly link to the Single IRB Exception Determinations webpage it mentions in this FAQ. We assume OHRP is referencing this website, however it is not clear as the guidance references exceptions for "classes of research" while the Single IRB Exception Determinations page describes exceptions based on policy reasons.

FAQ #3. Who decides which IRB will be the single IRB for the purposes of regulatory compliance?

The single IRB model requires HRPPs to be involved sooner in the research process, including for studies that may never come to fruition. In a typical scenario, the funding applicant identifies which participating institution is best qualified to serve as the reviewing IRB, and designates this IRB in their funding proposal. As such, before researchers can apply for funding, they need to talk with

their HRPP about what activities will take place at each site so that the sites can determine which IRB has the qualifications and staff resources to serve as the reviewing IRB.

The information presented in FAQ #3 emphasizes that Federal agencies or departments determine which IRB will serve as the Reviewing IRB. While UC understands that this language responds to the requirement in 45 CFR 46.114(b)(1), we want to underscore how important it is for HRPPs to be able to provide input on which site is best equipped to serve as the Reviewing IRB. It would be helpful if OHRP can elaborate on how Federal agencies and departments identify Reviewing IRBs, and how changes to the designated Reviewing IRB can be made. This information is especially important in instances when researchers do not contact or interact with the participating site IRBs prior to proposal submission. Should the research change between discussion with the IRB and the final proposal, we would appreciate that OHRP describe how to change the designated reviewing IRB if the original reviewing IRB is no longer willing or able to conduct the review. In addition, UC advises that OHRP make clear that site investigators need to communicate with their local IRBs early on.

FAQ #5. Can an institution involved in cooperative research choose to conduct its own IRB review of the research even though review is required by a single IRB that is located elsewhere?

UC believes that advising relying institutions that they may conduct internal IRB reviews is inconsistent with the cooperative research requirement. We suggest that instead the Draft Guidance state that a relying IRB is not obligated to re-review a study or ensure congruence with a reviewing IRB's determination. In addition, we recommend that OHRP describe when it is appropriate to conduct additional internal reviews. UC supports adding the language provided by COGR into this FAQ:

> ***An institution, through its human research protections program (HRPP), may conduct additional reviews of the research activities in which the institution is engaged, for local suitability and determination as to whether the research can be conducted at the local site, and/or requires additional changes to reflect local circumstances, local standards of care, and context. Although such HRPP reviews do not constitute IRB review, the institutional HRPP may determine whether the institution will participate in the research approved by the single IRB. Further, the institutional HRPP should report its determinations to the single IRB, and the single IRB may determine if the research must include additional changes to address local context.***

FAQ #6. Are there documentation requirements for use of a single IRB in cooperative research?

The single IRB requirement downplays the time-consuming and complicated nature of work that goes into developing a reliance agreement, which includes vetting and developing relationships with various institutions, creating legally binding agreements among the collaborating sites, and systemically managing information dissemination.

UC appreciates that the Draft Guidance recognizes flexible ways in which reliance agreements can be achieved, such as "through a written agreement between the institution and the single IRB,

through implementation of an institution-wide policy directive outlining the allocation of responsibilities between the single IRB and the institution, or through a description in the IRB-approved research protocol." However, in UC's experience, reliance agreements are increasingly used as a vehicle to legally shield institutions from a range of unforeseen problems rather than focusing on delineating responsibilities between the reviewing and relying IRBs. We ask that OHRP make clear that the purpose of a reliance agreement is to explain the respective roles of the participating institutions. Language beyond that is unnecessary and may create further delays in conducting single IRB reviews.

UC also asks OHRP to remove the mention of "indemnification and liability provisions" in the Draft Guidance. Such terms are complicated, especially for public institutions for which Regental policy (such as for UC) or state law outline such terms, and at times resolved in addendums to reliance agreements.

Lastly, UC strongly suggests that OHRP link to available template reliance agreements, such as OHRP's IRB Authorization Agreement and the SMART IRB Agreement, to encourage their use. Periodically, OHRP should assess whether these resources fit the needs of the community, and if additional resources should be created (such as a reliance agreement template better suited for social-behavioral research).

FAQ #8 and 9 regarding Local Context Reviews

Despite its intended purpose to streamline IRB review, single IRB review has not eliminated a relying site's workload since each site remains individually responsible for meeting regulatory obligations. Each participating site needs to complete local context reviews and inform the reviewing IRB of any site-specific issues that should be considered in the protocol review, such as special population knowledge, state law, and institutional policy. For example, unlike other states, California state law requires HIPAA authorization to be written in 14-point font or larger and separate from other text appearing on the same page, such as the research consent form. Even after the reviewing IRB approves a study, local IRBs will have continued oversight work, such as tracking and communicating reportable events to the reviewing IRB, and supervising any resulting management plans implemented by the reviewing IRB.

In addition, implementing a single IRB review does not mean forgoing other local reviews. Local reviews continue but without the unifying center that the IRB would provide. The IRB's review role is part of a larger oversight and administrative ecosystem that includes other entities (Conflict of Interest, Radiation Safety, Biosafety, Privacy, and Contracting, to name a few), each with their own regulatory requirements that are not easily modifiable to accommodate the single IRB review process. Coordinating and streamlining this ecosystem of processes are more complicated and difficult to address.

The language in FAQs #8 and 9 places the onus on the reviewing IRB to fully manage local context reviews when in reality local context review is a partnership between the various participating sites. Tweaks to the language throughout these two FAQs can bolster the collaborative nature of single IRB review. For example, rather than stating that the reviewing IRB should lean on its diversity of members for local context reviews, OHRP can identify the various factors that IRBs would need to consider in conducting such reviews. Drawing attention to the various ancillary committee reviews,

such as Conflict of Interest, Radiation Safety, Biosafety, Privacy, would make information in FAQ #8 more well-rounded.

Lastly, UC urges OHRP to develop and sustain a compendium of state laws relevant to human subject research. OHRP has been able to establish and maintain "a listing of over 1,000 laws, regulations, and guidelines on human subjects protections in ***131 countries*** and from many international organizations."[2] We strongly ask that OHRP invest in the incredibly important effort to maintain a similar database for ***50 states*** in order to facilitate efficiencies in single IRB review.

Thank you for the opportunity to comment. We welcome further discussions on this important topic. If you have any questions concerning these comments, please contact Agnes Balla, Research Policy Manager, at agnes.balla@ucop.edu.

Sincerely,

Deborah Motton, Ph.D.
Executive Director
Research Policy Analysis and Coordination
University of California, Office of the President

[2] International Compilation of Human Research Standards