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OFFICE OF THE VICE PRESIDENT – RESEARCH AND INNOVATION

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*Submitted via email: help@smartirb.org*

February 13, 2024

SMART IRB
c/o Harvard Catalyst
Harvard Medical School
1635 Tremont Street
Boston, MA 02120

**RE: UC Comments in Response to Revisions to the SMART IRB Reliance Agreement v3.0**

To Whom It May Concern:

I write on behalf of the University of California (UC) system regarding revisions to the SMART IRB Reliance Agreement v3.0. The UC system is comprised of ten campuses and three affiliated U.S. Department of Energy national laboratories.

Our office, Research Policy Analysis and Coordination (RPAC), provides guidance and assistance in the development, interpretation and implementation of policies and external rules in the conduct of research at the University of California. We regularly convene campus research administrators to provide a strong, systemwide voice to shape research policy in local, state and national arenas.

In response to the opportunity to comment on the SMART IRB Reliance Agreement 3.0, RPAC worked directly with each UC campus/location Human Research Protection Program (HRPP) to consolidate feedback on the proposed SMART IRB revisions. The table below consolidates feedback from across the UC HRPPs.

| Page # | Line # | Question/Objection | Proposed Revision | Rationale | Importance of Request |
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| 1 | 3-18 | The University of California has in place numerous reliance agreements under SMART IRB agreements v1 through v2. It would hamper research if those agreements were terminated without a sunset period, or if an existing study could not continue if one site signed v3, but other sites did not sign on to v3. | "INSTITUTIONS PARTICIPATING UNDER ANY OF THE PRIOR VERSIONS MAY CONTINUE UNTIL THE TERMINATION OF THE APPLICABLE STUDY. FOR ANY NEW STUDIES, INSTITUTIONS WILL HAVE [_____] DAYS AFTER THE V3.0 GO-LIVE DATE [_____], UNTIL [_____ ___, 20__] (THE "CUT-OFF DATE"), TO RE-EXECUTE A JOINDER AGREEMENT. DURING SUCH [_____]-DAY TIME, AND PRIOR TO RE-EXECUTION, THE INSTITUTION'S PARTICIPATION WILL CONTINUE TO BE GOVERNED BY THE TERMS OF THE VERSION IN WHICH THE INSTITUTION CURRENTLY PARTICIPATES. AN INSTITUTION THAT DOES NOT RE-EXECUTE A JOINDER AGREEMENT BY THE CUT-OFF DATE WILL BE CONSIDERED TO HAVE TERMINATED ITS PARTICIPATION IN THE AGREEMENT AS OF THE CUT-OFF DATE PURSUANT TO SECTION 7.2.1.2 HEREOF." | We recommend that SMART IRB agreement v1 through v2 remain active until the termination of the studies. With the effective date of v3, no *new* studies would be permitted to be issued under older versions of the SMART IRB reliance agreement. However, studies currently using v1 & v2 may continue in order to prevent a situation where, for example, 2 existing study sites sign on for v3, but other sites do not. A sunset period for v1 - v2 will: 1) reduce administrative burden, 2) the possibility of breach of the agreement, 3) ensure the continued protection of research participants and 4) limit disruption to the research. | Deal-breaker |

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| 6 | 17-20 | The language is confusing. | "A Reviewing IRB may determine based on significant cause that it must withdraw from providing review and oversight of the Research for a Relying Institution. The Reviewing IRB will provide sixty (60) business days' prior written notice to the Relying Institution explaining the significant cause for the Reviewing IRB's withdrawal." | The University of California suggests this modification for clarity. | Preference |

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| 9 | 17-20 | Instead of defaulting to the SMART IRB Standard Operating Procedures, the University of California supports flexibility in applying commensurate protections when agreed upon by Participating Institutions(s). | "For Research that is not subject to Mandated Policies, Participating Institutions are strongly encouraged to use and follow the Smart IRB Standard Operating Procedures ("SMART IRB SOPs") with respect to the conduct of their reliance relationships under this Agreement, or commensurate protections as agreed upon by Participating Institution(s)." | Instead of the agreement specifying the standard to be used for the review of the "unregulated" studies, the ORS and LoA should have options for the Relying and Reviewing IRB to agree to in such cases. The Common Rule could be one of those pre-built options along with "SOPs of the Reviewing IRB" and "SOPs of the Relying IRB" as well as "Other Standard (specify)." To keep the information clear between the Reviewing and Relying IRBs, the SMART IRB checklist, ORS, LoA or something similar should be used to document the commensurate protections, and a reliance under the Agreement will not be valid unless a standard is agreed upon. | Very Important |
| 15 | 10 | Liability "in connection with" participation in the Agreement is too broad. | "…allocation of liability or responsibility ~~in connection with~~ arising from participation in the Agreement." | University of California Legal opines that "in connection with" broadens the scope of responsibility to acts beyond the performance in the scope of work under an agreement. "Arising from" and "resulting from" are sufficiently narrow. | Deal-breaker |

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| 16 | 20-26 | IRBs that have "unchecked the box" should be permitted to use commensurate protections, as agreed upon by Participating Institutions, and there should be a space where this can be indicated in the Agreement. | "With respect to Research that is not subject to any federal human subjects protection regulations or policies (directly or through an Assurance) and is not subject to the FDA Clinical Investigation Regulations, a Reviewing IRB will review and oversee the Research in accordance with the standards ~~of the Federal Policy unless the Reviewing IRB and the Relying Institution(s) mutually agree on a different standard of review~~ agreed upon between the Reviewing IRB and the Relying Institution(s); provided, however, that nothing hereunder requires the external reporting to federal departments or agencies contemplated under 45 CFR 46.108(a)(4)) in connection with such Research." | Participating Institutions should retain the flexibility to review research not subject to federal regulations based on commensurate protections agreed upon by Participating Institutions. To keep the information clear between the Reviewing and Relying IRBs, the SMART IRB checklist, LoA, ORS, or something similar should be used to document the commensurate protections, and a reliance under the Agreement will not be valid unless a standard is agreed upon. | Very Important |

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| 25 | 16-20 | Does this refer to monitoring research activities or monitoring of the human research protection program? | "A Relying Institution will maintain, implement, or have access to a human subjects research quality assurance/quality improvement ("QA/QI") process, function, program, or service for the human research protection program that can conduct and report to the Relying Institution the results of for-cause and not-for-cause audits of the Relying Institution's and its Personnel's compliance with human subjects protections and other relevant requirements in the conduct of Research." | In the context of the SMART IRB agreement, the QA/QI function should be limited to the monitoring of the HRPP, rather than monitoring research activities. UC recommends separating the QA/QI requirement from the reporting element to avoid confusion about the content of the reporting. | Very Important |
| 25 | 16-20 | Not all University of California campuses have the resources to perform not-for-cause audits, so we propose deletion of that from clause 6.11. | "A Relying Institution will maintain, implement, or have access to a human subjects research quality assurance/quality improvement ("QA/QI") process, function, program, or service that can conduct and report to the Relying Institution the results of for-cause ~~and not-for-cause~~ audits of the Relying Institution's and its Personnel's compliance with human subjects protections and other relevant requirements in the conduct of Research." | The University of California campuses that do not have the resources to perform not-for-cause audits regularly conduct reviews of their program processes and have a process for investigating for-cause concerns about the research. Requiring not-for-cause audits adds unnecessary burden. | Very Important |

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| 27 | 1 | It is unclear when this reporting requirement applies. Is this referring to situations when the Relying Institution takes an action that is reportable in spite of the study being ceded (e.g. the institution learns of something untoward and suspends the study locally)? | | | Unclear |
| 27 | 10-15 | The University of California recommends including flexibility for DOE-managed labs as they may require earlier reporting to meet requirements under separate agreements with DOE. | "If the Relying Institution will make the Report pursuant to Section 5.13.2 hereof, the Relying Institution will promptly prepare the draft Report and will provide the Reviewing IRB/Reviewing IRB Institution with the opportunity (no fewer than five (5) business days, whenever possible, or as agreed upon by institutions) to review and comment on the draft Report, after which time the Relying Institution may finalize and send the Report to external recipients (such final Report will also be copied to the Reviewing IRB/Reviewing IRB Institution)." | The proposed revisions enable DOE-managed labs to meet their reporting deadline requirements to DOE. | Very Important |

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| 27 | 18-26 | • If the content of the communications is about any of the elements previously defined in 6.10-6.16, then it is already stated that the Reviewing IRB should be notified.<br>• Additionally, there is inconsistency in when the PI or study team members at the Reviewing Site are required to notify of such communications. | "When a Relying Institution is notified, ~~A Relying Institution~~ it will promptly notify the Reviewing IRB/Reviewing IRB Institution of communications regarding unanticipated problems. A Relying Institution will promptly notify the Reviewing IRB/Reviewing IRB Institution of suspension or termination of IRB approval, serious and/or continuing noncompliance, and/or other regulatory compliance concerns regarding Research conducted under the authority of the Relying Institution under Ceded Review that are received by the Relying Institution from, or made by the Relying Institution to, federal human subjects research regulatory agencies or funding agencies. ~~A Relying Institution will require its Overall PI (if any), Site Investigator(s), and other Personnel to do the same with respect to such communications between the Overall PI/Site Investigator(s)/other Personnel from, or made by the Overall PI/Site Investigator(s)/other Personnel to, such agencies."~~ | • This section may be redundant with reporting requirements in 6.10-6.16.<br>• This section is written in a way that institutions are at risk of being in breach of the agreement. This is because institutions can only comply when they are informed by PIs/others. If an institution is not notified, it cannot comply.<br>• For consistency, we recommend removal of the requirement for personnel to report, as not all IRBs have a mechanism to track non-PI/co-PIs personnel across studies. | Deal-breaker |

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| 32-33 | 25-10 | We recommend remaining silent on Governing Law and Venue. | Delete section 8.12 Governing Law and Venue. | Governing law and venue do not need to be identified in a reliance agreement. Participating Institutions retain greater flexibility if we remain silent. | Very Important |
| 48 | 4-6 | University of California Legal interprets "in connection with" to imply a very broad scope beyond the scope of the agreement. | "This SMART IRB Indemnification Addendum ("Indemnification Addendum") sets forth certain terms providing for indemnification between a Reviewing IRB/Reviewing IRB Institution and a Relying Institution ~~in connection with~~ resulting from their activities under the SMART IRB Reliance Agreement ("Agreement")." | "Resulting from" clarifies that the indemnification obligation is solely for acts directly tied to activities under the SMART IRB Reliance Agreement. We understand this sentence is not describing a specific indemnification obligation. However, we are requesting this revision for consistency with later parts of the Indemnification Addendum. | Preference |
| 51 | 17 | The obligation to indemnify is too broad. For the University of California to be able to accept the SMART IRB Indemnification Addendum, the obligation to indemnify should be limited "only *in proportion to* and to the extent such Losses are attributable to" the University of California's actions. | "but (a) only in proportion to and to the extent such Losses are attributable to the Responsible Party's, its IRB's, or its trustees', directors', officers', employees', agents', faculty's, or students'" | The University of California (UC) Board of Regents Standing Orders prohibit UC from assuming liability for non-UC acts. UC Legal has opined that UC's indemnification obligations must be limited "only in proportion to and to the extent" losses, etc. arise from UC's acts. If this change cannot be made, UC would need to individually negotiate indemnification provisions with each Reviewing/Relying IRB Institution, which negates the efficiency of signing the SMART IRB agreement. | Deal-breaker |

Thank you for the opportunity to comment. We look forward to continued engagement on this important issue. If you have any questions concerning these comments, please contact Ruchika Dhussa, Senior Research Policy Manager, at Ruchika.Dhussa@ucop.edu.

Sincerely,

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