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Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: UC Comments in Response to FDA's Proposed Guidance for Sponsors, Investigators, and Institutional Review Boards on Key Information and Facilitating Understanding in Informed Consent (Docket Number: FDA-2022-D-2997)

To Whom It May Concern:

I write on behalf of the University of California (UC) system regarding the FDA's Guidance for Sponsors, Investigators, and Institutional Review Boards on Key Information and Facilitating Understanding in Informed Consent. The UC system is comprised of ten campuses and three affiliated U.S. Department of Energy national laboratories and receives approximately $7 billion annually in funding for research.

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.

UC appreciates the opportunity to comment on the proposed guidance. In response to the opportunity to comment on the FDA's proposed guidance, RPAC worked directly with each UC campus/location Human Research Protection Program (HRPP) to consolidate the following feedback on the proposed guidance.

Elements of the Proposed Guidance Supported by UC

In general, UC supports the FDA's proposed guidance, and finds many of the recommendations to be helpful, such as:

- Harmonizing sections of the FDA regulations on human subject protections and institutional review boards (IRBs) with the Revised Common Rule, in accordance with the 21st Century Cures Act.
- Following plain language principles, including appropriate breakdown of complex information, use of simple language, and definition of technical terms.
- Disclosing Conflicts of Interests in the key information section.
- Presenting key information in the informed consent document in a way that is best suited to the study and context.
- Emphasizing that the FDA is providing guidance, and researchers and institutions should ultimately select the approach that fits the needs of their study.

Feedback on the Use of the Bubble Format in the Key Information Section

UC HRPPs support solutions that promote ease of reading and comprehension of informed consent documents in alignment with the Revised Common Rule. However, UC highlights the following concerns regarding use of the proposed bubble format for the key information section:

- The bubble approach may limit the use of screen readers for accessibility. Specifically, because bubbles need to be drawn around existing text, or a "shape" must be entered into a word processing document, the bubbles are not inherently readable by screen readers. Instead, in addition to visually adding text within the bubble, researchers/IRB administrators must add the text contained in the bubble into the "alternative text" associated with the bubble. If the bubble format recommendation is included in the final FDA guidance, it should be accompanied by guidance that alternative text is required to make the format accessible.

- UC recommends that the FDA's guidance explain the necessity of the bubble format and how to ensure that equity is maintained for all research participants as informed by the Belmont Report's principle of justice and the requirements of The Americans with Disabilities Act (ADA).

- The FDA guidance should indicate that IRBs need to review the information presented visually in the bubbles, as well as the alternative text, since it would be possible for a researcher to include inconsistent or incorrect information which may cause confusion and inadvertently withhold important information from some participants.

- The suggested bubble format may increase whitespace and the length of the informed consent documents, which may make it difficult to find content when participants return to reference the document. The FDA guidance should note that the bubble format should only be adopted if it is in line with the Revised Common Rule requirement that informed consent begin with a concise and focused presentation of the key information. Such information should be organized and presented in a way that facilitates understanding of the reasons why one might or might not want to participate. If the bubble format adds complexity, the

guidance should clarify that researchers or IRBs should seek alternatives to meet the Revised Common Rule requirements.

- In response to the FDA recommendations, sponsors of research may choose to require, rather than merely suggest use of bubbles. This could lead to administrative challenges for institutions if faculty have trouble creating the bubbles as part of the key information section. UC recommends that the FDA emphasize these recommendations are suggestions and may not be appropriate in all scenarios. For instance, the appendix that includes the sample bubble format examples can use a watermark like "optional" to clarify the bubbles are not required.

- UC notes that the FDA referenced one publication to support the recommendation of the bubble format. The cited study compared three different formats for the presentation of information on medication and sought to find if a particular format enabled participants to have greater comprehension and better application of the information. Per the abstract of the article, the bubble format improved comprehension but no significant difference was found in application of information in comparison to the control format. It would be helpful to see a comparison of the bubble format against the standard Office for Human Research Protections consent template to understand which format is better.

Recommended Additions to the Proposed Guidance

The UC HRPPs recommend the following additions to the FDA's proposed guidance:

- Include contact information, which is a basic element of consent, as noted in 45 CFR 46.116(b)(7) and 21 CFR 50.25(a)(7). Contact information is currently missing from section III.B of the FDA's proposed guidance, which discusses the basic and additional elements of consent that the FDA notes should be included in the key information section. UC HRPPs consider contact information to be key information for research subjects to have, and advocate for its inclusion in section III.B of the guidance.

- Use stronger language to emphasize the importance of the elements of informed consent. Section III.B describes the seven recommended basic and additional elements of informed consent to be included in the key information section. The first five elements listed (i.e., Voluntary Participation and Right to Discontinue Participation; Purpose of the Research, Expected Duration and Procedures to Be Followed; Reasonably Foreseeable Risks and Discomforts; Reasonably Expected Benefits; and Appropriate Alternative Procedures) are widely understood by the IRB community to be necessary components of the key information section; however, elements 6 and 7 (i.e., Compensation and Medical Treatments for Research-Related Injuries; and Costs Related to Subject Participation) may not be as universally recognized. UC recommends that clearer language be inserted in sections II.B.6 and III.B.7 to allow institutional IRBs to easily push back on research sponsors who may be more reluctant to include these components.

- Provide qualifiers for specific elements of consent. The addition of the italicized language below lends clarity to the recommendations:

    - From Section III.B.3: *"For greater than minimal risk studies*, we recommend providing information about the most common and serious risks and discomforts in the key information section to inform a prospective subject's decision about participation. Key information about risks and discomforts of research participation should be included on the first page of the key information section, if possible."

    - From Section III.B.4: "If *the study involves a clinical intervention and* there is no potential for direct benefit to the prospective subject, this point should be clearly stated."

- Add the status of participants' current medications or treatment. In Section II.B.2, lines 204-212, UC recommends inclusion of information on whether participants need to stop taking any current medications or treatments to participate in clinical trials using investigational medical products. This key information may also be added to Section II.B.3.

- Note any risks or discomfort to participant families and communities. In Section II.B.3, UC recommends adding information related to potential risks/discomforts to participants' family members or to the larger community (e.g., genetic studies).

- Increase guidance on key information for conditions, such as:
    - When short form versions of key information should be the same as the long form.
    - If study specific key information is required, whether HRPPs are expected to review translated short form key information before use of the short form consent process.
    - When to use variations in key information for exceptions from informed consent and expanded access.

Recommended Deletions from the Proposed Guidance

UC is concerned about the guidance in Section IV.B.2 that recommends providing glossaries, references, a table of contents, and page numbers. Though UC finds that a tiered presentation system could be useful for some studies, a recommendation for including these additional elements may burden researchers and subjects by significantly increasing the volume of material to be developed and read. Additionally, the use of page numbers to cross reference between key information and other sections of the consent form creates significant administrative burden of managing cross reference locations as modifications are made and content shifts. These sections could easily turn into bureaucratic opportunities to pack into consent forms all various defined terms and move away from using understandable lay language, in contradiction with Section IV.B.3 of the guidance. Thus, UC suggests deleting these recommendations from FDA's proposed guidance.

Thank you for the opportunity to comment. We look forward to continued engagement on this important guidance. 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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