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PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

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

RE: Docket No. FDA–2022–D–2997, Key Information and Facilitating Understanding in Informed Consent; Draft Guidance for Sponsors, Investigators, and Institutional Review Boards.

The Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) and Public Responsibility in Medicine and Research (PRIM&R) appreciate the opportunity to provide our combined comments on the proposed joint guidance entitled "Key Information and Facilitating Understanding in Informed Consent" issued by the US Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP), Office of the Assistant Secretary for Health, Office of the Secretary. Although AAHRPP and PRIM&R are responding with the same comments, our organizations submitted them separately to underscore that they reflect the thinking of more than one entity. Additionally, AAHRPP endorses the thoughtful comments on the draft guidance made by the Association of American Medical Colleges (AAMC), which align closely with those of AAHRPP and PRIM&R.

AAHRPP is a non-profit organization that accredits human research protection programs. Currently, more than 600 entities from diverse research settings—including hospitals, independent review boards, clinical research organizations, universities, and Veterans Affairs facilities—are accredited. AAHRPP's comments are based on our 20+ years of experience evaluating and working with a variety of HRPPs, most of which conduct research regulated by the FDA or fall under the purview of the Common Rule. We offer our feedback on this proposed guidance based on our deep knowledge of HRPPs and the regulations with which they must comply. The following comments on the proposed guidance reflect AAHRPP's views but do not necessarily reflect the opinions of AAHRPP's accredited organizations.

PRIM&R is a nonprofit organization dedicated to advancing the highest ethical standards in the conduct of research. Since 1974, PRIM&R has served as a professional home and trusted thought leader for the

research protections community. Through educational programming, professional development opportunities, and public policy initiatives, PRIM&R seeks to ensure that all stakeholders in the research enterprise appreciate the central importance of ethics to the advancement of science.

AAHRPP and PRIM&R applaud the FDA and OHRP for moving to provide harmonized guidance for the new informed consent provisions, which include the key information requirement, currently within the Common Rule and expected to become part of the FDA regulations for the protection of human participants. We were pleased that the proposed guidance generally aligns with what many organizations implemented to address the informed consent requirements in the more than five years since the revised Common Rule went into effect.

Comments for Consideration

Provide more guidance on what constitutes reasonably foreseeable risks in research

One of the prominent recommendations within the guidance is the suggestion to include reasonably foreseeable risks and discomforts in the key information section of informed consent documents. Confusion remains in the regulated community about what are considered reasonably foreseeable risks and discomforts, which can lead IRBs to err on the side of caution and include all potential risks in consent documents. As one expert in the regulated community noted, the amount of detail regarding the reasonably foreseeable risks and discomforts the guidance suggests "could be interpreted to encompass the entirety of a consent section regarding the risks of the study" and this dilute the impact and utility of the information.[1] In 2014, OHRP issued Draft Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care (https://www.hhs.gov/ohrp/regulations-and-policy/requests-for-comments/draft-guidance-disclosing-risk-in-standards-of-care/index.html), which could be immensely helpful to the community in identifying what information to include in terms of risks and discomforts within the key information section versus the body of the consent document. Consequently, we urge OHRP to return to this draft and collaborate with the FDA to issue new guidance regarding how reasonably foreseeable risks and discomforts may be identified in general and for standard of care specifically.

[1] Public Responsibility in Medicine & Research blog, Ampersand: Add Your Voice: Share Your Thoughts with the FDA and the Office for Human Research Protections (OHRP):https://blog.primr.org/add-your-voice-share-your-thoughts-with-the-fda-and-the-office-for-human-research-protections-ohrp/. Accessed April 16, 2024.

Incorporate into the guidance findings from research and other sources about what participants find important to know

As currently proposed in the guidance, the key information section would include the majority of the basic elements of informed consent and an expectation that these details can be boiled down to a few pages. We agree with a concern expressed by an expert in the community that the amount of detailed information the guidance suggests should be included in the key information section might contradict the goal of enhancing the understanding of participants and that the "example of the bulleted information in the guidance appendix is helpful, but seems somewhat inconsistent with the extent of the information proposed in the guidance itself."[2]

The guidance suggests that research teams consult in advance with patient advocacy groups or prospective subjects about their views on key information. Although AAHRPP strongly supports involving the community in the design and review of research involving human participants, the expectation that consultation with the community occur routinely to develop informed consent documents can be quite burdensome on smaller organizations that may not have the resources to do this in a meaningful way. Further, many organizations already have conducted such outreach to find out what potential participants want to know about participating in a study and drafted their key information templates and guidance based on that knowledge. For example, one organization found that potential research participants wanted to know the time commitment; where they had to go to participate; what they needed to do; and what was the reimbursement or compensation for participation or if they were injured in some way.[3] These priorities differ from what OHRP and FDA propose to include in the key information section of an informed consent document. We recommend OHRP and FDA follow their own guidance and take advantage of the work organizations already have done and incorporate that knowledge into their recommendations. OHRP and FDA might consider reviewing the key information sections of informed consent templates that organizations have posted publicly or conducting a survey of organizations about what they learned.

Additionally, a systematic review of what potential research participants want to know about research is somewhat at odds with the recommendations in the guidance as to what to include in the key information section.[4] For example, their study showed that most potential participants wanted to be offered information about result dissemination, the

[2] Public Responsibility in Medicine & Research blog, Ampersand: Add Your Voice: Share Your Thoughts with the FDA and the Office for Human Research Protections (OHRP):https://blog.primr.org/add-your-voice-share-your-thoughts-with-the-fda-and-the-office-for-human-research-protections-ohrp/. Accessed April 16, 2024.

[3] Public Responsibility in Medicine & Research blog, Ampersand: Add Your Voice: Share Your Thoughts with the FDA and the Office for Human Research Protections (OHRP):https://blog.primr.org/add-your-voice-share-your-thoughts-with-the-fda-and-the-office-for-human-research-protections-ohrp/. Accessed April 16, 2024

[4] Kirkby HM, Calvert M, Draper H, Keeley T, Wilson S. What potential research participants want to know about research: a systematic review. BMJ Open 2012; 2(3): e000509

purpose of the study, how long the research would last, and potential benefits. Result dissemination appears to be highly valued by potential research participants but apparently not suggested to be included as key information because it is not one of the basic elements of consent.

Provide guidance on the informed consent process and not just the informed consent document

The draft guidance document appears to focus on a written informed consent document to the exclusion of how the presentation of key information and organization of the presentation of information could enhance the informed consent process beyond the form. Although the informed consent document is important, research has shown how the information within those documents is presented to a potential participant makes a difference in their satisfaction with the informed consent process.[5] Extending the guidance to provide recommendations related to the process, especially if based on input from those skilled at obtaining informed consent, could help underscore for IRBs and others the importance evaluating the informed consent process and not just informed consent documents.

Acknowledge the variability in what may be perceived by individual research participants to constitute key information and the challenges this presents.

The revised Common Rule requires prospective subjects or their legally authorized representatives to be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate. This reasonable person standard, which can be logically inferred to be the standard that should be used to identify what to include in the key information section, is a challenging and potentially impossible to meet given the variability in what reasonable persons may consider to be key information.[6] Consequently, we urge OHRP and FDA to provide more concrete discussion in the guidance about how IRBs and others can attain the ideal of ensuring the informed consent process and documents meet the needs or preferences of each potential participant due to the expected variation in what is perceived as key information. Instead of relying on information in a single key information section, for example, skilled individuals who obtain informed consent know how to adapt their presentation of a consent document in response to questions and feedback from potential participants. The FDA and OHRP might consider ways of supporting the regulated community to develop and share what they learn and

[5] Suver CM, Hamann JK, Chin EM, et al. Informed consent in two Alzheimer's Disease Research Centers: insights from research coordinators. AJOB Empirical Bioethics 2020; 11(2): 114–124.

[6] Odwazny LM, Berkman BE. The "Reasonable Person" standard for research informed consent. The American Journal of Bioethics: AJOB 2017; 17(7): 49–51.

mechanisms they develop to better meet the needs of individual participants, such as efforts to develop more personalized approaches to informed consent.[7] [8]

Thank you for the opportunity to comment on this draft guidance. If you have any questions or require any further information, please feel free to contact me at 617.303.1872 or itillman@primr.org.

Respectfully submitted,

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cc: PRIM&R Public Policy Committee, PRIM&R Board of Directors

[7] Cobb NL, Edwards DF, Chin EM, et al. From paper to screen: regulatory and operational considerations for modernizing the informed consent process. Journal of Clinical and Translational Science. 2022;6(1):e71. doi:10.1017/cts.2022.379.

[8] Lawrence, CE, Dunkel, L, McEver, M, et al. A REDCap-based model for electronic consent (eConsent): Moving toward a more personalized consent. Journal of Clinical and Translational Science 2020; 4(4): 345–353.10.1017/cts.2020.30.