

April 30, 2024

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

*Submitted via Regulations.gov*

**Re: Key Information and Facilitating Understanding in Informed Consent; Draft Guidance for Sponsors, Investigators, and Institutional Review Boards (Docket Number FDA-2022-D-2997).**

The Association of American Medical Colleges (AAMC) appreciates the opportunity to respond to the proposed guidance, *Key Information and Facilitating Understanding in Informed Consent* issued by the Food and Drug Administration (FDA), the Department of Health and Human Services (HHS), and Office for Human Research Protections (OHRP).

The AAMC is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research, and community collaborations. Its members are all 158 U.S. medical schools accredited by the Liaison Committee on Medical Education; 13 accredited Canadian medical schools; approximately 400 academic health systems and teaching hospitals, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools, academic health systems and teaching hospitals, and the millions of individuals across academic medicine, including more than 193,000 full-time faculty members, 96,000 medical students, 153,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences. Following a 2022 merger, the Alliance of Academic Health Centers and the Alliance of Academic Health Centers International broadened participation in the AAMC by U.S. and international academic health centers.

**General Comments**

The AAMC appreciates the collaborative efforts of the FDA and HHS to address the "content, organization, and presentation" of informed consent information within FDA-regulated clinical investigations of medical products and HHS-supported or conducted nonexempt human subjects research. Since the finalization of the revisions to the *Federal Policy for the Protection of Human Subjects* in 2017 (the "revised Common Rule" 45 C.F.R. Part 46, Subpart A), the AAMC has supported member institutions with the implementation of these changes (e.g., develop policies, processes, educational resources), including navigating the compliance challenges stemming from the differences between the revised Common Rule and the FDA's regulations (21 C.F.R. Part 50).

Notably, in September 2022, the FDA issued two proposed rules to align key aspects of its regulations with the revised Common Rule.<sup>1</sup> The AAMC commented on both proposals, commending the FDA's interest in prioritizing the harmonization of specific elements in the revised Common Rule such as those pertaining to informed consent. The Association also emphasized the need for a closer evaluation of

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<sup>1</sup> See AAMC Comment Letters (January 13, 2023), <https://www.aamc.org/advocacy-policy/washington-highlights/aamc-comments-harmonization-fda-human-subject-protection-regulations> (Protection of Human Subjects and Institutional Review Boards, 87 Fed. Reg. 58733 (Sep. 28, 2022); Institutional Review Boards: Cooperative Research, 87 Fed. Reg. 58752 (Sep. 28, 2022)).

additional areas in the revised Common Rule that have raised implementation concerns and greatly impacted institutions.<sup>2</sup> We appreciate the FDA and OHRP’s recent efforts to develop guidance on informed consent, helping to better assist institutional review boards (IRBs), investigators, and, sponsors engaged in research subject to the FDA and/or HHS. This draft guidance provides important clarification on the requirements pertaining to the key information section in the informed consent form and facilitation of understanding for a prospective subject or their legally authorized representative (LAR). In the comments below we provide recommendations on four areas:

- **Informed Consent Process** —Need for additional guidance on the process not just the content or format of the consent form.
- **Innovative Approaches to Informed Consent**—Ensuring the draft guidance emphasizes the importance of engaging with diverse organizations and populations to develop new approaches to key information, including considering existing research and example consent forms.
- **Key Information and Elements of Consent** — Proposed recommendations for when the FDA and OHRP should discuss the necessity of the “key information” label in the draft guidance.
- **Facilitating Understanding**— Ensuring the draft guidance includes recommendations on the measurement of a prospective subjects’ comprehension of the information provided, as well as considerations for language fluency.

### **Informed Consent Process**

The draft guidance provides recommendations on how to facilitate discussions with a prospective subject or LAR and an investigator about participation in a clinical trial. The recommendations cover the appropriate length of the consent form and information that should be included, emphasizing “multiple strategies for providing key information to prospective research subjects [...] such as developing an approach that encompasses principles from a variety of sources for the key information section, depending on the distinctive attributes and design of the study, the prospective subject population, the condition being examined, and other relevant factors (lines 98-103).”

While we recognize the utility of guidance on the length, format, and structure of the consent form, we are also reminded by the OHRP that “[i]nformed consent is a process, not just a form. Information must be presented to enable people to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act.”<sup>3</sup> Similarly, in the AAMC’s comments on the Common Rule notice of proposed rulemaking, we suggested that:

“[...] there is an opportunity to re-envision the informed consent process and provide investigators and institutions with the flexibility to ensure that critical information is delivered in a way that is understandable to the research subject. Although the proposed changes to the informed consent document are not harmful, they are focused on rearranging and adding to a written document, not setting forth the types of information that is important for prospective subjects to know and giving investigators and IRBs the flexibility to determine how best to communicate the information and ensure understanding, given the research design, level of inherent risk to participants, target study population, and best evidence for effective communications.”<sup>4</sup>

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<sup>2</sup> AAMC Comments on HHS Common Rule NPRM (January 4, 2016), <https://www.aamc.org/media/11936/download?attachment>.

<sup>3</sup> Office for Human Research Protections. Informed Consent Tips (Rockville, MD 1993), <https://www.hhs.gov/ohrp/regulationsand-policy/guidance/informed-consent-tips/index.html> (Accessed Dec. 20, 2022).

<sup>4</sup> Supra Note 2.

**We suggest the FDA and OHRP collaborate with the research community to expand the recommendations on this topic.** This expansion would better reflect the significance of the consent process, beyond just the format, language, or form. Related, in August 2023, the FDA issued final recommendations titled "*Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors*," which should also serve as reference (see, Sect. II Summary of the Consent Process, Sect. IV. Review of the Consent Process).<sup>5</sup>

### **Innovative Approaches to Informed Consent and Public Consultation**

This draft guidance offers valuable recommendations for leveraging innovative tools and technologies to enhance flexibility in the informed consent process. Notably, lines 98-111 outline diverse approaches, including media, illustrations, videos, and electronic tablets. The guidance also underscores the significance of early engagement with patient advocacy groups, prospective subjects, and other interested parties to gather insights on key information in advance.

**While we support the recommendation for advance consultation with individuals and organizations, we propose that the guidance specify the necessity of engaging with diverse advocacy groups and prospective subjects, including those from underrepresented racial and ethnic groups, as well as populations with low literacy or limited English proficiency.** The timing of when public consultation should take place should also be better defined and should include who could serve as an appropriate party to initiate the process (e.g., sponsor, investigator, IRB, other parties). This approach aligns with the FDA's proposed strategies to improve participation from underrepresented racial and ethnic populations in clinical trials but also with the broader objectives of the Administration to promote racial equity across federal initiatives.<sup>6</sup>

Further, we urge the FDA and OHRP to consider the substantial body of existing research on the impact of the key information requirement.<sup>7</sup> This should also include a recognition of the organizations that have conducted extensive consultation with diverse populations to identify effective methods for enhancing comprehension, as well as development of consent templates informed by these efforts.

Missing from the draft guidance is a recognition of the use of innovative technologies and by the disability community. In the AAMC's letter to HHS Office of Civil Rights regarding the request for information on *Discrimination on the Basis of Disability in Health and Human Service Programs or Activities*, we addressed the use of web technology, an area that is also covered in this draft guidance. In our letter, we encouraged HHS "[...] to create opportunities for public feedback on additional approaches that better account for diverse experiences by type of disability."<sup>8</sup> In the context of this guidance, an assessment of how key information is presented in digital formats (e.g., hyperlinks) and the potential design constraints based on the type of disability should be assessed and included in the draft guidance if finalized.

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<sup>5</sup> Grant SC. Informed Consent—We Can and Should Do Better. *JAMA Netw Open*. 2021;4(4):e2110848. doi:10.1001/jamanetworkopen.2021.10848

<sup>6</sup> Re: Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry [Docket No. FDA – 2021 – D – 0789 <https://www.aamc.org/media/61296/download?attachment>

<sup>7</sup> Gelinis L, Morrell W, Tse T, Glazier A, Zarin DA, Bierer BE. Characterization of key information sections in informed consent forms posted on ClinicalTrials.gov. *J Clin Transl Sci*. 2023 Aug 14;7(1):e185. doi: 10.1017/cts.2023.605. PMID: 37745937; PMCID: PMC10514692.

<sup>8</sup> AAMC Comments to HHS (Nov 13, 2023) Re: Discrimination on the Basis of Disability in Health and Human Service Programs or Activities (88 FR 63392) <https://www.aamc.org/media/71091/download?attachment>.

## **Key Information — Title and Elements of Consent**

In the introduction to Section III. (Key Information), the draft guidance discusses the length and format of the consent form, recommending that the form be “relatively short” (lines 73-83). However, almost three pages later, it is stated that “[c]ertain studies, such as those involving no more than minimal risk, may have relatively brief consent forms. In such cases, the key information section could constitute the majority of or even the entire consent document” and does not need to be labeled as “key information” (lines 149-151). **To improve clarity, we suggest incorporating the rationale for when to use the “key information” label (as outlined in lines 149-151) into the discussion in lines 73-83. This would ensure a better understanding of when it is appropriate to label a consent form, particularly as it relates to the form’s length for certain studies.**

Section B of the draft guidance states: “we do not recommend that the key section of the consent form necessarily include each element of informed consent” (lines 118-120). The guidance cites the FDA’s August 2023 *Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors* for a “full discussion of how to address the elements of informed consent during the informed consent process.”<sup>9</sup> Notably, there is limited discussion and supporting rationale regarding *which elements* of consent could be deemed “key.” The FDA’s 2023 guidance on informed consent provides comprehensive recommendations on the basic elements of consent but also the consent process related to each unique element. We believe including a direct reference to the 2023 guidance within the body of the draft guidance, rather than relegating it to a footnote, would be beneficial.

## **Facilitating Understanding**

In the final section of the draft guidance, the FDA and OHRP provide recommendations on ways to enhance prospective subjects’ understanding of participation and the importance of making informed decisions, an important perspective that is also emphasized in the revised Common Rule. **However, the draft guidance does not address how IRBs, sponsors, or other parties can appropriately measure a prospective subjects’ comprehension as part of the consent process (e.g., through interactive questions or other testing methods). Therefore, we recommend including suggestions for assessing comprehension of informed consent information, a topic that would also greatly benefit from community discussion and feedback.**

Subsection 3 (*Understandable Language*) advises that “[i]nformation should be provided in the primary language of a prospective subject with limited English proficiency.” It is critical for the FDA and OHRP to recognize that fluency in one’s primary language doesn’t always equate to proficiency in reading that language.


In closing, we commend the FDA and OHRP for their continuous efforts to harmonize and clarify their respective human subjects protection regulations through proposed rulemaking, draft guidance, and other educational resources. We look forward to further opportunities for public input on aspects of this draft guidance that require additional clarification, as well as other areas within the FDA and HHS regulations in need of clarification. These crucial steps toward alignment are not only mandated by the 21st Century Cures Act (sect 3023) but eagerly anticipated by the research community.

For questions about these comments, please contact me or my colleague, Daria Grayer, MA, JD, Director of Policy and Regulations ([dgrayer@aamc.org](mailto:dgrayer@aamc.org)).

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<sup>9</sup> Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download> (Accessed April 22, 2024).

Sincerely,

A handwritten signature in blue ink that reads "Heather Pierce". The signature is written in a cursive style with a large initial 'H' and 'P'.

Heather Pierce, JD, MPH  
Acting Chief Scientific Officer

cc: David J. Skorton, MD, President and Chief Executive Officer