AMA
AMERICAN MEDICAL ASSOCIATION

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Jerry Menikoff, MD, JD
Director
U.S. Department of Health & Human Services
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Re: Federal Policy for the Protection of Human Subjects, Docket number HHS–OPHS–2015–0008

Dear Dr. Menikoff:

On behalf of the physician and medical student members of the American Medical Association (AMA), I applaud the ongoing efforts of the Office of Human Research Protections to better safeguard the interests and well-being of research participants. We appreciate the opportunity to comment on the proposed changes in the Federal Policy for the Protection of Human Subjects (referred to as the federal Common Rule). As we have previously noted, there is compelling need to modernize the Common Rule to address significant changes that have taken place in biomedical and behavioral research over the past 20 years and to ensure that oversight of research involving human participants meets the needs of patients, investigators, research institutions, sponsors, and the public at large. The goals and activities surrounding the President's Precision Medicine Initiative highlight many of the challenges, opportunities, and risks in this area that must be addressed as the capacity and methods for clinical research have expanded rapidly and will continue apace into the foreseeable future. We strongly support the development of guidance specific to research involving biospecimens or identifiable private information, including the secondary use of specimens or information initially collected for non-research purposes.

Overall, the proposed changes successfully address many of the concerns by those engaged in clinical research, particularly with regard to clarifying the scope and application of the Common Rule. Also, for the most part, the proposed changes effectively balance enhancing protection for research participants while minimizing regulatory and administrative burdens for investigators, institutional review boards, and research sponsors. Nonetheless, we are concerned that some of these changes may have unintended consequences.

Calibrating Review to Risk Level

We appreciate changes that explicitly specify activities that are not subject to the Common Rule. The defined category of "excluded activities" appropriately recognizes that some activities are not research and thus should not fall within the purview of the Common Rule or pose low risk and are already subject to independent control such that regulatory oversight by means of the Common Rule is not warranted. We particularly appreciate proposed changes that clearly define activities covered by the Health Information Portability and Accountability Act as "excluded activities" since important patient protections are already in place and this clarification will significantly facilitate important quality

assurance/quality improvement activities by removing regulatory confusion and administrative duplication.

Other proposed changes expand the category of "exempt" research to include: (1) secondary research use of identifiable private information; and (2) collection of identifiable private information or biospecimens for research purposes when these activities meet conditions newly defined in the regulation. We appreciate that the intent of these changes is to facilitate appropriate research that poses low risk while protecting the well-being of individuals who provide private information or biological samples.

We believe that new provisions permitting the determination of exempt status to be made using a decision tool, which will be developed by the Secretary of the Department of Health and Human Services, have the potential to significantly reduce confusion and decrease administrative burden and will help ensure greater consistency in such determinations. We support this innovative approach, which could have value as an educational resource as well as a tool for research oversight.

Protection of Biospecimens and Identifiable Private Information

Ensuring that the privacy, security, and integrity of biological samples and identifiable private information are adequately protected is a central concern for AMA. We support the development of a single, well-defined list of clear, specific measures for institutions and investigators to use to meet these fundamental ethical requirements. However, while such a list could effectively define a threshold of protection, care must be taken that the Secretary's list not become a disincentive to the development of more stringent measures where the nature of the research or the sensitivity of information warrant a higher level of protection. Institutions and investigators should not be expected or required to adopt these measures if other, more robust protections are already in place within the institution or required by local institutional policies. We look forward to the opportunity to offer comment on the list of proposed measures when it is available.

Informed Consent

As we indicated in our earlier comments on the advanced notice of proposed rulemaking, we are strongly in favor of improving the process of informed consent and support new provisions requiring that consent forms be designed to provide succinctly the information a reasonable person would want to have to make a well-informed decision about participating in research. Exhaustive lists of risks and highly granular descriptions of research protocols or interventions serve more as tools to protect the interests of institutions than to promote meaningful understanding on the part of research participants.

New provisions for informed consent in research that involves the collection and use of biospecimens or identifiable private information address a significant gap in previous guidance. Requiring that participants be informed as part of the consent process that their biospecimens may be used for commercial profit (and whether they will share in that profit), that they be informed whether and under what conditions clinically relevant findings will be disclosed to them, and that they explicitly be offered the opportunity to consent or refuse to be re-contacted enhances transparency and meaningful decision making. Requiring that participants be informed about the conditions under which their identifiable private information may be used for future research or distributed to other investigators offers the same enhancements.

We support the concept of "broad consent" as defined at 116(c)(1) for storage, maintenance, and secondary research use of biospecimens or identifiable private information. We believe that this concept offers a viable response to the challenges posed by rapidly evolving research methodologies using biorepositories or clinical datasets and support the disclosure requirements set out in the new regulations. However, we are concerned that clarification is needed with respect to the implications of new consent requirements for secondary use of specimens or data originally collected for non-research purposes. Research using collections created for research or non-research purposes prior to the compliance date of these new regulations need not comply and is not problematic. Questions arise, however, with respect to how and by whom consent should be obtained for research access to biospecimens or identifiable private information originally collected for non-research purposes, e.g., secondary use of pathology specimens or data collected for purposes of treatment. Must investigators separately re-contact patients whose specimens or data were collected by non-research personnel in the process of providing clinical care? Or should broad consent for possible future use of biospecimens or identifiable private information routinely be sought by clinical personnel, who may not be affiliated with research activities, at the time specimens or data are collected as part of consent for clinical care? This issue is of considerable concern among investigators who currently rely on pathology specimens, for example.

We note that criteria for waiver of consent for research with biospecimens require investigators and institutional review boards (IRBs) to make determinations about potential adverse effects on participants' welfare and rights, but also about scientific questions about the rationale for study design and the feasibility of carrying out the study using biospecimens for which consent has already been obtained or which could be collected with appropriate consent. These are complex judgments, and IRBs will require appropriate scientific expertise among members or access to such expertise through other channels.

Oversight of Cooperative Research

We support changes in the Common Rule designed to facilitate timely, appropriate, coordinated oversight of large-scale, multi-site research. These provisions reflect well-established practices of existing clinical trials networks. Requiring review and approval of such research by a single IRB will provide more consistent, uniform protection for participants at all study sites and will significantly reduce the administrative burden, delays, and potential conflicts currently associated with participation by multiple, site-specific IRBs. The regulations identify ethically appropriate exceptions to this requirement.

Conclusion

The state of clinical and biomedical research will continue to evolve rapidly as are the norms around the engagement and participation of human subjects/participants. We appreciate the effort to provide flexibility and careful consideration of important protections that benefit participants in such research. We look forward to providing comment and outreach on the new policy when it is finalized.

Sincerely,

James L. Madara, MD