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Jerry Menikoff, MD, JD

Office of Human Research Protections

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Rockville, MD 20852

RE: Docket ID Number HHS-OPHS-2011-0005

Dear Dr. Menikoff:

On behalf of C-Change, we thank you, the Office of Science and Technology Policy (OSTP), and the Office of the Secretary of the Department of Health and Human Services (HHS) for this opportunity to submit comments on the advance notice of proposed rulemaking (ANPRM), "Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators."

The mission of C-Change is to eliminate cancer as a major public health problem at the earliest possible time by leveraging the expertise and resources of our members. A 501(c)(3), C-Change is comprised of approximately 150 of the Nation's cancer leaders from the private, public, and non-profit sectors. Working together, we are able to address system and societal level issues spanning the continuum of care - *that cannot be solved by one organization or even one sector alone.*

C-Change recognizes that all people with cancer want and need cures for cancer now. We are committed to accelerating research by illustrating, in particular, the man-made barriers to progress, proposing solutions, and advocating for change. Improving patient privacy protection and reducing impediments to research remains one of C-Change's strategic priorities. The 2009 Institute of Medicine (IOM) report, [Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health through Research](#), concluded that the HIPAA Privacy Rule does not adequately protect patient privacy and that it significantly impedes research. In the spirit of the IOM report, C-Change aims to change research and health data policies to strengthen patient privacy protection and accelerate cancer research.

The IOM report described the barriers imposed by HIPAA to the research process in terms meaningful to researchers such as selection bias, inefficiency, procedural burdens, and abandoned studies. The ANPRM addresses many of these concerns. Of note, these concerns are of importance to researchers and patients alike. Translating these documented barriers into a patient perspective, HIPAA-driven selection bias creates challenges to finding cures for all types of patients so that health disparities are not perpetuated. HIPAA-driven inefficiencies add challenges for finding cures rapidly that are also affordable. HIPAA-created procedural burdens make the patient experience more complex and unpredictable. HIPAA-driven closure of studies undermines the trust that patients have imparted to researchers by

participating in research and threatens access to experimental treatments. In addition, the resulting cost burden of these barriers weighs heavily on the healthcare and research system in terms of time, dollars, and the opportunity cost of now infeasible research.

C-Change truly appreciates the effort to harmonize and streamline the current research environment, to “Enhance Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators.” Below, we will describe support for many of the proposed changes as well as some specific concerns and objections. However, to fully achieve the goals embodied by the ANPRM title, HHS must address issues that are outside the scope of this ANRPM and OHRP. Harmonizing privacy and security provisions across all agencies involved in health research will best position our nation’s research enterprise to meet the needs of people at risk for and living with cancer and other disease. With recent advances made in the understanding of genetic diseases, we stand on the brink of being able to tailor medicines to the specific needs of individual patients. Information-based research is critically important to making strides in personalized medicine targeting more and more refined subpopulations. Patients and researchers need a consistent and modern regulatory framework to realize this potential.

A major hurdle identified in the IOM report that is being expanded and perpetuated in several aspects of the ANPRM is the use of the HIPAA de-identification standards. HIPAA de-identification standards remove so much information, that the data are often made useless to researchers. We strongly oppose proposals to incorporate the HIPAA de-identification standards into Common Rule practices. That said, we strongly support the use of HIPAA Security Rule standards to improve patient privacy protection. We aim to make the maximal and most responsible use of the data entrusted to us by patients.

Below you will find C-Change’s specific recommendations to the ANPRM.

1. Modifications to categories of research that do not require patient consent

ANPRM proposed change for pre-existing medical records and electronic medical records:

The ANPRM proposes to use medical information originally collected for non-research purposes, written consent would not be required if the researcher obtains data that are de-identified in accord with the HIPAA standards. This proposal does not change the current consent rules, but it introduces the HIPAA concepts of “de-identified data or a limited data set” into the Common Rule.

C-Change Comments:

We support the current rule that a researcher need not obtain written consent if the researcher does not have information that identifies the research subject. However, we strongly oppose incorporating or substituting the HIPAA Privacy Rule definitions for de-identified data or a limited data set into the Common Rule because that would dramatically reduce the types of research that could be done without any improvement in the privacy of the patients. The restrictive nature of the HIPAA data sets means that very little useful research could be done without patient consent. Further, the ANPRM proposal would mean that consent for research would be required even where data sets are anonymized. This proposal would undermine the quality of epidemiological and outcomes research, and adverse event detection analyses because an inability to find every patient for consent will mean that the data sets will be biased samples and not appropriate for some critical population-based studies. Health disparities pose an enormous challenge to our Nation for reasons that are difficult to control. Controllable, man-made regulations should not perpetuate health disparities.

In addition, this proposal ultimately could result in less privacy protection because researchers would have no incentive to request anonymous data. The same type of consent would be required for

anonymous data as for data that includes the patient's name and address so that instead of being anonymous, researchers and analysts might have names and addresses in their datasets. We believe adopting the HIPAA Security Rule standards and increasing enforcement against re-identification would better protect research subjects from harm than incorporating the HIPAA Privacy Rule definitions into the Common Rule. *Therefore, we propose that the Common Rule should be left as written without adding the HIPAA Privacy Rule concepts.*

ANPRM proposed changes for pre-existing research data:

To use data originally collected for research purposes, the proposal would require written consent for future research on the data set regardless of whether the researcher obtains identifying information. This proposal would mean that the current practice of telling research subjects during the initial research consent that the data they are providing will be used for one purpose and then using the data for another purpose after it has been stripped of identifying information would no longer be allowed.

C-Change Comments:

We oppose this change and believe it would significantly inhibit clinical research activities without improving privacy protections for the research subjects for three reasons. First, if not all participants consent to future research, researchers would be unable to rely on the randomization and other research controls that were applied in the original study, making comparisons to the earlier study less reliable and potentially invalid. Second, not all types of future research questions can be anticipated, making it possible that the scope of the future consent was ineffective under the regulations. Finally, where researchers propose to combine anonymized data from multiple research protocols, as the FDA recently did in its proposal to speed innovations, research could not proceed without first considering whether every one of the consents used with different patients permitted the particular type of research analysis for each specific study.

In effect, this proposal causes the money spent on developing innovations to be wasted because the data cannot be reused without serious degradation of the sample that the data represents. Moreover, there is no evidence that the current practice of allowing a researcher to use pre-existing anonymized data for new research purposes causes harm to research subjects. So, the primary effects of the proposal are to de-value the contribution made by the research participants, increase the cost of research, make the data useless for some types of research, and delay bringing innovations to patients. *Instead, we believe that research subjects are better protected if all researchers handling health data are subject to minimum security standards and unauthorized attempts to re-identify research subjects are criminally prosecuted.*

ANPRM proposed changes for pre-existing biospecimens: (i.e. biospecimens collected for a purpose other than the currently proposed research):

Under the ANPRM, written general consent would be required for all research use of pre-existing biospecimens, regardless of whether or not the researcher possesses information that would allow him/her to identify the subject. Researchers would no longer be allowed to conduct research using biospecimens for which the researcher does not possess identifying information without consent.

C-Change Comments:

We oppose this change. *Instead, we propose that a better way to protect research subjects from any risk of harm posed by research on de-identified biospecimens is to increase enforcement of current*

federal laws and regulations that are designed to address specific risks of harm, such as the Genetic Information Non-Discrimination Act, and to extend the data security standards to all entities handling biospecimens in order to guard against the risks of inadvertent disclosure.

II. Proposed changes regarding consent to research

The ANPRM proposes to simplify and consolidate the forms used to obtain consent to research

C-Change Comments: In principle, we support making forms simpler and taking out the legalistic warnings that seem to serve no purpose other than frightening patients and without helping them better understand the research risks. We think this is a difficult task and that patients and their families should be consulted and listened to in developing these changes. We do not want to increase the liability for researchers and research institutions but we do not think that a legal perspective should be the only view considered when designing these forms. Participation in research is a very personal decision and risks should be discussed in relation to patients' and families' expectations. At a minimum, once HHS has made the HIPAA security rule standards applicable to researchers and strengthened the penalties for unauthorized re-identification of an individual, *we think that HHS should determine that the Common Rule consent requirements supersede the separate research authorization requirements that the HIPAA privacy rule created.* Adding the HIPAA requirements to the research consent has merely complicated the informed consent process without improving the privacy protections available to the research participant.

The ANPRM proposes to permit researchers to obtain consent to future research:

The proposal would permit (but not require) researchers to simultaneously obtain general consent for future research that covers open-ended, unspecified future research and that would not need to be study-specific.

C-Change Comments:

C-Change strongly supports this proposal where it is appropriate to the research situation and the data being collected because it is consistent with research subjects' expectations and because it reduces burdens to conducting important research. Where this future research consent relates to clinical research data, the future consent should be a very simple permissible addition to the informed consent to research. However, we do not believe that this future research consent should be the only mechanism for permitting research, either with medical records or research data, as it is neither appropriate or necessary for certain types of epidemiological, outcomes, adverse event detection and other studies requiring some degree of certainty regarding sampling. *Again, we believe that most of the significant risks posed by future research use of data will be best addressed by requiring all research entities to meet minimum data security standards and by increasing enforcement against unauthorized attempts to re-identify research subjects.*

The ANPRM asks about the retroactive applicability of consent (Question 52):

HHS seeks response to the following question: "Should the new consent rules be applied only prospectively, that is, should previously existing biospecimens and data sets be "grandfathered" under the prior regulatory requirements? If so, what are the operational issues with doing so?"

C-Change Comments:

Regardless of what changes HHS ultimately makes to the consent requirements, we strongly support applying those changes prospectively only. Applying changes to the consent requirements for pre-existing data and biospecimens retroactively would destroy researchers' ability to use most existing tissue banks and data repositories that have been lawfully established. Moreover, such changes might fundamentally alter the research norms and ethics that have already been explained to research participants, so researchers would be required to obtain new consent from current research subjects. Most importantly, making any such change retroactive would adversely impact research without any increase in the privacy protections offered to the patients.

III. Proposed changes for establishing mandatory data security and information protection standards

HHS is considering adopting data security standards modeled on the HIPAA Security Rule. The proposal would also strengthen the enforcement mechanisms to protect against the inappropriate re-identification of information that is collected or generated as part of a research study in order to minimize informational risks and eliminate the need for IRBs to review the informational risks in proposed research.

C-Change Comments:

C-Change supports establishing mandatory data security and information protection standards because we agree that doing so will minimize the risk of inadvertent disclosure of data or harm to individual research subjects. We think applying the HIPAA security standards would be appropriate. We would further support extending those standards to all entities as a prerequisite to conducting health research. Further, we agree that it is ethically inappropriate for researchers to attempt to re-identify research subjects except when necessary under certain limited circumstances. We believe that the unauthorized attempt to re-identify a research subject should be a criminal offense.

However, we disagree with the ANPRM proposal to add in the HIPAA privacy rule standards for de-identifying information into this security proposal. We strongly oppose using the HIPAA Privacy Rule to define what constitutes "individually identifiable information", a "limited data set", and "de-identified information." It has already proved difficult to define or enforce these concepts, and instead the terms have created great uncertainty for researchers without adequately protecting privacy (because even the most rigorously de-identified data may be re-identified with sufficient time and effort). Moreover, applying the HIPAA privacy standards for purposes of the Common Rule would impede needed research because information that has been de-identified to the HIPAA standard is generally useless for research.

Therefore, we propose that HHS retain the Common Rule concepts of "anonymized" and "coded data" and combine them with regulations prohibiting any attempt to re-identify research subjects in an unauthorized manner and providing that any such unauthorized attempt shall be treated as a prosecutable criminal offense.

IV. Other proposed changes regarding event reporting, multi-site studies, continuing review requirements, and exempt study requirements.

ANPRM proposed change to simplify and consolidate event reporting

C-Change Comment: We support creating a single website to report adverse events into a single database with common reporting requirements across agencies to promote patient safety and efficiency.

ANPRM proposed change to mandate that multi-site studies seek approval from central IRBs.

C-Change Comment: We support this change in general. While a mandate to use central IRBs seems like a rigid approach, we suggest that HHS highly encourage their use and provided additional assurance to reduce the liability concerns of individual institutions. Specifically, we believe additional clarification is needed on selection of the lead IRB, the division of responsibility between central and institutional IRBs, and a mechanism to recognize local issues to ensure the participation of diverse populations and to deal with concerns about local IRBs and research institutions' liability.

ANPRM proposed change to eliminate continuing review requirements for certain studies.

C-Change Comment: We support eliminating continuing review requirements for 1) research approved as "minimal risk" studies that qualify for expedited review, 2) research for which the only remaining tasks are data analysis, and 3) research for which the only remaining aspects are standard clinical care.

ANPRM proposed change to revise and expand standards for categories of research that are exempt from prior review by an IRB.

C-Change Comment: We support expanding the categories of "excused" studies to include research using pre-existing data and biospecimens, educational tests/surveys, and some social/behavioral research on competent adults. However, we believe that the use of existing data and anonymized data should adhere to Common Rule standards, rather than HIPAA Privacy Rule standards.

Thank you for considering this input. C-Change remains committed to accelerating research so that patients receive timely, affordable, and effective treatments. By streamlining and strengthening privacy and security regulations in health research as discussed, we can minimize the man-made barriers to progress.

If we can be of further assistance, please contact Alison Smith, Vice President, Strategic Initiatives asmith@c-changetogether.org or (708) 267-5166.

Sincerely,



Tom Kean, MPH
Executive Director