January 4, 2016

Jerry Menikoff, M.D., J.D.
Office of Human Research Protections (OHRP)
Department of Health and Human Services
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

**Re: Docket No. HHS-OHPS-2015-0008: Federal Policy for the Protection of Human Subjects; Notice of Proposed Rulemaking**

Dear Dr. Menikoff,

On behalf of the American Association for Cancer Research (AACR), Association of American Cancer Institutes (AACI), American Society of Clinical Oncology (ASCO), and American Society of Radiation Oncology (ASTRO), we thank you for the opportunity to comment on the Notice of Proposed Rulemaking (NPRM) put forward by the Department of Health and Human Services (HHS) and eighteen other agencies (collectively, the Common Rule Agencies). AACR, AACI, ASCO, and ASTRO are the nation's leading professional and scientific organizations representing cancer researchers, cancer centers, and oncology care professionals. Information about each organization appears at the end of this letter.

Our members value the safety and privacy of individuals who choose to participate in cancer research, and we are pleased to comment on the important changes under consideration to better protect these individuals. We believe that many of the proposed reforms to the Common Rule set forth in the NPRM will more effectively safeguard human subjects and reduce excessive regulatory burden on researchers. For instance, we support the proposals to streamline and simplify informed consent, create an "excluded" category with ten types of research that would not be subject to the Common Rule, specify "exempt" research eligible for limited review based on the risk involved, institute mandatory data security and information protection standards, apply the Common Rule to all clinical studies conducted by institutions receiving funding from the Common Rule Agencies, require use of a single IRB for most multi-site research studies, and harmonize guidance among the Common Rule Agencies. We encourage the Common Rule Agencies to proceed with finalizing these changes.

We support the efforts to modernize the Common Rule to keep pace with the substantial changes in ways that human research is conducted; however, we have significant concerns with some areas of the proposed rule. Specifically, we urge the Common Rule Agencies to refrain from finalizing the proposals under the following three areas of the NPRM that do not further

the primary goal of the rulemaking process "to better protect human subjects involved in research, while facilitating valuable research and reducing burden:"

1. The proposed classification of all biospecimens as "human subjects," regardless of whether the biospecimens contain identifiable information.
2. The lack of clear and consistent privacy standards across all research, including possible confusion between the HIPAA Privacy Rule and the Common Rule.
3. The absence of harmonized guidelines for reporting unanticipated problems and adverse events and the decision to abandon a harmonized electronic database for reporting.

These issues are discussed in greater detail below.

**1. The proposed classification of all biospecimens as "human subjects," regardless of whether the biospecimens contain identifiable information.**

As organizations representing professionals engaged in cutting edge cancer research, we have serious concerns with the proposed modification of the definition of human subjects to include all biospecimens. The proposed approach to the regulation of secondary research uses of non-identified biospecimens is not appropriate for the very low level of risk inherent in this type of research. Because of the lack of publically available genomic data, the risk of re-identification of de-identified biospecimens is very low now and during the foreseeable future. There is insufficient benefit to implement this change at this time, especially given that this change would significantly increase the administrative burden and undermine the viability of research involving de-identified or non-identified biospecimens.

Research involving biospecimens is essential to cancer research. Investigators are able to use biospecimens to link genetic aberrations to specific cancers and bring molecularly-targeted therapies to patients, and to identify novel drug targets and prognostic markers. The NPRM would require that secondary research on non-identified biospecimens be subject to broad consent, documentation, and IRB review requirements. These proposed changes would significantly impede the ability of researchers to use non-identified tissue samples, specifically archival tissues collected prior to implementation of the Common Rule and samples collected during routine clinical care.

We are concerned that these proposals would inadvertently undermine our ability to conduct research to answer important clinical questions, resulting in significant, adverse effects on individuals with cancer. In general, future research use of biospecimens is not always anticipated before surgery, and requiring broad consent from every surgical patient would add significant burden, time, and resources toward compliance, to the point of having detrimental effects on research programs. Moreover, administrative costs to implement such procedures for storage and future research use could impact early career investigators and have the

greatest impact on institutions that have fewer resources to support their research programs. Institutions with fewer resources may disproportionately serve low-income, minority, inner-city, and rural populations. If these institutions choose to abandon use of non-identified biospecimens for research, it would have a negative impact on the representativeness of data on under-represented populations and hinder our ability to understand health disparities. Our continued success in developing molecularly-targeted treatments relies heavily on research use of these non-identified biospecimen samples.

Although we understand and support the goal of the Common Rule to balance respect for autonomy with respect for beneficence, requiring patient consent where the opportunities to develop innovative and life-saving therapies and to bring these treatments to thousands of cancer patients outweighs an individual's desire to control all possible future uses of their biospecimens.

We strongly oppose the proposal to modify the definition of human subjects to include non-identified biospecimens under any of the alternative proposals put forward in the NPRM. Rather than proceed with the proposal to classify non-identified biospecimens as human subjects at this time, we recommend closely monitoring the issue with reconsideration in future years of a stepwise strategy to update the Common Rule, if necessary, to address any future changes in technology or other methods that somehow increase the risk of re-identification of biospecimens.

We support protecting the privacy of individuals and ensuring compliance through documentation and limited IRB review. In addition, we would strongly support efforts to ensure that an individual's data are protected through appropriate data security measures. However, placing broad consent requirements on this type of the research would result in significant and unreasonable administrative burdens for researchers as described above. If biospecimens are deemed to be human subjects, then we strongly urge the Common Rule Agencies to remove the consent requirement for biospecimens through the exemption mechanism for the foreseeable future.

Although our priority is the removal of broad consent requirements for secondary research use of biospecimens, we are also concerned about the 10-year limit on collection under broad consent. There is a common misconception that the 10-year time limit applies to research use of biospecimens and that research would be prohibited on biospecimens collected more than 10 years ago. However, we understand that this proposal would require a new broad consent form to be signed by patients every 10 years if additional biospecimens are to be collected. We understand and oppose this requirement because it would create unnecessary administrative burdens for providers without providing enhanced protection to patients.

Some research institutions are developing approaches to obtain consent for subsets of biospecimens. As best practices begin to emerge in the area, this may inform future

rulemaking in the event that federal mandates seem warranted when policymakers revisit this issue in future years.

**2. The lack of clear and consistent privacy standards across all research, including possible confusion between the HIPAA Privacy Rule and the Common Rule.**

The NPRM does not fully address our significant concerns regarding the current fragmented approach to the regulation of research. We value the privacy of health information and the importance of health research, and we believe that privacy considerations warrant a single, uniform set of criteria. As recommended by the 2009 Institute of Medicine (IOM) report examining privacy safeguards, the Secretary of HHS should take a leadership role in designing uniform standards that specifically address the secure use of information in research.

Nonetheless, if the fragmented privacy provisions proposed in the NPRM are finalized, it is important that the Common Rule Agencies promulgate additional guidance with specific examples that delineate what types of research are subject to Common Rule regulations and what types of research are subject to the HIPAA regulations. This clarification could be implemented through regulations or subregulatory guidance, or both. Additional clarity is needed to eliminate confusion and promote the efficient use of the limited resources available for research, and we urge the Common Rule Agencies to work closely with our organizations to develop such clarifications and examples.

**3. The absence of harmonized guidelines for reporting unanticipated problems and adverse events and the decision to abandon a harmonized electronic database for reporting.**

Despite the urgency to harmonize the existing system to enhance human subject protections, the NPRM failed to include plans for a harmonized electronic database to report unanticipated problems and adverse events. A carefully planned system that uses standardized data elements to simplify and consolidate the reporting of information that is already required, as suggested in the 2011 Advanced Notice of Proposed Rulemaking (ANPRM), has the potential to improve safety among research participants, decrease confusion surrounding reporting requirements, and promote the efficient use of the limited resources available for research. A database of this nature would eliminate the multiplicity of reporting portals, increasing efficiency in research. The development and implementation of such a system aligns with the overarching goal of this rulemaking process to increase human subject protections while facilitating valuable research.

We urge the Common Rule Agencies to reassess stakeholder comments to the ANPRM on implementation of a harmonized electronic database to report unanticipated problems and adverse events. Many concerns brought up about this proposal, such as the lack of a uniform definition of “unanticipated problem” or “adverse event” and confusion about oversight responsibility, could be addressed and resolved through further guidance and examination.

The complexity and difficulty of developing harmonized reporting is not a sufficient rationale to drop the 2011 proposal – in fact, the complexity of this issue highlights the need for the Common Rule Agencies to resolve the inefficiencies, inconsistencies, and counterproductive differences in reporting requirements.

Developing standardized terminology and reporting requirements across the Common Rule Agencies and creating a uniform database for reporting would enable regulators and manufacturers to compare safety data across research studies and across diverse populations of research participants. With the current system of disconnected databases, it is difficult to identify concerns by comparing across patient experiences. We strongly urge the Common Rule Agencies to ensure that regulations outlining plans for a harmonized database are promulgated in an expedited manner.

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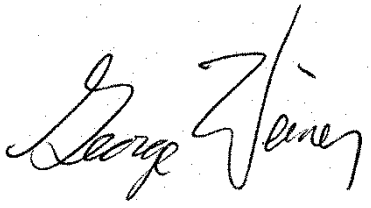
We offer our sincere thanks for your consideration of our comments as you deliberate on these important issues. In many areas, we support the NPRM, and we are eager for the federal government to move forward with these changes. Nonetheless, as summarized above, we have significant concerns with a few key aspects of the NPRM, and we urge the Common Rule Agencies to refrain from finalizing these proposals without addressing the concerns of the cancer research community.

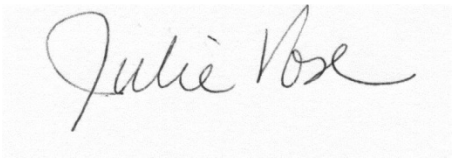
If we can provide any additional information or assistance at this time, please contact Michael Francisco at ASCO at michael.francisco@asco.org.

Sincerely,

José Baselga, MD, PhD
AACR President



George Weiner, MD
AACI President



Julie M. Vose, MD, MBA, FASCO
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Founded in 1907, the American Association for Cancer Research (AACR) is the world's oldest and largest professional organization dedicated to advancing cancer research and its mission to prevent and cure cancer. AACR membership includes more than 39,000 laboratory, translational, and clinical researchers; population scientists; other health care professionals; and patient advocates residing in 101 countries.

The Association of American Cancer Institutes comprises 95 leading cancer research centers in the United States, including National Cancer Institute-designated centers and academic-based cancer research programs that receive NCI support.

ASCO represents more than 39,000 physicians and health care professionals involved in cancer clinical care and research from all oncology disciplines and subspecialties.

Radiation oncologists, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants and practice administrators comprise ASTRO's more than 10,500 members, making it the largest radiation oncology organization of its kind. ASTRO provides members with the continuing medical education, health policy analysis, patient information resources and advocacy that they need to succeed in today's ever-changing health care delivery system.