January 5, 2016

Jerry Menikoff, MD, JD
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Docket #: HHS-OPHS-2015-0008

Dear Dr. Menikoff:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the Department of Health and Human Services' (HHS') Office of Human Research Protections (OHRP) September 8, 2015 proposed rule, which suggests changes to the current Common Rule governing federally funded human subject research. Although we support the Department's efforts to ensure that consumers are appropriately informed of their rights, and the privacy of their personal health information maintained, we recommend that HHS policy permit the continued use of residual, de-identified specimens without patient consent.

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. AACC brings together more than 50,000 clinical laboratory professionals, physicians, research scientists, and business leaders from around the world focused on clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management, and other areas of progressing laboratory science. Since 1948, AACC has worked to advance the common interests of the field, providing programs that advance scientific collaboration, knowledge, expertise, and innovation.

AACC's primary concern centers around the requirement of obtaining informed consent for the research use of any biospecimen collected for clinical purposes, including de-identified residual specimens. This proposal would alter the longstanding Department policy that permits Institutional Review Boards (IRBs) to grant permission to clinical laboratories, researchers and other providers to utilize these leftover samples for improving patient care as long as the patient identifiers have been removed. Furthermore, AACC is worried that this proposed change, if implemented, could hinder quality improvement (QI) efforts and the refinement and development of new laboratory tests.

Quality Improvement
Currently, clinical laboratories rely upon the use of residual de-identified samples in the protocols used to validate or verify the analytic and clinical performance of a broad variety of assays. Residual specimens are needed for these protocols as synthetic materials do not perform as well as real samples and, in many instances, are not commercially available. The clinical laboratory uses only patient samples that would normally be discarded—maintaining only minimal clinical information (e.g., age, gender, and diagnosis) associated with the specimen. Direct patient identifiers are removed from the specimen. The purposes of these studies are to establish or verify the performance of testing and are not related to the well-being of a particular patient.

Many QI activities performed by clinical laboratories are required under the federally mandated Clinical Laboratory Improvement Amendments (CLIA) regulations. For example, laboratories use de-identified specimens to validate the test methodologies they employ, refine the normal range for patient results and compare instruments performing the same tests—all functions required under CLIA. For rare disorders, clinical laboratories also use de-identified samples as an additional quality control measure when commercial products are not available. While the proposed rule would permit clinical laboratories to utilize leftover specimens for QI under certain circumstances it does not fully define those areas. AACC suggests that permitted QI activities be further defined and those required by CLIA, other government agencies or private accrediting organizations be excluded from the informed consent requirements.

New Test Development and Validation
Clinical laboratories also use residual specimens to develop and validate new laboratory tests. We are concerned the narrowness of the proposed exemption will significantly impede these activities. OHRP states that healthcare facilities can use existing specimens without informed consent "if the research is designed not to generate any new information about the person, but only confirm what is already known." The agency further adds that any IRB waivers from this requirement would be "very strict" and in "rare circumstances." Without modification, these limitations may impede the efforts of manufacturers and clinical laboratories to develop new tests and validate their performance.

One area where this policy change may hinder advancements in patient care is newborn screening. A newborn bloodspot that tested normal for sickle cell disease could not be used to validate a new marker for the same condition if it presented different risks or prognosis for the 'known' condition. In addition, a clinical laboratory could not use the same bloodspot to test for a different inborn error or marker for another condition. We strongly oppose these limitations. In this instance, OHRP's efforts to increase patient protection may unintentionally diminish patient care.

Obtaining Informed Consent
The proposed rule states that providers could use "a broad consent template" developed by HHS to obtain patient permission to use residual specimens. Although the objective is laudable, it does not address many of the administrative hurdles that healthcare providers may encounter, such as:

- tracking and keeping separate specimens with and without informed consent;
- the lack of staff to explain and answer questions about the consent forms; and
- the inability to provide information on samples that will be stored in repositories for future research.

AACC is concerned that the introduction of these new, burdensome, costly requirements may discourage institutions from retaining these specimens—which would be a tremendous setback for ongoing efforts to advance laboratory medicine and improve the quality of healthcare.

Clinical Studies
Laboratory scientists seek a representative patient population when performing clinical studies to ensure the test can be effectively utilized among diverse patient groups. Unfortunately, one of the unintended consequences of the proposal is that it significantly narrows the types of groups included in clinical studies thus diminishing the value and usefulness of any findings.

For example,

- it is well established that certain patient populations, such as the poor and minority populations, refrain from providing consent;
- individuals in emergency room and critical care settings are unlikely to participate in clinical studies because of the need for immediate patient care; and
- few healthcare providers would have personnel available 24 hours a day to obtain patient consent, thereby resulting in many institutions only using specimens obtained during normal 9-5 working hours.

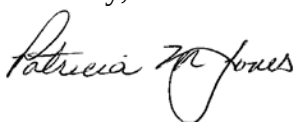
All of these scenarios may result in certain patient populations being systematically excluded from important life-saving research. Similarly, the informed consent requirements would undermine the usefulness of newborn screening samples, which have been an invaluable source of specimens for many fields since they provide a large representative sample of a state's entire population. Unfortunately, with the adoption of the informed consent requirements, the value of many studies utilizing these specimens could decline precipitously.

Penalties for Re-identification of De-identified Specimens
OHRP states that one of the reasons for introducing the new informed consent requirements is that with newer technologies it will be increasingly difficult to prevent the re-identification of an individual "from the use of a biospecimen or a combination of data sources." If this is the primary

concern of OHRP, AACC suggests that stiffer penalties be adopted and enforced to prevent such practices rather than developing and implementing new, costly regulations that may hinder the development of newer technologies and better quality assurance and quality improvement activities.

We look forward to working with you on this most important issue. If you have any questions, please email Vince Stine, PhD, AACC Director of Government Affairs, at vstine@aacc.org.

Sincerely,



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