October 26, 2011

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

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

Dear Dr. Menikoff:

This letter is a comment in response to the Advanced Notice of Proposed Rulemaking (ANPRM) referenced above, as published in the Federal Register, Vol. 76, No. 143 (Tuesday, July 26, 2011), from and on behalf of the International Society for Biological & Environmental Repositories (ISBER), a division of the American Society for Investigative Pathology (ASIP), which is submitting a comment in response to the ANPRM separately. This submission is in addition to, and in supplement of any other response submitted by ISBER, endorsing in full the views and comments of the ASIP response.

In short, ISBER is an international organization addressing the technical, legal, ethical, and managerial issues relevant to repositories of biological and environmental specimens (see www.isber.org for additional information). Although not restricted to human specimens intended for research, the great majority of ISBER members focus on human tissues procured for research purposes, either directly or indirectly (e.g. from clinical specimens procured for non-research purposes). ISBER membership and expertise in the area of human tissues used for research is extensive, longstanding, ongoing, and representative of the best practices. ISBER's thought leaders in this area are worldwide, including many in the United States. As such, we have a keen interest in the ANPRM and are pleased to submit for your consideration our comments and views as follows:

• **We fully endorse the ASIP comments in response to the ANPRM (which you will have received separately from ASIP), with only the following clarifications:**

Regarding the Use of "Left-Over" Tissue Without Consent (ANPRM Question 47)

In general, we believe the use of "left-over" clinical biospecimens for research purposes should be permitted, provided that there is continued oversight by Institutional Review Boards (IRBs) of research protocols intending to access clinical biospecimens for research purposes. It is our view however, that while a waiver of informed consent or other form of permission may be granted in most cases, every protocol intending to access these biospecimens should be reviewed and approved. Absence of informed consent should not equate to a lack of research oversight. A continued oversight mechanism engenders public trust and confidence in the research enterprise.

Where procured biospecimens might fall outside the boundaries of "human subjects research" under current or future definitions, IRB determination of that exclusion remains appropriate, and could engender trust among populations of participants that view biospecimens as collective property, common ancestry, or parts of their soul, whether or not such biospecimens are identifiable at the individual participant level. Other countries' views on this subject are informative. In New Zealand for example, consent is always required unless waived by ethical review committees, a system that has reportedly functioned well since 2004.

Were consent to be mandated in all instances in order to access clinical "left-over" biospecimens for research purposes, it has been estimated by ISBER members that the additional cost of utilizing archival paraffin embedded tissue that was collected for clinical purposes, even to large academic medical centers in the U.S., could amount to over $200,000 per year. .

We would also like to clarify that our position regarding consenting patients "at the door" differs slightly from that of ASIP. While we fully endorse the concept that the informed consent process should ideally take place as remote in space and time from the clinical tissue removal event as is necessary to avoid undue influence, duress, or coercion, we do not believe that consenting prior to a procedure scheduled to occur in the near future, even the same day, is always unwarranted. Other facts must be considered such as the type of procedure, the condition of the patient, the location within the institution where consent occurs, etc.--all factors that should be weighed and evaluated by IRBs when reviewing protocols and research plans involving access to biospecimens obtained from patients.

Regarding Considering Human Biospecimens in and of Themselves Identifiable (ANPRM Question 56):

We agree with the ASIP's position that biospecimens should not be considered in and of themselves identifiable. We agree that in order to link a biospecimen to a participant's identity, the biospecimen alone is insufficient. In order to link even a fully genetically characterized sample to participant identity, there must be a reference sample that positively links to participant identity for comparison.

Further, we would like to add that biospecimens lacking nucleic acids (such as red blood cells, expiratory gases, etc.) should be excluded from any rule that were to determine that other types of biospecimens (containing DNA) were in and of themselves identifiable. In other words, if biospecimens are to be considered in and of themselves identifiable, the definition of biospecimen should be carefully crafted to exclude sample types lacking DNA.

As mentioned, other than the above, ISBER views are those stated in the ASIP response to the ANPRM.

Respectfully submitted,