



July 8, 2013

Public Commentary, Presidential Commission
for the Study of Bioethical Issues, 1425
New York Ave. NW., Suite C-100,
Washington, DC 20005

Delivered via email to info@bioethics.gov

Dear Sir:

This letter is a comment in response to the Request for Comments on Issues Related to Incidental Findings That Arise in the Clinical, Research, and Direct-To-Consumer Contexts, from and on behalf of the International Society for Biological and Environmental Repositories (ISBER).

Introduction and Focus

The International Society for Biological and Environmental Repositories (ISBER) is an organization that addresses 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 providing human tissues for research, either procured for research purposes, or from residual clinical specimens obtained during the course of routine medical care. 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. As such, we have a keen interest in the matter of incidental findings and their implications for research.

ISBER welcomes the opportunity to respond to the Presidential Commission for the Study of Bioethical Issues request for comments on the return of incidental findings. Although the Commission requested comments on the return of incidental findings in the clinical research settings, our comments are focused upon the return of incidental findings from biorepositories, defined for the purpose of this response as a repository of biological specimens and associated information for future use in research, in the conduct and support of research.

Objection to Potential Mandate

ISBER is committed to the ethical conduct of research. However, the society objects to any general mandate to return incidental findings from research to research participants.

The return of incidental findings from research to participants by biorepositories represents a fundamental change in the underlying principles of biomedical research which could potentially inhibit the primary goals of discovering new knowledge and finding ways to implement this. That is, the obligation to accomplish a therapeutic responsibility by those neither qualified to do

so, nor properly resourced, could actually produce unintended and undesired outcomes, causing immediate harm to patients, and long term harm to society through a very likely reduction in research productivity.

Notwithstanding that the return of incidental research findings to participants would be a large and costly undertaking by biorepositories that would detrimentally affect their support of research on human diseases, there are other important considerations that are the basis of our objection to the return of incidental research findings to participants, specifically:

- 1) Research findings like all good science require validation, and until adequately reproduced, should not be the basis of therapeutic decision making. Providing unvalidated incidental findings to participants may cause harm if poorly supported and/or wrong medical decisions are made based upon incorrect results. For example, wrong results from forensic laboratories have proven to be problematic in the criminal justice system (Innocence Project, <http://www.innocenceproject.org/>). Because research findings are sometimes wrong or can be misinterpreted, there is also potential liability with returning such results to participants.
- 2) ISBER supports the requirement for information potentially used in patient care to be provided only by Clinical Laboratory Improvement Amendments (CLIA) certified laboratories.

Existing concerns regarding this requirement however, include (1) most research laboratories are not CLIA certified and do not have the infrastructure required for a CLIA laboratory; (2) an equivalent approved diagnostic test must be available and this is not the case for many research assays; (3) additional tissue is required to perform the diagnostic test, which could be problematic in cases where the original tissue sample was depleted in the research process.

- 3) Because one biorepository may supply tissue specimens to hundreds of investigators, the return of incidental findings to participants from the secondary research that follows is impracticable. Hence, the biorepository community views any such requirement with great concern. Biorepositories serve as an intermediary between patients from whom specimens are collected and processed, and investigators to whom specimens are provided and who generate research results. Most biorepositories do not have access to secondary research results, and have no infrastructure for the return of incidental findings to participants. Developing such an infrastructure, including informatics necessary to support the return of incidental findings would be extremely costly for biorepositories, most of which have marginal funding. Requiring the return of incidental findings would change the primary focus of biorepositories from supporting research to providing medical information to participants. Such a requirement would extensively disrupt biorepository operations and additionally subject the biorepositories to liability secondary to any harm caused by provision of inaccurate incidental findings.

- 4) The primary goal of medical research should be to understand and optimize the treatment of human diseases. Creating administrative and cost burden associated with the return of incidental findings from medical research would not result in improved patient outcomes for the reasons stated above.

Context and Consequences

The impracticality of a requirement for biorepositories to return incidental findings from research should be viewed in the context that most investigators receiving human tissue specimens from biorepositories receive a coded specimen, typically with only the age, race and sex of the patient who is the tissue source, and with whom they have no direct relationship. In many cases, investigators who receive specimens cannot know the identity of the source of the specimens because of privacy limitations. Thus, even for medically trained investigators, the identification and interpretation of medically important incidental findings would be held in a vacuum; investigators who have no medical background would be unable to identify medically important incidental findings, and biorepository personnel would be unaware of potentially medically important incidental findings from the hundreds of research projects to which specimens are provided.

These issues are of special concern as the discussion shifts to requirements for seeking incidental research findings, and whether or not research data beside genome wide sequencing (GWS) results also are considered as a source of incidental research findings that are expected to be returned to participants.

In most cases, investigators do not know the identities and/or contact information of the participants who are the sources of the tissue they study. Therefore, the biorepository would be central in the return of incidental research findings. The concern of ISBER is that in a worst case scenario, the biorepository would have to (1) query investigators periodically and collect incidental research results; (2) consent participants for repeating incidental research results in a CLIA approved laboratory; (3) pay for CLIA testing; (4) return CLIA results to participants; (5) arrange and pay for genetic or clinical counseling of the participant; (6) follow the consequences of the return of research results and (7) assume liability for the entire process.

This may have the unintended consequence of leading biorepositories to anonymize all tissue samples provided to investigators since research results would not be able to be linked back to the original specimens and the research results from multiple investigations could not be combined to further knowledge of the disease being studied. Such anonymization would greatly reduce the usefulness of tissues provided by biorepositories. Of note is the fact that biorepositories could not operate *without* anonymization if the return of incidental findings from research were to be required.



Summary

In summary, ISBER is concerned that a decision to require the return of incidental research findings to participants will be made without an adequate understanding of how such a mandate will negatively affect biorepositories and in turn, greatly reduce the amount and quality of research they support. Unanticipated consequences will result that are sure to be detrimental to research. ISBER strongly encourages the development of a very careful and informed cost benefit analysis before a general recommendation is made as to whether incidental findings generated from research should be returned to research participants.

In addition, rather than mandating the return of incidental findings in the conduct of research, ISBER suggests that biorepositories be encouraged to develop and document individual related policies, and that these policies be reflected in the informed consent document signed by biorepository participants.

Respectfully submitted,

Andy Zaayenga, ISBER President Elect (2013 – 2014)
for Fay Betsou, ISBER President (2013 – 2014)