

## Advisory Panel Meeting Attendance and Discussion Content

### Advisory Meeting I

#### Attendees

**Pathology:** Michael Blechner MD, Bioinformatics/EMR Director, Blood Bank; George H. Barrows, MD, Department of Pathology, Saint Francis; Melinda Sanders MD, Chair, Pathology, UCHC

**IRB:** Sandra Alfano PhD Chair, Yale IRB; Mary R. Raum, CIP, CCRP Human Protections Administrator/IRB Middlesex Hospital

**ELSI:** Audrey Chapman PhD, Chair, Medical Humanities and Bioethics, Dept of Community Medicine, UCHC; Stephen Latham JD, PhD, Director, Interdisciplinary Center for Bioethics, Yale

**CT Cancer Partnership:** Linda Mowad, Former Director, CIS at Yale, CT Cancer Partnership Chair of Board

**Cancer Centers:** Andrew Salner, MD, Director, Cancer Center, Hartford Hospital, CT Cancer Partnership

**DPH:** Joan Foland, Planner, Office of Genomics; Lloyd Mueller, Principal Investigator, CT Tumor Registry; Lou Gonsalves, Epidemiologist, CT Tumor Registry, DPH

**Research/Biobank:** Sean Altekkruse, Residual Tumor Repositories, NCI; Bruce Mayer PhD, UCHC; Paul Pescatello, CEO, Connecticut United for Research Excellence (CURE); Bonnie Gould Rothberg, MD, Lung Cancer Repository, Yale; Kathy Wiggins, Histology Supervisor, UCHC; Herbert Yu MD PhD, Cancer Epidemiologist, Yale School of Public Health

**Consultant:** Lisa Miranda, President and CEP, Biobusiness Consulting Inc.

**Project Team:** Richard Everson, MD, MPH, Deputy Director for Cancer Prevention and Control, UCHC; Helen Swede, PhD, Cancer Epidemiologist, UCHC; Rajni Mehta, RCA

**Evaluators listening via telephone:** Anne Betzner, PDA; Ann Wendling, PDA

#### Overview of discussion

**Tissue availability and quality:** Small tumors may be confined to a single block and may not be available for release until ten years. Since tissues are often discarded after the required holding time of 10 years or shortly thereafter, they would no longer be available through ATA and would need to be moved to a physical repository. Tissues are often stored offsite after a couple years and are labor intensive to retrieve. It was noted that there may be a wide variation in tissue quality and accuracy of sub-typing at hospitals. It was suggested that hospitals perhaps could store and protect extra uncut tumor blocks for future research. Perhaps, the biorepository should focus on selecting tissues based on tissue characteristics that would be most useful to researchers. Maximal access would require a hybrid model: ATA for the first ten years and a physical repository (RTR) for tissues over 10 years old. It was noted that there may be wide variation in tissue quality at hospitals and a pilot study was suggested to test quality of RNA and DNA in tissues across various hospitals.

**Consent:** Current surgical consents may not be compliant with informed consent principles for future research. They might not have meaningful consents or opt-out clauses for research. For the ATA, it is important to assess the willingness of hospital IRBs to provide waivers of consent. It was suggested that it might be helpful to review forms from other states also, such as New

Jersey, where the language in the consent form is adequate for pathology departments to release tissue for IRB approved studies.

*IRB issues:* IRB issues should be linked with ELSI and public education

*Funding for infrastructure and maintenance:* The costs and other resources are significant. Could fees from investigators offset costs, or could funding and infrastructure be part of BioScience Connecticut?

*Assessment:* It is important to try to determine demand for access with data from researchers, other biorepositories, and organizations. Support was expressed for asking a few key questions of Pathology Departments and IRBs that did not respond to the surveys.

*Public Education:* Public support and understanding might count more than the legal status of who owns tissue. In states with legal suits, parents were unaware that blood spots were taken in the first place. Cancer survivor support groups may be helpful in obtaining feedback on models.

## **Advisory Meeting II**

### **Attendees**

*Italicized attendees did not attend Advisory Meeting I.*

**Pathology:** Michael Blechner MD, Bioinformatics/EMR Director, Blood Bank; Melinda Sanders MD, Chair, Pathology, UCHC; Daniza Mandich, Dept. of Pathology and Laboratory Medicine, Hartford Hospital; George Barrows, Dept. of Pathology, St. Francis Care Medical Group

**IRB:** Sandra Alfano PhD Chair, Yale IRB; Olinda Morales, JD, Human Investigations Committee

**ELSI:** Audrey Chapman PhD, Chair, Medical Humanities and Bioethics, Dept. of Community Medicine, UCHC; Stephen Latham JD, PhD, Director, Interdisciplinary Center for Bioethics, Yale

**CT Cancer Partnership:** Lucinda Hogarty, Director of CT Cancer Partnership

**Cancer Centers:** Patricia Checko, Dr. P.H, Board of Directors, Tobacco & Health Trust Fund

**DPH:** Joan Foland; Lou Gonsalves; Catherine Phillips, Manager CT Tumor Registry

**Research/Biobank:** Paul Pescatello, CEO, Connecticut United for Research Excellence (CURE); Bonnie Gould Rothberg, MD, Lung Cancer Repository, Yale; Kathy Wiggins, Histology Supervisor, UCHC

**Consultant:** did not attend

**Project Team:** Richard Everson, MD, MPH, Deputy Director for Cancer Prevention and Control, UCHC; Helen Swede, PhD, Cancer Epidemiologist, UCHC; Rajni Mehta, RCA

**Evaluators:** Anne Betzner, PDA; Ann Wendling, PDA

**Others:** Susanne Morrill, Hartford Hospital (not listed in Advisory Group Membership)

Individuals that did not attend either meeting are:

Marianne Horn, JD, RN Chair, Human Investigations Committee DPH; John Fontana, PhD, Laboratory Director, DPH; Lorrie Perpetua, Coordinator, Research Tissue Repository Core

Facility, UCHC; Pramod Shrivastava, MD, PhD, Professor of Immunology; James Thibeault, MS, Director, Signature Programs at UCHC

### **Overview of discussion**

The meeting started with a follow-up discussion on some key issues raised at Meeting I. Highlights of this discussion included follow-up on consent issues. Dr. Everson noted that there were many different consent forms used across all hospitals. He reported that it took many versions for UCHC Biorepository informed consent form to be approved by IRB for non-specific future research purposes of cryopreserved tissues. Dr. Everson noted that, currently, research using existing specimens is permitted without consent (via waivers) if all identifiers are stripped. A proposed US Department of Health and Human Services (USDHHS) reform is to re-consent for use of existing tissues even if identifiers are stripped by use of a small form. If enacted, the change would apply only to specimens collected at the start of the new regulation. This means that we might need to develop a system to track the consents, which can be a very difficult. The other proposed regulation is that for multi-site studies that all IRBs would accept the mandated IRB of record. In response to questions about tissue quality and annotation, Dr. Everson noted that it was probably not feasible to analyze tissue for quality and biomarker status in the statewide repository, but suggested developing a tracking system by researchers who use tissues. He also emphasized that funding for the establishment of RTRs at SEER sites is no longer available through NCI. Dr. Everson noted that Pharma representatives had been invited to the meeting to provide input on their possible use of the repositories as well as funding, but were unable to attend.

The remainder of the meeting centered on discussions of the RTR and ATA options, protocols and projected costs. Two tables cataloging a range of options related to operation of an ATA and RTR were used to structure the discussion. The draft procedures and protocols were informed by the two surveys conducted for this project, general literature on biobanking, consultations with experts at University of Southern California and Cancer Institute of New Jersey, and NCI, and comments from Advisors. Topics included operational considerations (e.g., hospital participation, clinical data associated with specimens, governance) and issues related to Ethical, Legal and Social Implications (ELSI) of research conducted using the ATA and RTR approach (e.g., Informed Consent, IRB). The preferred option was highlighted with rationale provided where possible (e.g., Advisory Panel discussion, survey, standard procedures.) A number of the considerations were applicable to either an ATA or RTR. The ATA repository was the focus of the discussion with the significant and uncertain funding for the RTR.

Some highlights of the RTR discussion included housing the facility at a physical site to be determined, possibly under contract with DPH. Before tissues would be released to researchers, the RTR would require IRB approval of the research protocol. Adherence to strict standard procedures for storing human tissue for research would be required, but the RTR would not have to be compliant with the more rigorous mandates of the Clinical Laboratory Improvement Amendments (CLIA), which govern tissue testing for clinical use, cutting costs and more complex oversight. By not being a CLIA-compliant tissue archive, tissues housed in the Statewide RTR could not be returned to hospitals for future clinical uses (see Final Project Report Appendix D). A variant of the RTR, the post-diagnosis RTR (pdRTR) requiring CLIA compliance, in which tissue blocks would be donated prior to the ten year mandate, previously addressed in the Surveys, was also discussed with the Advisory Panel.

A cost estimate handout for the ATA was provided to the Panel as well as a handout on suggestions for future planning by statewide work groups. These were categorized into ways to move forward with the ATA, developing a viable business model for the RTR and cross-cutting issues. Steps in the ATA planning included developing and supporting a Master Agreement based on the protocol developed for CICATs, enlisting the support of Pathology and IRB Chairs, engaging the Yale RCA to assist with hospital IRB approvals and record keeping, and tracking tissue requests to gauge demand. For the RTR, it was suggested that a Bio-Business consultant be engaged; that tissue demand, optimal acquisition periods and fees be quantified; benefits to hospitals be characterized; other financial funding be explored; a CT Cancer Research Consortium be defined and possible storage sites be explored. Some of the cross cutting issues included more definition of public education outreach, including the scientific community, proposing new wording for surgical consent, addressing medical retention with the legislature and exploring other funding.

The meeting closed with the suggestions for future planning. The investigators noted that they were planning to have a meeting(s) on sustainability aspects, and would be in touch with some advisors. They also stated they were in the process of identifying external reviewers of Final Report due at the end of February.

### **Third Meeting (Sub-group of Advisory Panel)**

A third small meeting with the investigators and consultant, Lisa Miranda, to discuss sustainability occurred on December 29, 2011. Lisa Miranda is a market consultant with expertise product development that touches a lab and setting up biobanks for academic centers and industry. Additional attendees included Drs. Everson and Swede, and several Advisors: Paul Pescatello, Pramod Srivastava, James Thibeault, and, later by telephone, L.Gonsalves, L. Mueller, and P. Checko, for additional input.

The discussion focused on funding and sustainability issues for the ATA and RTR with Ms. Miranda recommending a hybrid model of the two. Various funding and their associated challenges were discussed, especially those associated with including Pharma. Although Pharma involvement would have unique challenges, it likely would also increase demand for tissue, another significant concern for sustainability. Ms. Miranda stated that best practice would be to start with a business plan to seek funding from multiple sources. It was suggested that target value-added support, e.g., aggregate samples for research should be added to the business plan. Benefits to stakeholders, e.g. Path, IRB, CTR, researchers and the state need to be delineated. She suggested a case could be made for Pharma involvement being “good for society”. As a follow-up to the meeting, she would give examples of industry partnerships, potential federal grants; and contact information at Pharma, noting that small Pharma might be easier to contract with than big Pharma. Pharma could provide services (e.g., set up lab) as well as funding. They would likely want to pilot test samples for quality and for adequate annotation and might be considered for access to fast-track access. About \$7 million was estimated to be in the business plan discussed at the meeting. Dr. Everson described the BioTrust Model in which multiple efforts in Connecticut such as pre-term delivery, newborn blood spot, cord blood would join to develop common protocols and procedures like the Massachusetts Biotechnology Council (Mass Bio). Another idea, expanding ATA to a consortium, would use the conventional R01 mechanism to build a biorepository through hypothesis-driven questions. CURE, a non-profit educational

and business support network organization for bioscience in Connecticut, might be willing to spearhead and fund the consortium. CURE's membership includes major pharmaceutical companies, emerging biotechnology companies, and major research universities. Ms. Miranda suggested legal review of any ATA plans.

DPH representatives were invited to attend the latter part of the meeting so that they could learn about some of the proposals and consider some of the implications for DPH. Challenges to Pharma involvement included possible DPH limitations, public perception, possible IRB issues, and lack of sufficient tissue to be available to Pharma. Jackson Lab, a potential funder, might need a couple of years before knowing its potential to support a statewide RTR and critical value would need to be established, including consideration of adding RNA and DNA extraction. The possibility of providing funding to John Dempsey Hospital to run a statewide biorepository, referred to as a joint venture mode, was mentioned. Justification for including Pharma would need to be provided.

Regarding the demand for tissue, it was noted that demand might be currently artificially low because of the cumbersome processing. The market could be expanded by including Pharma in addition to academic researchers. Legal opinion would be needed shipping tissue out of state. Ms. Miranda noted the revenue stream might be enhanced by expanding beyond FFPE to Fresh Frozen, and others.