

Management of Human Biological Samples in the NIH Intramural Research Program

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Discussion Topics

- Historical Background
- Issues related to conflict of interest
- Issues related to technology transfer
- Issues related to human subjects protections

Background Information

- NIH has been changing policies related to conflict of interest; policies related to human subjects protections and technology transfer of human samples are defined, but there is need for clarification
- News stories have highlighted outside activities of several NIH intramural scientists that appear to conflict with their official duty responsibilities
- Hearings were held by the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, House of Representatives, on June 14, 2006

Outline of Concerns

- An NIH intramural scientist consulted (with remuneration) with a large pharmaceutical company
- Human CSF samples collected under research protocols over several years were transferred to the company under a Material Transfer Agreement to be assayed for potential biomarkers associated with Alzheimer Disease
- Questions were raised about this coi, why the samples were not part of a formal biorepository, and what oversight was provided to regulate transfer of human samples

Conflict of Interest Regulations at the NIH

- Since August, 2005, no NIH employee has been allowed to consult for a fee as part of an outside activity with a significantly affected organization (SAO--biotech or Pharma)
- Stock holdings in SAOs are limited to de minimis amounts (\$15,000) and are discouraged for all clinical investigators
- All senior scientific staff and leadership and all clinical investigators must submit annual reports of stock holdings
- There is a central computer system with this information so that if an official action is taken (submitting a clinical protocol, proposing a collaboration or material transfer, etc.) the approving authority will know of any potential conflict

Relevant Pre-existing Rules Governing Technology Transfer

- Every transfer of material (human or otherwise) should be accompanied by an appropriate official document (material transfer agreement, letter of collaboration, cooperative research and development agreement (CRADA))
- These documents should be signed by a scientific director, but this authority can be delegated

Actions Taken about Technology Transfer to Respond to Concerns

- Senior level committee charged with improving rules and communications regarding technology transfer
- Any transfer of human tissue samples must be approved by a senior official (scientific director or higher)
- The standard MTA form is being modified to indicate the need for human subjects oversight when human samples are transferred

Human Subjects Protection Issues

- According to the Office of Human Research Protections (OHRP), DHHS, all linked samples *and data* obtained under research protocols must be under the continuing oversight and review of an Institutional Review Board (IRB)
- This means that linked samples kept in freezers by individual PIs cannot be used for research purposes not specified in the informed consent while a protocol is open, and cannot be used at all once the protocol is closed unless the PI returns to the IRB for approval

Steps Taken at NIH to Assure Appropriate Oversight of Human Samples

- Memo to all clinical investigators reminding them of OHRP requirements
- Updating of Office of Human Subjects Research (OHSR) information sheet on use of human samples
- Formation of a committee on biorepositories to determine how best to provide oversight for human samples at the NIH

Biorepository Issues

- Millions of human samples currently reside in NIH freezers with oversight by individual PIs (who keep individual records), and, in some cases, with separate biorepositories controlling collection and distribution
- Should there be a central biorepository at the NIH (real or virtual), with standard procedures for collection and distribution?
- Can oversight by IRBs of use of human samples be streamlined?

How do these issues affect intramural-extramural collaborations?

- Conflict of interest restrictions should have no effect on official collaborations
- We cannot control conflicts of interest that extramural collaborators may have, but we do report these or the possibility of their existence in informed consent documents
- Other than specifying IRB oversight of transfer of human materials, collaborative research can continue

How are we assuring compliance by intramural investigators with these rules?

- Training: Computer-based training courses are available for coi, tech transfer, and human subjects protections; frequent reminders are sent; working on better approaches
- Administrative support: Has been increased in these areas
- Penalties: For violation of rules ranging from reprimands to termination of government employment
- Auditing: Computer-based central system will pick up conflicts unreported by employees