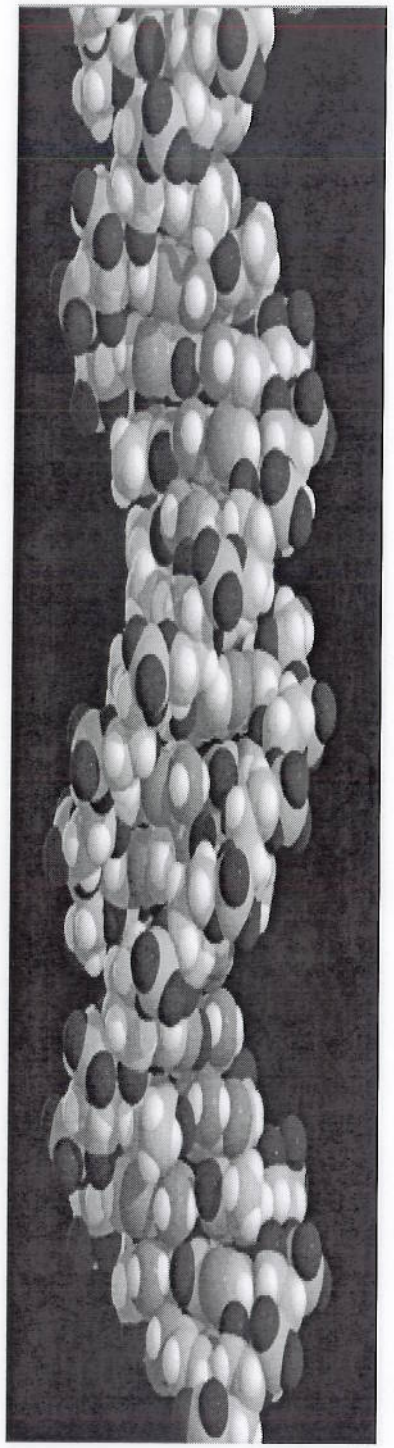

Ethical and Regulatory Considerations in Research using Residual Specimens

Jeffrey R. Botkin, M.D., M.P.H.

Professor of Pediatrics and Medical Ethics

Associate Vice President for Research

University of Utah

Reasons for NBS Specimen Storage

- Confirmation of test results
- Quality assessment of current test modalities
- Forensic uses
  - Post-mortem disease identification
  - Identification of remains
- Research
  - Related to newborn screening
  - Unrelated to newborn screening

Terminology

- Identifiable specimens (the identity of the tissue source can be determined)
  - Linked or coded specimens (someone has the key)
- De-identified specimens ("anonymized" – no one can identify the tissue source)
  - 45CFR46 "not readily identifiable by the investigator"
  - HIPAA – 18 potential identifiers must be removed

Research Options

"Anonymized" specimens

- Pros
  - Valuable for epidemiologic research
  - Research does not involve "human subjects" under US regs
  - Minimal IRB review
    - IRB defines exempt research
    - IRB may review de-identification process
  - No consent usually necessary for anonymous *use* (consent may be appropriate for collection and storage)
- Cons
  - Unable to link with health outcome of child
    - Cannot discriminate false positives and false negatives
  - Unable to contact family with beneficial health information

Research Options

Linked samples (identifiable)

- Pros
  - Health tracking possible
  - Return of health information possible
- Cons
  - IRB review and oversight necessary
  - Informed permission may be necessary
    - Undermines value of having a specimen already
  - Return of information may pose risk to child and/or family

2004 OHRP Guidance

- Investigator A obtains tissues in the conduct of research. Banked with identifiers
- Investigator B obtains specimens from A but without identifiers. Specimens remain linked with key held by Investigator A.
- Investigator B signs agreement that she will not seek identities of tissue sources
- Investigator B is <u>not conducting human subjects research</u>

htttp://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf

Informed Permission in NBS

- Permission usually not sought for NBS
  - Only 2 states and DC have permission process for NBS
  - No infrastructure for obtaining permission
  - Opposition to permission by public health and nursery personnel
- Acquire permission for *retention* of sample for research purposes?
- Acquire permission for research *use*?
  - Research specific to newborn screening conditions?
  - Broad authorization for other research uses?

AAP/HRSA Task Force Recommendations (2000)

- Use of unlinked specimens
  - Can retain demographic information
  - IRB review for epidemiologic research
  - No consent required

AAP/HRSA Task Force Recommendations (2000)

- Use of identifiable samples
  - IRB approval should be obtained
  - Parental permission should be obtained
  - Optimal source of tissue for the research?
  - Unidentified samples will not suffice?
  - Acceptable samples from consenting adults not available?

Community "Consent"?

- Conflict between individual consent model and public health model
  - An individual consent requirement and process undermine the public health approach
- ? Use community "consent" for identifiable samples without individual consent.
- Research on emergency interventions permit waiver of consent but with community disclosure and consultation

Policy Considerations

- Public dialogue on the value of retention and research uses
  - Sensitive issues need public dialogue and support
  - Substantial funding needs
  - ? Restrict use to research purposes or other child welfare uses
- Notification and opt-out option for research use at the time of education for NBS
- Affiliation with IRB for protocol reviews
- Process for prioritizing access to limited sample resource

The Need for NBS Research

- Availability of effective treatments does not mean early detection will be beneficial
- NBS is a *system* with many links in the chain from screening to beneficial outcomes

Use of Residual Specimens in Program Assessment

- Applicable when new NBS test is being introduced
- Retain residual specimens for 1 - 2 years prior to implementation
- Analyze retained specimens "retrospectively" when new program is initiated (control group)
- Identify and track children who screen (+)
- Compare health outcomes for children identified prospectively (intervention group) versus retrospectively (control group)

Retrospective Screening

- Approach avoids detection bias from comparing screened population with unscreened population
- Consent process undermines the validity of the study -- the *system* is a test article and NBS programs do not include consent
- Avoids the large challenge of permission process for thousands of parents

Waiver of Consent

Permitted under 45 CFR 46.116d if all criteria are met:

1) research involves no more than minimal risk
2) waiver would not adversely affect rights and welfare of the subject
3) research could not be practicably carried out without waiver
4) when appropriate, subjects can be provided with pertinent information after participation

Waiver of Consent

- Contention: retrospective screening for genetic/metabolic conditions confers minimal risk if:
  - Preliminary data suggest screening is likely to be beneficial
  - Disclosure of abnormal results occurs through a carefully designed protocol
  - Consent obtained at the time of results for subsequent data collection
  - Public discussion/consultation over protocol
  - Public notification of research

NHGRI 1 R01 HD058854-01

- *"Methods for promoting public dialogue on the use of residual newborn screening samples for research" (*PI - Botkin)

- Duration: 3 years (9/08 – 8/11)

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- Specific Aim 1:
  - **To conduct a comprehensive assessment of health department policies and procedures in the Mountain States region relevant to retention of residual NBS samples and the role of public input on policy development.**

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- Specific Aim 2:
  - **To compare responses from 3 methods for obtaining public input on the retention and use of residual NBS samples.** Methods to obtain public input will differ by elements of information about the issues and opportunities for deliberation about the topic.
    - Surveys
    - Focus Groups
    - Knowledge Networks®

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- Specific Aim 3:
  - **To conduct a regional working group meeting of representatives of newborn screening advisory committees, regional NBS laboratory directors, and national thought leaders and lay advocates to address ethical, regulatory, and policy issues relevant to the retention and research use of residual NBS samples and methods to obtain informed public input.**

Initial Impressions

- Research use of residual specimens is not necessarily a high priority for health departments
- Members of the public are not aware of retention and use
- High levels of public and professional concern over use of residual specimens without individual consent