



Ethical and Regulatory Issues in the Use of Stored NBS Samples for Research

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Uses of Stored Specimens

- Quality assessment of current test modalities
- Forensic uses
- Research

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- Quality management of current test modalities
- Forensic uses
- **Research**

Research with Stored Tissue Specimens

- Controversial
 - ❖ Estimated 282 million clinical and research specimens stored in 1999
 - ❖ Increasing by 20 million per year
- DNA as a “future diary”
- Collection types
 - ❖ Prospectively acquired specimens
 - ❖ Existing specimens

Alder Hey Children's Hospital

BBC News

1999

- “The hospital retained hearts to help doctors carry out complex, life-saving surgery, but was unaware that other organs had also been retained for research purposes.”
- “...[T]he hospital is devastated to learn that so many organs have been retained for research without the knowledge of the hospital, its doctors or the parents.”

NBS Sample Retention

- Mandl et al. Pediatrics 2002;109:269.
- 70.6% of programs retain samples
 - ❖ 91.7% retain with identifiers
- 74.5% of programs notify parents of sample collection
- 14% of programs that retain samples explicitly do so for research purposes
- 19.6% neither notify parents nor obtain consent

Residual NBS Specimens

- Resource of potentially enormous value
 - ❖ Expanding use of population studies for genetic and environmental research
 - ❖ DNA repository on the entire pediatric population over time
 - ❖ Future: Linkage of electronic medical records (health outcomes) with DNA repository

Human Subject Protections

- Peer review of research protocols
- Prevention of harm to participants
- Respect for individual autonomy by honoring choice about participation
 - ❖ Not absolute
 - ❖ Minimal risk research is permitted without consent

Ethical Concerns in Use of Residual NBS Specimens

- Psychological or social harms to child or parents from health information generated
- Invasion of privacy for research without permission
- Dilemmas for professionals in the return of research results
- Allocation of limited and valuable resource
- Use of specimens for non-public health purposes

Research Regulations

- Federal Regulations: 45 CFR 46
- Human subjects:
 - ❖ “Human subject means a living individual about whom an investigator ... obtains (1) data through intervention or interaction with the individual, or (2) **identifiable private information**. ... Private information must be individually identifiable (i.e., the identity of the subject is or may be **readily ascertained by the investigator** ...”
- Research with identifiable tissue specimens constitutes research with human subjects

Research Options

- “Anonymized” specimens (de-identified, unlinked)
- Pros
 - ❖ Valuable for epidemiologic research
 - ❖ Research does not involve human subjects
 - ❖ 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
 - Detect false positives and false negatives
 - ❖ Unable to contact family with beneficial health information

Research Options

- Linked samples (identifiable)
- Pros
 - ❖ Health tracking possible
 - ❖ Follow-up possible with health information
- Cons
 - ❖ IRB review necessary
 - ❖ Informed permission usually necessary
 - Undermines value of having a specimen already
 - ❖ Research information may pose risk to child and/or family

Research Options

- Retrospective testing of stored NBS specimen of children after they have developed a target condition.
- Does not involve predictive testing for the child
- Results may have genetic implications for family members
- Consent feasible

Lay Attitudes

- Wandler and Emmanuel 2002 Arch Intern Med
162:1457
 - ❖ Survey of 504 individuals
 - ❖ **65.8%** would require consent for research on tissue samples obtained through clinical care
 - ❖ **27.3%** would require consent even if samples were anonymized

Informed Permission in NBS

- Permission usually not sought for NBS
 - ❖ Only 3 states have permission process for NBS
 - ❖ No infrastructure for obtaining permission
- ?Acquire permission for retention of sample for research
- ?Acquire permission for research use
 - ❖ Specific to newborn screening conditions
 - ❖ Broad authorization for other research uses

AAP/HRSA Task Force

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

AAP/HRSA Task Force

- Identifiable samples
 - ❖ IRB approval
 - ❖ Parental permission obtained
 - ❖ Optimal source of tissue for the research
 - ❖ Unidentified samples will not suffice
 - ❖ Acceptable samples from consenting adults not available

Waiver of Consent

- Can research be conducted on identifiable samples without consent?
- Federal regulations require that 4 criteria be met:
 1. Minimal risk research
 2. Not practicable without the waiver
 3. No rights infringed
 4. Participants will be informed of research when appropriate

Community Consent?

- ?Use for identifiable samples without individual consent.
- Generally not consistent with current regulations or research ethics in the U.S.

Health Department Policies

- 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 NBS uses
- Consider permission process for research use at the time of permission/education for NBS
- Affiliation with IRB for protocol reviews
- Process for prioritizing access to limited sample resource