Translational Research in the Context of Newborn Screening— How Can We Make it Work?

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I have no financial or commercial interests or conflicts of interest to reveal

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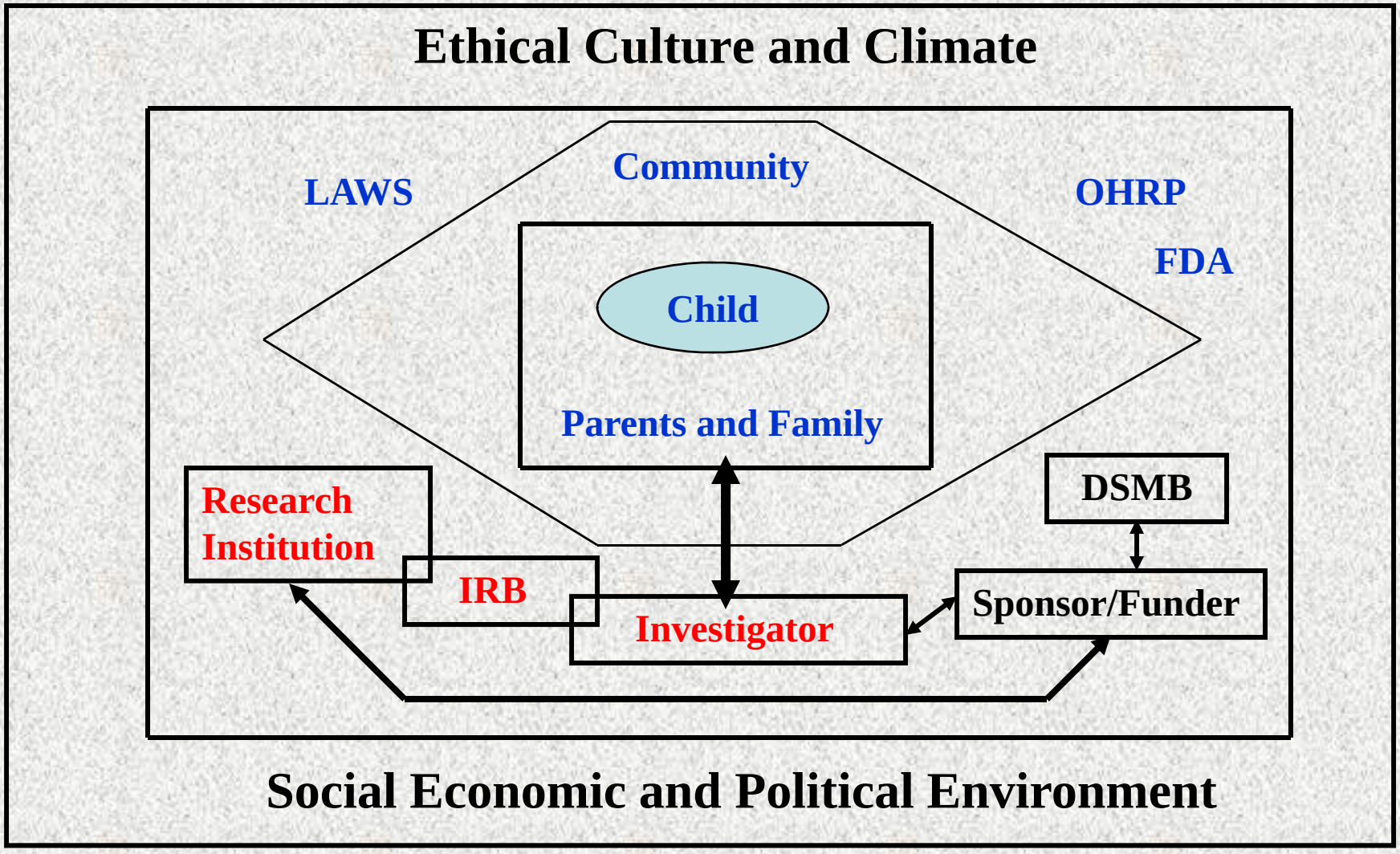
Human Subjects Protection Program



Newborn Screening -- Tension in Research Involving Human Subjects

Scientists and Clinicians

Child

Family

Newborn Screening -- Tension in Research Involving Human Subjects

Scientists

Generate new knowledge

Clinicians

- **Develop new screening methods**
- **Assess population prevalence**
- **Identify affected children**
  - **Assess long term health status**
  - **Enroll in clinical trial**

Newborn Screening -- Tension in Research Involving Human Subjects

Government

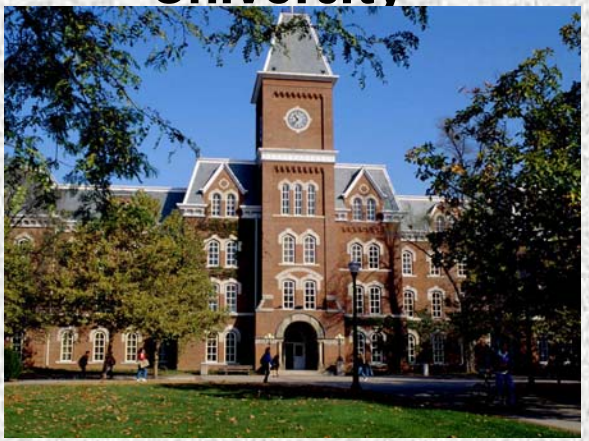
Create Laws and Regulations

Public Health Department

- **Protect interests of population—enforce laws/regulations**
- **Monitor health status--Disease surveillance**
- **Investigate health hazards, epidemics, bioterrorism**
- **Assure clinical services for underserved**
- **Protect confidentiality of individual**
- **Research (?)**

Newborn Screening -- Tension in Research Involving Human Subjects

University



Institutional Review Board

- Protect human subjects
- Facilitate research
- Assure compliance with federal and state regulations and laws
- Protect institutional interests

Newborn Screening Research--
The Massachusetts Approach

- **Two population-based studies**
  - **Expansion of Newborn Screening (1999)**
  - **Prevalence testing for HIV (1987)**
- **Screening for conditions to obtain new and generalizable scientific knowledge without evidence-based proof of benefit to the child, constitutes research**

Anne Comeau and Donna Levin. Two Models for Compliance with the Common Rule in the Massachusetts Newborn Screening Program. Forthcoming, 2009: *Ethics and Newborn Genetic Screening*

Newborn Screening Research--
The Massachusetts Approach

- Expansion of Newborn Screening (1999)
  - Mandate screening for 10 disorders
  - Pilot program – Cystic fibrosis screening
  - Pilot program – 19 additional disorders
- Review by two IRBs—MA Dept Public Health and Univ. Mass Medical School
  - Parental permission required—written consent waived
  - Brochure distribution – verbal consent documented on form

The New England Newborn Screening Program
University of Massachusetts Medical School
State Laboratory Institute

ROUTINE NEWBORN SCREENING

· In Massachusetts, there are ten treatable diseases that are included in ROUTINE NEWBORN SCREENING.

· Under Massachusetts law, it is a requirement that all babies born in Massachusetts be screened for signs of these ten diseases unless parents object on the basis of religious beliefs.

OPTIONAL NEWBORN SCREENING

· For your benefit, Massachusetts is offering newborn screening for an additional twenty disorders.

· *There is no extra cost and no extra blood required for your baby to participate.*

· The OPTIONAL NEWBORN SCREENING is two research studies to develop the best screening programs for the additional twenty disorders.

· Under Massachusetts guidelines for the OPTIONAL PROGRAM, after your baby is born, you will be asked whether you want to take advantage of the OPTIONAL NEWBORN SCREENING.

· If for some reason, you decide that you do not want to participate in the OPTIONAL program, your baby will still have all the benefits of ROUTINE NEWBORN SCREENING.

The New England Newborn Screening Program
University of Massachusetts Medical School
State Laboratory Institute

PARENT"S COPY

declines CF

declines MET

LAB ID # 100001

BABY'S NAME (Last) (First)

Dear Parent

This sheet is your record to show that a small blood specimen was taken from your baby for routine newborn screening.

This routine service ensures that your baby will be screened for each of 10 treatable disorders as mandated by the Massachusetts Department of Public Health.

In addition, this sheet records your instructions to your hospital nursery/pediatrician on your decisions about optional services (public health research initiatives) that are being made available to all babies born in Massachusetts.

- If your sheet has an X in the "declines CF" box, your baby will NOT be screened for cystic fibrosis.
- If your sheet has an X in the "declines MET" box, your baby will NOT be screened for any of the new set of 19 metabolic disorders.

The New England Newborn Screening Program of the University of Massachusetts Medical School provides all newborn screening services, as described in your brochure entitled "Answers to Common Questions About Newborn Screening".

Newborn Screening Research--
The Massachusetts Approach

- Prevalence Testing for HIV in child bearing women (1987)
  - Measure maternal antibody in de-identified residual newborn blood spots
  - Results reported as rate of HIV positivity per 1000 births
- Justification:
  - Exempt from IRB review--Not human subjects research -- no consent required for anonymous prevalence study
  - Knowledge of HIV status for newborn—not beneficial
  - Confidential HIV testing widely available to women

Newborn Screening Research--
The California Experience

- 2000—CA State legislature mandated pilot testing of tandem mass spec technology for newborn screening to determine effectiveness
- 2001—decision to require parental consent – CA Health and Human Services Committee for the Protection of Human Subjects
- Process:
  - Some hospitals required local IRB review
  - Hospital staff distribute booklet, obtain signature, and place YES or NO sticker on blood collection card

Lisa Feuchtbaum, George Cunningham, and Stan Sciotino. Questioning the Need for Informed Consent: A Case Study of California's Experience with a Pilot Newborn Screening Research Project.
Journal of Empirical Research on Human Research Ethics, 2007

Newborn Screening Research--
The California Experieince

- Outcome:
  - 47% of eligible births were enrolled – hospitals faced serous logistic problems in obtaining consent
  - 90% of parents offered participation in the research study consented
- Conclusion:

  "the legitimate needs of society and the interests of newborns should not be sacrificed to respond to the autonomy interests of the few parents who do not wih their infant to participate in the study"

  "in the future parental consent should be waived"

Newborn Screening Research--
How Can We Make it Work?

Critical Questions

- Is the study research?
- Does the study involve human subjects?
- Is the study exempt from IRB review?
- Does the study require consent? Can consent be waived?
    - Is oral consent justifiable?
- How many institutions will be involved?
    - Multiple individual reviews
    - Joint review arrangements
    - Cooperative agreements

Newborn Screening Research--
How Can We Make it Work?

Critical Questions

- Is the study research?
  - Definition of Research – seek generalizable knowledge
  - Nature of the study—laboratory methods, population prevalence, individuals
  - Distinction from Surveillance, Quality Improvement, Clinical Care

Newborn Screening Research--
How Can We Make it Work?

Critical Questions

- **Does the study involve human subjects?**
  - **Can the study be done with fully de-identified data?**

"OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
(1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
(2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain"

Newborn Screening Research-- How Can We Make it Work?

Critical Questions

- **Is the study exempt from IRB review?**
  - **Public data sets**
  - **Study of existing de-identified data or specimens**
  - **Study of public benefit or service programs**

§46.101

(b)4. ***"Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects."***

Newborn Screening Research--
How Can We Make it Work?

Critical Questions

- **Does the study require consent? Can consent be waived?**

§46.116

(d) "*An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:*

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

***(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation*."**

Newborn Screening Research--
How Can We Make it Work?

Critical Questions

- How many institutions will be involved?
  - Multiple individual reviews
  - Joint review arrangements
  - Cooperative agreements

- Current Approaches:
  - Children's Oncology Group
  - National Children's Study

Newborn Screening Research--
How Can We Make it Work?

Children's Oncology Group—Central IRB

…If the LocalIRB accepts the PedCIRB review, the PedCIRB becomes the IRB of record for that protocol and takes responsibility for the review of subsequent protocol amendments, adverse events and continuing reviews. Since starting in November 2004, the PedCIRB has reviewed 59 protocols. Initial reviews resulted in 44 approvals pending modification and 15 protocols being tabled for further information. The time from protocol submission to final approval by the PedCIRB has ranged from 3 to 28 weeks with an average time of 16.9 weeks during year one and 12.7 weeks during year two of the project. As of November 2006, 117 of a possible 197 U.S. COG institutions (59%) have signed on to the PedCIRB initiative and 70% of the participating institutions have conducted facilitated reviews (total 750) for the 30 protocols available on the PedCIRB website…

Journal of Clinical Oncology, 2007 ASCO Annual Meeting Proceedings (Vol 25, No 18S (June 20 Supplement), 2007: 6632
B. D. Anderson, J. Goldberg, J. Adler, L. Covington, D. Olson, B. Gordon, G. Reaman, J. Everett, M. Smith and M. Christian

Newborn Screening Research--
How Can We Make it Work?