NIH Bioethics: *Research to Inform Policy*

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OD Funds for Bioethics Research: $5M

- NIH invests about $50 million per year in bioethics research
- IC's often focus on issues related to their mission and portfolio
- The Office of the Director received $5M for bioethics research beginning in 2010
- Increasingly, these funds are used to generate data to help inform policy and program development

Research to Inform Policy
FY 2012

Research to develop evidence to inform changes to protections for human research subjects

1981: HHS regulations on the protection of human subjects

1991: Common Rule published; 15 federal agencies

Since then: Science has changed dramatically; time for a revision

2011: HHS publishes ANPRM with 2 overarching goals: Enhance protection of research subjects & Increase efficiency of oversight

Research to Inform Policy
FY 2012

Common Rule ANPRM: 7 Key Reforms

1. Refine existing risk-based framework.
2. Utilize single IRB review of record for domestic multi-site studies.
3. Establish single source of guidance on federal regulations
4. Establish mandatory data security and information protection standards
5. Establish systematic approach to collection & analysis of data on unanticipated problems and adverse events
6. Extend federal regulatory protections to all research conducted at US institutions receiving federal funding
7. Improve informed consent

Research to Inform Policy
FY 2012 (Competing Supplements)

Research to develop evidence to inform changes to protections for human research subjects

Four Awards

- Easy-to-read consent in high-risk clinical trials
- Harmonized procedures for informed consent for biospecimens and repository operations
- Preferences for consent models for secondary use of biospecimens, including diverse populations
- Tools for consent for data-sharing

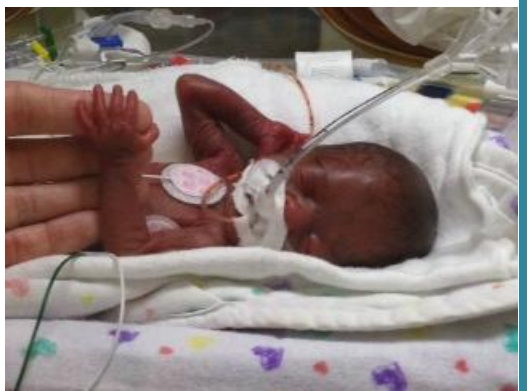
Research to Inform Policy
FY 2013

- Spring of 2013 – an unanticipated controversary in human subjects research emerged
- Will require new policy development/guidance
- OD bioethics funds could be used to generate data to guide the next steps

SUPPORT: *Surfactant, Positive Pressure and Pulse Oximetry Randomized Trial*

- DESIGN: 1,316 infants (24-27 wks ga) randomized within standard of care: **85-89%** or **90-95%** oxygen saturation (AAP rec. 85-95)
- STUDY: Carried out at >20 Sites from 2004 – 2009
- QUESTION: Ideal oxygen saturation targets for preterm infants?
- GOAL: Identify the target that would minimize the risk of ROP; **no known increased risk of death within SOC range**
- RESULTS:
  - ROP was reduced at lower range
  - Incidence of death increased at lower range;

    16.2% to 19.9% (P = 0.04) – **Unexpected**



SUPPORT: The Controversy

TIME LINE

- Feb, 2005 – Feb 2009: Infants enrolled in the SUPPORT Study
- May, 2010: NEJM article reporting the results of SUPPORT
- 2012: New Oxygen saturation clinical guidelines from AAP
- Feb 8, 2013: OHRP compliance letter to UAB

SUPPORT: OHRP's Position

- Study involved "substantial risks" that were not disclosed.
- "the level of oxygen being provided to some infants, compared to the level they would have received had they not participated, could increase the risk of brain injury or death."
- Randomizing to arms both within the standard of care places participants at risk.

"Their position is apparently that informed consent forms need to inform parents not only of known risks and of possible risks, but also of risks that the investigators did not think were possible – even after those risks have been shown not to exist."

John Lantos, 4/18/13
Hastings Bioethics Forum

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- April 10, 2013: Letter from Public Citizen – call for apology
- April 15, 2013: NYT story and editorial, An Ethical Breakdown

  "startling and deplorable"
- Many voices enter the debate…

SUPPORT: Divided Community

And those who don't

Those who agree with OHRP

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

The OHRP and SUPPORT

TO THE EDITOR: We are a group of scholars and leaders in bioethics and pediatrics with extensive

that the institutional bodies responsible for reviewing SUPPORT failed to exercise appropriate

NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

RP and SUPPORT — Another View

TO THE EDITOR: We are a group of physicians, bioethicists, and scholars in allied fields who agree with the Office for Human Research Pro-

from usual clinical care, and that information should have been included in the consent forms. About half the forms indicated that because

April 15, 2013

An Ethical Breakdown

By THE EDITORIAL BOARD

Despite reforms to protect patients from being harmed by medical research in recent decades, 23 academic institutions authorized a re project that failed to meet the most basic standard: providing an informed consent document to parents that accurately described the r benefits of the research to be conducted on extremely premature babies.

This failure was startling, and deplorable. Federal officials have rightly demanded that the University of Alabama at Birmingham, the le

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- June 4, 2013: OHRP revised letter to UAB
- June 5, 2013: NIH publishes NEJM perspective disagreeing with OHRP; HHS announces plans for a public meeting

NIH weighs in, OHRP halts action on UAB, HHS plans public meeting

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

In Support of SUPPORT — A View from the NIH

Kathy L. Hudson, Ph.D., Alan E. Guttmacher, M.D., and Francis S. Collins, M.D., Ph.D.

Each year in the United States, nearly 500,000 infants — 1 in every 8 — are born prematurely, before 37 weeks of gestation. Despite substantial advances in their care, premature infants face a daunting array of challenges; they are at high risk for death in infancy and face severe and lifelong health problems if they survive.[1] The National Institutes of

ized Trial (SUPPORT), carried out at more than 20 sites between 2004 and 2009, sought to identify, in infants born very prematurely at 24 to 27 weeks' gestation,

ence in mortality between the two treatment groups in SUPPORT — one with the oxygen saturation target of 85 to 89%, the other with the target of 91 to 95%.

An important finding of the study was a reduced incidence of ROP in the lower oxygen-saturation range. However, contrary to what was known at the time, the study also showed a slightly but

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- August 28, 2013: Public meeting

Moving Forward: Where are we today?

- Many studies slowed due to uncertainty
- Some new studies not being launched
- OHRP Draft Guidance coming…
- NIH workshop:
  - What are reasonably foreseeable risks?
  - Are there risks inherent to randomization?
  - Perspectives from the entire community

Moving Forward: Research to Inform Policy

NIH-funded studies on ethical issues surrounding standard of care, FY13

- **Laura Dember, U Penn**

  Understand how patients value physician autonomy to choose treatment strategies within the standard of care

- **Susan Huang, UC Irvine**

  Insight into expected improvements in healthcare (QI) and what constitutes research

- **Rob Califf, Duke**

  Preferences about research & consent in the setting of usual care

- **Mary Disis, U Washington**

  Understand how patients, general public, IRBs view the ethical implications of randomization within the standard of care

Moving Forward: Research to Inform Policy

Some of the ethical questions that we're interested in include:

- Should the risks of SoC interventions be considered risks of the research and what are the ethical dimensions of this question?
- How should risks of research done within the standard of care be disclosed to participants? What are patient's preferences?
- What are the obligations of IRBs and trial investigators in identifying and disclosing risks for SoC research?

Research to Inform Policy
Also in FY 2013

NIH funded the eMERGE network to study participant preferences surrounding consent for future use of biospecimens and data

- **eMERGE: Electronic Medical Records and Genomics Network**
  - Nine sites, including a Coordinating Center
  - Goal: to understand the best ways of incorporating genetic information into EHRs
  - Also focuses on ELSI in the use of EMRs for genomics research

Research to Inform Policy
FY 2014 – NEW RFA

- NIH will fund **$1.4 million** in new bioethics research in FY2014
- RFA here: http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-14-002.html
- Applications due: April 18th
- Propose to fund research in the following areas:
  - Central IRBs overseeing multisite studies
  - Research using clinical records and data

Research to Inform Policy
FY 2014 – NEW RFA

Central IRBs overseeing multisite clinical trials

- Principles to guide the formation and conduct
- SOPs for routine functioning
- Resources or tools to support the operation
- Other ethical or logistical issues

Research using ***clinical records and data***;

- Participant preferences
- Type/duration of consent for research use of data
- Research vs QI
- Privacy *and* data sharing