Absent Informed Consent Research is Unethical

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A Primer on Human Subject Research: Federal and State Law

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Authority of Nuremberg Code

"The voluntary consent of the human subject is absolutely essential."

Nuremberg Code, 1947

"The Nuremberg Code is the most complete and authoritative statement of the law of informed consent to human experimentation. It is also part of international common law and may be applied, in both civil and criminal cases, by state, federal and municipal courts in the United States."

Maryland Court of Appeals, Grimes / Higgins v Kennedy Krieger, 2001

"The subjects must be volunteers and informed participants in the research project."

Declaration of Helsinki, Rev. 2000

"No human research may be conducted in this state in the absence of the voluntary informed consent subscribed to in writing by the human subject."

NYSC Law 24-A

The US regulatory system was established to safeguard human subjects by implementing the ethical principles articulated in codes such as the Nuremberg Code and the Declaration of Helsinki—both of which are affirmed in the Belmont Report.

However, the system is geared toward lending the appearance of legitimacy to ethical corner-cutting and commercial expediency at the expense of safety.

Nowhere is this more evident than in non-consensual emergency and pediatric research.

FDA Emergency Consent Waiver

21 CFR 50.24 “narrow” Exception Criteria:

“Life-threatening situation;

Available treatments are unproven or unsatisfactory;

Prospect of direct benefit to the subjects;

Risks are reasonable in relation to...medical condition... standard therapy... and what is known about the risks and benefits of the proposed intervention.”

“Additional protections”

- “consultation with community”
- “public disclosure”
- “independent data monitoring committee”

Who enforces “narrow exception” criteria?

Impact of Waiver of Consent

"Emergency research creates a special set of circumstances.

In a way, all of our usual approaches to research ethics

to protecting human subjects,

to trying to get informed consent –

just go out the window."

Kelly Fryer-Edwards, medical ethicist, Wired, 2004

Two federal legal / regulatory changes have undermined safety of human subjects.

1996: FDA Waiver of Informed Consent in Emergency Research

1997: FDA Modernization Act (FDAMA)

Expanded use of children as human subjects.

Incentives for testing patented drugs in children: + 6 month patent exclusivity

For best selling drugs = +$ 1 billion

Children forced to assume burden of risk:

children forced to ingest toxic, harm producing drugs for others' profit.

1998, FDA Consent Waiver: Artificial Blood Trial

In US urban centers, blood is available, its safety / benefit proven and satisfactory.

FDA's “narrow exception” first applied in 1998:

- Baxter’s blood substitute, HemAssist, was tested without informed consent.
- Trial was halted after 24 of 52 patients died compared to 8 of 46 who received real blood.

Waiver of informed consent opens the gate to preventable medical disasters.

What does “community consent” mean?

FDA waiver substitutes “community consent“ for personal informed consent.

- Historically, when others decide, risks to subjects escalate.
- How does "community consent" protect the rights of an individual human being?
- Who is responsible / accountable for bad choices resulting in preventable deaths?
- How many non-consenting people will be sacrificed?

Communal consent = illegitimate infringement of individual rights, degrades one’s humanity.

Artificial blood products tested since 1970s.

At least four companies attempted to produce a blood substitute to transport oxygen like blood does, is compatible with all people, and can be stored for long periods (real blood expires after 42 days).

—Baxter, Biopure, Hemosol, Northfield—

Artificial blood is made with hemoglobin molecules which tend to seep into the walls of blood vessels and cause inflammation. They can constrict blood vessels causing blood clots—

increasing risk of heart attacks.

ALL substitute blood products produced significant toxicity, myocardial infarction and renal failure.

Systemic Compromised Oversight

Lack of transparency:

Unsuspected conflicts of interest, secrecy, tensions, gaps in the local & national oversight of research, and absence of reliable enforcement mechanism compromise local and national oversight system.

FDA complicit shielding corporate secrets:

undisclosed: research protocols
risks
consent forms
deaths, negative results

Human subjects at increased risk of harm / exploitation

FDA Waives Consent, Violates Its Own Exemption Criteria

FDA approved 2-part PolyHeme blood trial --in ambulance and in hospital ER—

even though the experiment violates FDA's Exception Criteria:

The issue is whether or not it is ethical to withhold blood from trauma patients in a hospital setting to test an experimental product, without their consent?

2003: FDA Approved PolyHeme Waiver

AHRP Raised Concerns:

In prior trials, what was the survival rate of trauma patients who received an artificial product compared to those who received human blood?

How many suffered harm compared to controls?

-- myocardial infarction?
-- stroke?
-- renal failure?

FDA Complicit in public deception

Northfield misrepresented trial as "ambulance trial"

- Community not informed blood would be withheld in hospital 12 hours
- PolyHeme benefits, overstated
- Prior lethal trial results, concealed

OHRP: PolyHeme experiment is unethical

Patients exposed to experimental product without consent—even when real blood is available in the hospital ER

Sen. Grassley Letter to Sec. HHS, 2006
http://www.ahrp.org/cms/content/view/108/55

FDA Complicit in Cover-Up of Deaths

2004-2005: Northfield Labs lied to communities:

"In clinical trials to date, PolyHeme has demonstrated no clinically relevant adverse effects. Up to now, PolyHeme has not caused any clinically bad problems."

2001 trial stopped, results concealed:

10 of 81 patients who received fake blood suffered a heart attack within seven days

2 died.

None of the 71 patients who received real blood had a heart attack. Wall Street Journal, 2006

FDA: Deaths “Not a Show-Stopper”

Dr. Jay Epstein, FDA director of blood-products:

"Of course it's alarming there were excess deaths in the treatment group. We are highly mindful of the adverse events.

But the adverse-event profile in the trial, while significant, was not a show-stopper...”

WSJ, 2006

http://www.ahrp.org/cms/content/view/86/80/

Sen. Charles Grassley

"I am personally troubled that, for all intents and purposes, the FDA allowed a clinical trial to proceed, which makes the inhabitants of 32 communities in 18 states, and anyone living or traveling near these communities, potential "guinea pigs," without their consent and, absent consent, without full awareness of the risks and benefits of the blood substitute."

Sen. Grassley Letter to Sec. HHS, 2006

Non-consensual Trial Results

PolyHeme killed more patients than saline:

- 46 of 349 patients given PolyHeme died.
- 35 of 363 patients in the saline control group died.

How many preventable deaths before FDA stops lethal “show?”

In the absence of independent oversight / enforcement, penalties, research abuses, exploitation, abound.

Children Are Non-Consenting Subjects

A review of 561 research reports in five American medical journals: 40% of reports involving children failed to indicate that ethical standards were followed.

British Medical Journal, 2001

IRBs fail to protect children from dubious, non-therapeutic experiments involving risk and pain such that an autonomous adult would likely refuse.

NIMH, 1996: 45 boys, age 6-11, subjected to painful lumbar punctures, without any medical justification --simply to test a speculative hypothesis:

Does cerebrospinal fluid homovanillic acid predict behavioral response to stimulants in boys with ADHD?

Castellanos, Neuropsychopharmacology, 1996

A National Scandal-Foster Children

1989-2001: 13,878 Foster children "guinea pigs"
in > 48 toxic AIDS Drug / Vaccine trials.

Experiments violated federal regulations

--45 CFR 46.409 and 21 CFR 50.56—

10 deaths in one study; in another study,

26 of 52 infants suffered severe adverse effects.

Participating states: Illinois, Louisiana, Maryland, New York, North Carolina, Colorado and Texas.

Associated Press, 2005 http://www.ahrp.org/infomail/05/05/04.php

NYC foster children 75→ 465→ 650→714→ ?

NYS Law, Article 24-A (Public Health) violated.

2004: AHRP Filed Complaint

http://www.ahrp.org/ahrpspeaks/HIVkids0304.php

Fed. regs. prohibit use of children—wards of state—

from greater than minimal risk research;

mandate an independent guardian to protect foster children. (45 CFR 46.409 and 21 CFR 50.56)

OHRP NYC investigation determined:

Most children were denied protection of mandated independent advocate.

"Columbia University IRB failed to obtain sufficient

information to make the determinations

required for approval of research under 45 CFR 46.111"

National Institute of Child Health / Development (NICHD)

Example of non-therapeutic, invasive, painful clamp experiment in children:

100 obese children + 93 normal weight children aged 6 – 10, enrolled in 2000.

Battery of painful tests in-hospital:

- Insertion of multiple intravenous blood lines (one attached for 18 hours); 2- hour hyperglycemic clamp; 3-hour euglycemic clamp; hyperinsulinemic clamp.
- Children required to experience extremely high-low blood sugar levels for hours at a time.
- Children suffered undue pain, risk of allergic reactions, and risk of blood clots or phlebitis.

Pediatric “protections” inconsistent

- NICHD IRB approved experiment as “minimal risk” declaring that the risks involved were no greater than "what a child might encounter while playing in traffic."
- OHRP ruled that normal weight children "do not have a disorder or condition," and their inclusion in the experiment violated federal regulations. Experiment was suspended, 2000.

  http://**ohrp**.osophs.dhhs.gov/detrm_letrs/nov00a.pdf
- In 2001, OHRP accepted NICHD-IRB claim: “children of obese parents are at risk of condition.”
- No consistency in pediatric research protections.

PATS, NIMH Preschool ADHD drug experiment:

303 Children aged 3-5 recruited to test a drug that stunts growth, causes abnormal heart beat, and induces hallucinations in young children. *FDA ADHD Drug Review 2006*

Parents offered $645 if child completed protocol.

Results: 40% of children suffered adverse effects; 1 in 10 dropped out "intolerable side effects"

J Am Acad Child /Adolesc Psychiatry, 2006

Long-term consequences for young children

?

Two Landmark Court Decisions Cite research atrocities

New York State: TD v NYSOMH, 1995

"The mere mention of experimental medical research on incapacitated human beings—the mentally ill, the profoundly retarded, and minor children—summons up visceral reactions, with recollections of the brutal Nazi experimentation.... Even without the planned brutality, we have had deplorable instances of over-reaching medical research in this country."

Court restricts surrogate consent: "Parents may be free to become martyrs themselves. But it does not follow they are free, in identical circumstances, to make martyrs of their children before they have reached the age of full and legal discretion when they can make that choice for themselves."

Justice Greenfield, TD v NYSOMH, 1995

Maryland Court of Appeals orders Judicial Review

"Failure in the informed consent process leads to serious inequities in research, specifically for the poor and less educated who bear most of the research burden [and that] the problem is perpetuated in pediatrics..."

"The scientific and medical communities cannot be permitted to assume sole authority to determine ultimately what is right and appropriate in respect to research projects involving young children."

Grimes v Kennedy Krieger, 2001

Currently Recruiting Children, 3-7 years

Absent Informed Consent...

Protocol NCT00221403

"Valproate and Risperidone in 60 Young Children ages 3-7 with Bipolar Disorders"

"Many of these young BPD patients have been treated with stimulants or antidepressants"

Rebecca Riley, dubiously "diagnosed" at age 2-1/2 "Bipolar Disorder." Rx multiple toxic psych drugs. Dead at age 4 of drug toxicity, 2007.