

Evidence-based Research Ethics: Enhancing Biomedical and Behavioral Research in HIV/AIDS and Substance Abuse Conference  
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# Mission Creep: What Is Effective, and What Is Not?

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Attitudes of  
research consumers,  
potential participants,  
IRB members,  
and federal regulators  
come from many  
sources...

...spooking us about all  
research, fostering  
mission creep, and  
trivializing real problems

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Powell's Mission Impossible

**TIME**



HOW  
**MEDICAL  
TESTING**  
HAS TURNED  
MILLIONS OF  
US INTO ...

**HUMAN  
GUINEA  
PIGS**



# The Need for Regulation

Motivated by medical research abuses in the 20th century, especially these, run by Western governments:

- Nazi physicians / Nuremberg trials
- “Tuskegee Study of Untreated Syphilis in the Negro Male”

Funded by the U.S. Public Health Service 1932-1972 (!)

Research question: is nontreatment better than the available treatments (in 1932, all toxic)?

Free physicals and routine medical treatment, free rides to the clinic, hot meals on exam days: excessive inducement for African American sharecroppers during the Depression?

To study long-term effects of syphilis: withheld penicillin, even when it became the standard treatment

# Tuskegee and HIV / AIDS

“Infamous examples of real racism in the past such as Tuskegee Syphilis Study (1932-1972) have injured the level of trust in the black community towards public health efforts...

The AIDS epidemic has exposed the Tuskegee study as a historical marker for the legitimate discontent of blacks with the public health system.

The belief that AIDS [or barriers to research on and treatment of it] is a form of genocide is rooted in recent experiences of racism...

Researchers in public health hope that open and honest conversations about racism in the past can help rebuild trust and improve the health of people in these communities.”

# Balancing Goals

Serious abuse can happen - protection is needed

But opportunities – for participants and for  
researchers – must be fostered

What principles and practices, applied by whom,  
applied to what types of work?

What voice for participants?

# Belmont Principles (1978)

- 1) **Respect** for persons, including their autonomy
- 2) **Beneficence** – maximizing benefits and minimizing risks for society and for individuals
- 3) **Justice**, including representativeness of participant samples

How to balance free inquiry,  
respect for autonomy, and participant protection?

And who gets to decide?

# The IRB Decides

In the history of medicine, IRBs are a very recent invention...

National Research Act of 1974 defined IRBs

IRBs chartered to regulate all research receiving DHHS funding

IRBs overseen by DHHS' Office for Human Research Protections

# The Common Rule (1991)

15 federal agencies agreed to rely on Title 45 of the Code of Federal Regulations Part 46 subpart A

The Belmont Principles and the Common Rule are now bedrock reference points for Institutional Review Boards

How to get from principles to policies to action?

Who decides?

# Community Voices: Does Your IRB Deliver?

“(a) Each IRB shall have at least five members, with **varying backgrounds** to promote complete and adequate review of research activities commonly conducted by the institution.

The IRB shall be sufficiently qualified through the **experience and expertise** of its members, and the diversity of the members, including consideration of **race, gender, and cultural backgrounds** and sensitivity to such issues as **community attitudes**, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects...

(d) Each IRB shall include at least one member who is **not otherwise affiliated with the institution...**”

# IRB Purview: No Consensus

Only research posing risk of **physical harm** should be covered

– American Association of University Professors, 2001

Research on **autonomous adults** whose methodology consists entirely in collecting data by surveys, conducting interviews, or observing behavior in public places, be **exempt from the requirement of IRB review** ... [with] no requirement of IRB approval of the exemption

– American Association of University Professors, 2006

All **federally funded** research on a given campus vs. **all research**, regardless of funding source

– institution-elected option in current federal regulations

**All research**, whatever source of funding, should be covered

– Institute of Medicine Committee, 2002

(emphasis added)

# Mission Creep, Version 1

Journalism and oral history scholarship have well established professional ethics...and are very different from biomedical research

In journalism, the primary responsibility is to the public, not the subject

Protection of the subject is not paramount

Relation to subject may be inherently adversarial

1<sup>st</sup>-amendment issues / speaking truth to power

Do we want IRBs regulating journalism?

Should IRB criteria, procedures, and membership be sensitive to type of activity potentially being regulated?

# Mission Creep, Version 2

"It's been my feeling that the IRB, while sometimes making helpful suggestions, more often delays and micromanages projects.

It recently took them a month to look at a recruitment poster, and they then rejected it because they wanted us to unbold some text.

Now the poster is back [at the IRB office] for a week and we can't get a response."

- Anonymous colleague, another university, used with permission

# Illinois IRB Study Group

Interdisciplinary panel of scholars

Extensive IRB experience

Application (not just intention) of regulations

Ways to improve regulations

Ways to improve implementation of regulations

→ Focus on “Mission Creep”



The Illinois White Paper

**Improving the System for Protecting Human Subjects:  
Counteracting IRB "Mission Creep"**

## Mission Creep in the IRB World

C. K. Gunsalus, Edward M. Bruner, Nicholas C. Burbules, Leon Dash, Matthew Finklin, Joseph P. Goldberg, William T. Greenough, Gregory A. Miller, and Michael G. Pratt.

The authors are all at the University of Illinois Urbana-Champaign and participated in the Center for Advanced Study Steering Committee to Study Human Research Protections.

THE SYSTEM IN THE UNITED STATES FOR PROTECTING HUMAN PARTICIPANTS IN RESEARCH engages the earnest efforts of thousands of scientists, community volunteers, and administrators. Through untold hours of service on Institutional Review Boards (IRBs), they watch over the safety of human research subjects. Unfortunately, much of that effort is increasingly misdirected as the system succumbs to "mission creep" that could compromise its central goals. Our IRB system is endangered by excessive paperwork and expanding obligations to oversee work that poses little risk to subjects. The result is that we have simultaneous overregulation and underprotection.

IRBs were established following the 1979 Belmont Report from the Department of Health, Education, and Welfare, with the goal of protecting human subjects involved in potentially risky medical and behavioral research. But IRBs' burdens have grown to include studies involving interviews, oral history, journalism, secondary use of public use data, and similar activities that others conduct regularly without oversight. Most of these activities involve minimal risks—surely less than those faced during a standard physical or psychological examination, the metric for everyday risk in the federal regulations. And IRBs are pressured to review an expanding range of issues from research design and conflicts of interest to patient privacy and other record keeping. These are beyond the scope of research protection and are best left to others.

The IRB system is being overwhelmed by a focus on procedures and documentation at the expense of thoughtful consideration of the difficult ethical questions surrounding the welfare of human subjects, especially as complex clinical trials burgeon. Their work is afflicted by unclear definitions of terms like "risk," "harm," and "research." Because ethical behavior is difficult to measure, many IRBs rely on stylized documentation over substantive review, out of concern that one case in a thousand could slip through and generate bad publicity or penalties, or potentially shut down research. The result is that many protocols receive exaggerated review, and the paper piles up. Society loses as potentially productive research is discouraged or self-censored.

Ironically, this obsession with paperwork and mechanical monitoring may undermine protection of human subjects. IRB members spend too much time editing documents, marking typos, and asking for more details. One researcher, 10 years into a longitudinal study, was asked by an IRB to remove the term "anemia" from consent forms because participants might not understand it. Such actions, about which we hear frequently, carry a serious risk: They reduce trust in the guidance of IRBs and may alienate some researchers enough to turn them into scofflaws.

Oversight of the IRB process by federal agencies reinforces these tendencies. "Poor or missing Standard Operating Procedures" and "poor minute-keeping" account for about half of all U.S. Food and Drug Administration citations, and quorum failures for another 13%, according to one review. In seeking compliance, universities have multiplied the number of IRBs, depleting the supply of willing and competent faculty. All this has generated a trend in which researchers increasingly think of IRBs as the "ethics police." In fact, all researchers must take primary responsibility for professional, ethical conduct. Our systems should reinforce that, not work against or substitute for it; the IRB should be a resource, not the source, for ethical wisdom. All compliance systems require the buy-in and collaboration of the regulated, and it will be a sad day if scholars come to see human protection in research as the source of frustrating delays and expensive paperwork.

What can be done? Our University of Illinois white paper,<sup>8</sup> based on 2 years of study following an interdisciplinary conference of researchers and IRB leaders, addresses the problems of mission creep and offers possible solutions. Our recommendations include the exemption from IRB oversight of some activities that have ethical standards of their own, distinct from the biomedical tradition. We also support gathering information in a national clearing-house that supports IRBs and researchers alike. This would provide examples of good and poor practices rooted in disciplinary standards, and help IRBs make priority determinations about what constitutes risk and harm in different human research settings.

The IRB system is in trouble, and that means trouble for the safety and efficacy of research on human subjects. We should refocus our efforts on the core issues and stop expanding the mission into less productive territory.

—C. K. Gunsalus, Edward M. Bruner, Nicholas C. Burbules, Leon Dash, Matthew Finklin, Joseph P. Goldberg, William T. Greenough, Gregory A. Miller, Michael G. Pratt



# Primary Findings

More fields being regulated, including

ethnography, journalism, creative writing...

...using definitions, policies, and standards developed for quite different (biomedical) contexts

Ambiguous, even contradictory review criteria – e.g.,

IRB and IRS both claim to hold trump cards re: payment records

Long, complex consent forms instead of truly informed consent

More and more tasks assigned to IRBs

Burgeoning workload for all players and their budgets

Increasing discontent among IRB staff and researchers

# Federal Audits of IRBs

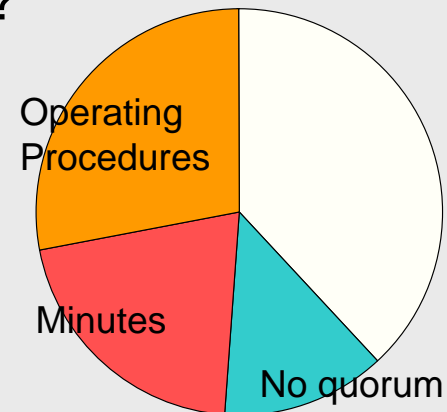
Widespread fear of liability, scandal, institutional “death penalty”...

Yet what are the frequently cited lapses in IRB audits by the 2 main federal oversight agencies, OHRP and FDA?

28% poor or missing standard  
operating procedures

21% poor minute-keeping

13% quorum failures



From Getz (2004) & Illinois White Paper (2005)

→ Almost 2/3rds of the citations were about internal IRB processes and were relatively trivial - not directly related to research protocols or participant protection or opportunity

# Critical Concepts

Not defined in federal regulations:

“research”, “covered research”, “risk”, “harm” (!)

“Research subject to regulation” defined circularly:

“...encompass those activities, for which a federal department or agency has specific responsibility for regulating as a research activity...”

45 CFR 46.102(e)

# One Size Fits All?

HIV / AIDS demographics

Community psychology

HIV / AIDS prevention

Ethnography

HIV / AIDS intervention

Journalism

Substance abuse

Oral History

Cognitive neuroscience

Behavioral economics

Chemotherapy clinical trials

Psychotherapy clinical trials

Should the IRB approach all of these the same way?

# One Size Fits All?

Do researcher and participant have the same type of relationship in all these contexts?

On which side are community leaders? community activists?

Does “informed consent” have the same meaning?

Some research is so embedded in or emergent from the context that there’s no “before” stage for IRB review to take place

# One Size Fits All?

Will people with low literacy and low trust in conventional institutions read long, complex consent?

Will under-served, under-resourced participants walk away from high-compensation research?

How to communicate potential risks and benefits to such potential participants so that they will make informed choices?

# Mission Creep: What Is Research?

“One of the most prevalent issues that leads to unnecessary burden for IRBs and investigators is the **lack of understanding of the definition of human subjects research.**”

Many institutions are including activities [for review] ... as human subjects research... [that] **do not meet the federal definition of human subjects research.**”

- Marjorie Speers, Executive Director, Association for the Accreditation of Human Research (2005)

(emphasis added)

# Mission Creep: What Is Minimal Risk?

“Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those **ordinarily encountered in daily life** or during the performance of routine physical or psychological examinations or tests.”

- 45 CFR 46.102(i)

“...federal regulations specify that expedited review procedures apply for certain kinds of research involving no more than ‘minimal risk.’

The problem, of course, is that **IRBs interpret ‘minimal risk’ in different ways** -- there is no uniformity or strong guidance on this.”

- Steven Breckler, *APA Psychological Science Agenda*, v. 19, #10, 11/2005

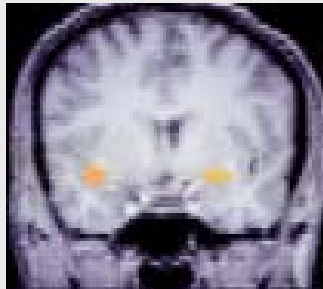
(emphasis added)

# Mission Creep: Decision-Making Biases

IRB members are subject to the same biases as anyone else

In many circumstances, anticipation of risk or danger is emotionally more powerful than the actual event

→ Intriguing neuroimaging research on brain mechanisms...



Amygdala activation to emotional stimuli

Mohanty et al. (2005), *J. Abnormal Psychology*

Yet IRB application forms (and IRB culture) press more for information on risks than for information on rewards and opportunities for individuals and communities

# Mission Creep: Expanding in a Vacuum

Failure to use research already available

Failure to encourage research on the ethical issues

Judging risk of harm subjectively, without good external data

→ Leaving IRB members to guess based on anecdote or personal comfort

→ The “I’m not comfortable with...” criterion or ethics by consensus rather than principle

# Mission Creep: The IRB Knows Best

Top-down decisions about opportunities and risks for participants

- rather than respecting their autonomy: IRBs could ensure that potential participants will be well informed, then let them decide

Projects disallowed that would trouble some potential participants

- rather than identifying the small %age who would be troubled and encouraging them not to participate

# Particularly for HIV / AIDS Research

Business as usual is especially damaging here...

Failure to expedite or exempt eligible research

Failure to use or encourage research on relevant risks  
or ethical issues, or decisional capacities

Top-down decisions about opportunities and risks for  
participants, acting as gatekeeper, rather than:

- acting as educator
- respecting their ability to make their own decisions
- relevant community expertise input

# Who Decides, on What Basis?

Hypothetical project involving mental illness → 3 views:

IRB members without training in psychopathology asked to judge how and how well psychotic outpatients would respond to being informed that identifying information may have been stolen

- 1) “If participants were competent to consent in the first place, they’re competent to deal with this information”
- 2) “Deciding to withhold the information is paternalism”
- 3) “Informing them would likely do much more harm than the extremely low probability of partial identity theft”

# Who Decides, on What Basis?

A hypothetical project on HIV / AIDs and other STDs proposes:

- To use snowball sampling to identify subjects
- To provide extensive oral discussion of the protocol with potential participants but no written informed consent
- To compensate participants with cash rather than a check
- To not require participants tested for HIV receive the results

These features of the research violate common IRB practice but arose from the researchers' extensive consultation with and ongoing involvement of community members

How to persuade (educate) your IRB?

# Research on Research Regulation

Virtually no scientific evidence brought to bear in the debate about how IRBs do, or should, function...

“It is quite remarkable how little we really know about the structure and function of IRBs.”

- Steven Breckler, APA Psychological Science Agenda, volume 19, #10, 11/2005

The White Paper calls for systematic research on IRBs

- How they operate
- How they define “minimal risk”
- Catalog best practices, common problems / solutions

A promising new venue:

Journal of Empirical Research on Human Research Ethics

[www.jerhre.org](http://www.jerhre.org)

# A Few Potential Research Topics

Numbers of protocols reviewed, numbers of serious abuses by discipline, common turnaround time

What is adequate and respectful informed consent

What participants perceive as risk or discomfort

How much risk or discomfort is “minimal” – varies!

How benefits to participants and communities balance risk and discomfort 2° community

How to approach, respect, inform, recruit, and retain stigmatized (even fugitive) participants ethically

Oh, and... effectiveness of the IRB system in protecting participants and in fostering the best science

# Says a Tennessean...

“At the base of our investment in research lies the trust of the American people and the integrity of the scientific enterprise.

If that trust is threatened . . . then not only are the people placed at potential risk, but the welfare of science itself is undermined.”

Senator Albert Gore, Jr.

1981 Congressional Hearings on *Fraud in Biomedical Research*

Thank you