

When is it Research and When is it Not? The  
Special Cases of Quality Assurance Studies and  
Medical Device Improvement

David Hoffman, Chief Compliance Officer, Carthage Area Hospital  
Lecturer in Bioethics, Columbia University  
Presentation to the  
Health Care Compliance Association  
Research Compliance virtual Conference  
June 2, 2020

1

Why are we here?

When Johns Hopkins launched its quality assurance study of central line infection control practices, they exposed a fault line in the medical research community that continues to generate strong opinions about when IRB approval is appropriate

2

In addition to the ongoing debate about whether their intervention required IRB approval due to human exposure to harm, the OHRP reaction to the Hopkins study triggered a debate about the need for IRB review as a condition of scholarly publication

3

This presentation will explore the lingering impact of the OHRP-Johns Hopkins confrontation. We will discuss how to evaluate application of the common rule to non-patient focused research and medical device improvement efforts

4

So, what's the problem?

5

So, what's the problem?

It's the word RESEARCH.

It's a Homonym Problem.

6

Research

What does the word mean from a IRB perspective?

7

Which begs the question,

why do we have IRBs?

8

Which begs the question,  
what is an IRB?

9

## 45 CFR 46

### **Subpart A—Basic HHS Policy for Protection of Human Research Subjects**

Source: 82 FR 7259, 7273, Jan. 19, 2017, unless otherwise noted.

[Back to Top](#)

#### **§46.101 To what does this policy apply?**

(a) Except as detailed in §46.104, this policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency that takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States. Institutions that are engaged in research described in this paragraph and institutional review boards (IRBs) reviewing research that is subject to this policy must comply with this policy.

10

# 45 CFR 46

- (l) *Research* means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
  - (1) Scholarly and journalistic activities (*e.g.*, oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
  - (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
  - (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
  - (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

11

And Yet,

IRB approval is required for other reasons and in other settings.

12

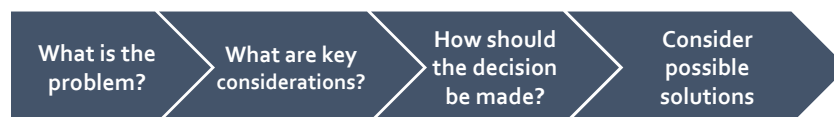
# The requirement for publication

What does that have to do with IRB protection of Human Subjects?

How do we solve this problem?

13

## ELEMENTS IN AN ETHICAL DECISION-MAKING PROCESS



Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

14

**1. What is the problem?**

- o What are the key ethical issues/questions?
- o Gather the facts (who, what, when, where, why?)
- o Identify the affected parties (e.g., stakeholders)

**2. What are the key considerations?**

- o Assess relevant laws– Identify the relevant ethical principles
- o Identify the risks and benefits (short/long-term, magnitude/probability)
- o Identify the rights/role of autonomy
- o Consider issues of justice
- o Consider other obligations/responsibilities
- o Consider your moral intuitions (“gut feelings”)
- o Consider your biases
- o Weigh competing principles
- o May need to revisit Step 1, to gather additional facts

**3. How should the decision be made?**

- o Consider processes– Transparency– Consulting with others
- o Experts– Stakeholders – e.g., community representatives

**4. What are the possible solutions?**

- o Think creatively about potential actions/solutions
- o Consider possible objections/alternatives
- o Decide on the proper ethical action

Note: This presentation is for educational purposes only.

15

## THE CENTRAL LINE INFECTION CONTROL STUDY

- Every year, physicians insert catheters into the blood vessels of millions of patients, of whom 80,000 unfortunately develop infections, and 28,000 die.
- In 2003, Peter Provonost, a prominent researcher at Johns Hopkins, and his colleagues, with support from a grant from the Agency for Health Care Research and Quality, studied whether a five item check list that included use of certain type of approved central lines and cleansers, and hand washing would reduce these infections at 67 hospitals in Michigan.
- Regulations exempt from IRB review studies that are not “research”, defined as, “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”
- Federal agencies have clarified:
  - Investigators who intend to publish their results are, by definition, conducting “research that requires IRB review,” because the researchers are thereby seeking “to contribute to generalizable knowledge.”
  - Studies may be exempt if they are of normal educational practices or QI studies of “public benefit and service programs” (i.e., are not seeking to contribute to “generalizable knowledge”).

Note: This presentation is for educational purposes only.

16



## THE CENTRAL LINE INFECTION CONTROL STUDY

- The researchers submitted the protocol to the Hopkins IRB as research and requested an exemption from IRB review, saying the study was only quality improvement research. The IRB granted the exemption.
- The Hopkins IRB thus did not review the study, and said the protocol was exempt from IRB review at Hopkins or at any the 67 hospitals, and that informed consent was therefore not needed.
- After three months, the study found that the median rate of infections dropped dramatically from 2.7 to 0 infections for every 1,000 patient days with a catheter (i.e., the total number of days on which patients, cumulatively, have these tubes in them). Over the next 16 to 18 months, the mean rate continued to fall (from 7.7 to 1.4).
- Yet the Office for Human Research Protections (ORHP) then rebuked the investigators and the IRB.

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

17

## THE CENTRAL LINE INFECTION CONTROL STUDY

### Questions:

1. Should the IRB have reviewed the study?
2. Should the researchers have obtained informed consent and if so, from whom?
3. What if the researchers were including in the protocol the use of a new type of central line, the safety and efficacy of which have not yet been established, and which therefore does not yet have FDA approval?
  - Would that change your considerations?, and if so, how?
4. Should the current regulations be changed?

Note: This presentation is for educational purposes only.


 COLUMBIA UNIVERSITY  
School of Professional Studies

18



1. **What is the problem?**
  - o What are the key ethical issues/questions?
  - o Gather the facts (who, what, when, where, why?)
  - o Identify the affected parties (e.g., stakeholders)
2. **What are the key considerations?**
  - o Assess relevant laws– Identify the relevant ethical principles
  - o Identify the risks and benefits (short/long-term, magnitude/probability)
  - o Identify the rights/role of autonomy
  - o Consider issues of justice
  - o Consider other obligations/responsibilities
  - o Consider your moral intuitions (“gut feelings”)
  - o Consider your biases
  - o Weigh competing principles
  - o May need to revisit Step 1, to gather additional facts
3. **How should the decision be made?**
  - o Consider processes– Transparency– Consulting with others
  - o Experts– Stakeholders – e.g., community representatives
4. **What are the possible solutions?**
  - o Think creatively about potential actions/solutions
  - o Consider possible objections/alternatives
  - o Decide on the proper ethical action

Note: This presentation is for educational purposes only.

19



SUBSCRIBE OR RENEW →

SEARCH  

**CASE RECORDS OF THE MGH**  
Case 15-2020: A 79-Year-Old Man with Hyponatremia and Involuntary Movements of t...

**Notable Articles of 2019**  
1 exclusive collection

**EDITORIAL**  
Atezolizumab plus Bevacizumab  
— A Landmark in Liver Cancer

**CASE RECORDS OF THE MGH**  
Case 17-2020: A 68-Year-Old Man with Covid-19 and Acute Kidney Injury

**ORIGINAL ARTICLE**  
Rivaroxaban or Enoxaparin in Nonmajor Orthopedic Sur...

A correction has been published 1

**ORIGINAL ARTICLE**

## An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

Peter Pronovost, M.D., Ph.D., Dale Needham, M.D., Ph.D., Sean Berenholtz, M.D., David Sinopoli, M.P.H., M.B.A., Haitao Chu, M.D., Ph.D., Sara Cosgrove, M.D., Bryan Sexton, Ph.D., Robert Hyzy, M.D., Robert Welsh, M.D., Gary Roth, M.D., Joseph Bander, M.D., John Kepros, M.D., et al.

Article **Figures/Media**

25 References 2558 Citing Articles Letters

### Abstract

**BACKGROUND**  
Catheter-related bloodstream infections occurring in the intensive care unit (ICU) are common, costly, and potentially lethal.

December 28, 2006  
N Engl J Med 2006; 355:2725-2732  
DOI: 10.1056/NEJMoa061115

---


**Related Articles**

**EDITORIAL** DEC 28, 2006  
Team-Based Prevention of Catheter-Related Infections  
R.P. Wenzel and M.B. Edmond

PDF

Help

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

20

10

# Peter Pronovost

From Wikipedia, the free encyclopedia

**Peter J. Pronovost**<sup>[3]</sup> is Chief Clinical Transformation Officer at [University Hospitals](#) (UH) health system in [Northeast Ohio](#). At UH, Pronovost is responsible for improving value across the health system, helping people stay well, get well and manage their most acute medical conditions. He is the clinical lead for population health and the lead for high-reliability medicine, with direct responsibility for the UH employee accountable care organization. He is also responsible for telehealth and virtual health programs serving patient and provider communities.

He previously served as an [intensive care specialist physician](#) at [Johns Hopkins Hospital](#) in [Baltimore, Maryland](#).<sup>[4]</sup> He is a Professor at the [Johns Hopkins School of Medicine](#) in the Departments of Anesthesiology and Critical Care Medicine, and Surgery, Professor of Healthcare Management at the [Carey Business School](#), Professor of Health Policy and Management at the [Johns Hopkins Bloomberg School of Public Health](#), and is Medical Director for the Center for Innovation in Quality Patient Care.

He introduced an intensive care [checklist](#) protocol that during an 18-month period saved 1500 lives and \$100 million in the State of [Michigan](#).<sup>[5]</sup> According to [Atul Gawande](#) in [The New Yorker](#), Pronovost's "work has already saved more lives than that of any laboratory scientist in the past decade".<sup>[6]</sup> In 2008 [Time](#) named Pronovost one of the [100 most influential people](#) in the world.<sup>[7]</sup> That same year, Pronovost was awarded a [MacArthur Fellowship](#).<sup>[1]</sup>

Pronovost's book *Safe Patients, Smart Hospitals: How One Doctor's Checklist Can Help Us Change Health Care from the Inside Out* was released in February 2010.<sup>[8]</sup>

**Contents** [\[hide\]](#)

- 1 [Early life and education](#)

Note: This presentation is for educational purposes only.

**Peter J. Pronovost**



**Born** February 22, 1965 (age 55)<sup>[1]</sup>  
Waterbury, Connecticut

**Citizenship**  United States

**Alma mater** [Fairfield, B.A., Sc.D. \(hon\)](#)<sup>[2]</sup>  
[Johns Hopkins, M.D., Ph.D](#)

**Known for** Intensive care [checklist](#) protocol

**Awards** 2008 [Time 100](#)  
2008 [MacArthur Fellow](#)

**Scientific career**

**Fields** [Anesthesiology](#)  
[Critical Care Medicine](#)

**Institutions** [Johns Hopkins Hospital](#)

 COLUMBIA UNIVERSITY  
School of Professional Studies

21



The NEW ENGLAND JOURNAL of MEDICINE

## Perspective

FEBRUARY 21, 2008

### Quality-Improvement Research and Informed Consent

Franklin G. Miller, Ph.D., and Ezekiel J. Emanuel, M.D., Ph.D.

Tens of thousands of patients die each year because of hospitals' failure to adhere consistently to standard procedures of safe and effective medical care. Accordingly, improving the quality

of routine hospital care is a public health imperative. An effective way to promote quality improvement is to conduct evaluative research on programs designed to implement standard practices for the safety and care of hospitalized patients.

opportunity to decide whether or not to participate. Can it be ethical to conduct such research without informed consent?

A recent investigation by the Office for Human Research Protections (OHRP) — the federal agency charged with overseeing

using chlorhexidine for skin cleansing before catheter insertion, minimizing the use of the femoral site for catheter insertion, and removing unnecessary catheters. In addition to the training of clinicians in such standard infection-control procedures, the project involved the use of a checklist to ensure adherence to the protocol. The result was a dramatic decrease in catheter-related infections: at baseline, the participating hospitals had a median

N ENGL J MED 358:8 WWW.NEJM.ORG FEBRUARY 21, 2008

765

Downloaded from [www.nejm.org](#) at UNIV OF FLORIDA HEALTH SCIENCE CENTER LIBRARY on April 23, 2008.  
Copyright © 2008 Massachusetts Medical Society. All rights reserved.

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

22

Tens of thousands of patients die each year because of hospitals' failure to adhere consistently to standard procedures of safe and effective medical care. Accordingly, improving the quality of routine hospital care is a public health imperative. An effective way to promote quality improvement is to conduct evaluative research on programs designed to implement standard practices for the safety and care of hospitalized patients.

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

23

Such research, however, poses an apparent ethical conundrum: it is often impossible to obtain informed consent from patients enrolled in quality-improvement research programs because interventions must be routinely adopted for entire hospitals or hospital units. When, for instance, research on a quality-improvement initiative that affects routine care is conducted in an intensive care unit (ICU), surgical suite, or emergency room, individual patients have no opportunity to decide whether or not to participate. Can it be ethical to conduct such research without informed consent? A recent investigation by the Office for Human Research Protections (OHRP) — the federal agency charged with overseeing human-subjects research — places this issue in bold relief.<sup>1</sup>

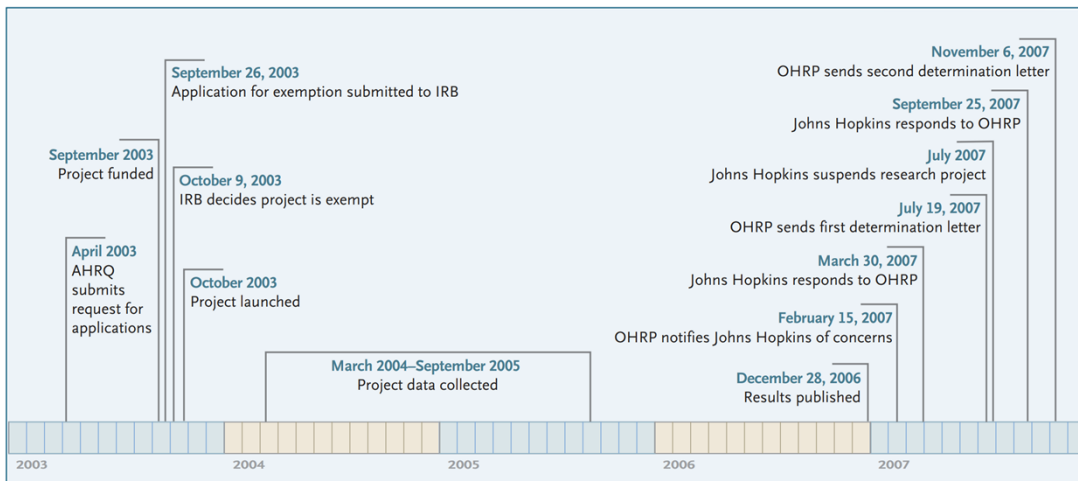
Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

24

Researchers at Johns Hopkins University coordinated a quality-improvement research project aimed at reducing catheter-related infections in 103 ICUs at 67 Michigan hospitals.<sup>2</sup> The study evaluated a protocol designed to routinely implement five evidence based procedures: having clinicians wash their hands, using full-barrier precautions during insertion of central venous catheters, using chlorhexidine for skin cleansing before catheter insertion, minimizing the use of the femoral site for catheter insertion, and removing unnecessary catheters. In addition to the training of clinicians in such standard infection-control procedures, the project involved the use of a checklist to ensure adherence to the protocol. The result was a dramatic decrease in catheter-related infections: at baseline, the participating hospitals had a median of 2.7 infections per 1000 catheter-days; after 3 months, the median had dropped to 0, and it remained there for 18 months. Publication of the results, however, triggered an investigation by the OHRP (see timeline).<sup>1</sup>

Note: This presentation is for educational purposes only.



**Timeline of Johns Hopkins Quality-Improvement Project.**

The October 9 decision by the institutional review board (IRB) was made by the IRB chair and one committee member, in accordance with Johns Hopkins policy. AHRQ denotes Agency for Healthcare Research and Quality, and OHRP Office for Human Research Protections.

Note: This presentation is for educational purposes only.

MILLER, EMANUEL:

In view of the provision for waiving consent, the OHRP's about the need for patients or surrogates to grant "legally effective informed consent" in its two determination letters seems unjustifiable.

N ENGL J MED 358:8 WWW.NEJM.ORG FEBRUARY 21, 2008

765

Downloaded from www.nejm.org at UNIV OF FLORIDA HEALTH SCIENCE CENTER LIBRARY on April 23, 2008 .  
Copyright © 2008 Massachusetts Medical Society. All rights reserved.

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

27

Can we live in a world where the word  
RESEARCH means two different things?

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

28

OF course we can.

In the Hopkins study who needed the protection of the IRB?

Who was the subject?

Who was the participant?

Note: This presentation is for educational purposes only.

What did OHRP accomplish by its investigation?

**ANYTHING?**

Note: This presentation is for educational purposes only.

IN CONCLUSION,

Let's stop tripping over the  
English language.

Note: This presentation is for educational purposes only.

 COLUMBIA UNIVERSITY  
School of Professional Studies

31



**BIOETHICS**  
Master of Science &  
Certificate Programs

Questions, Concerns?

David N. Hoffman  
[dnh2101@columbia.edu](mailto:dnh2101@columbia.edu)

<http://sps.columbia.edu/bioethics>

32