Flagler Hospital, Inc. Human Subjects Research Training: Based on Flagler Hospital, Inc. Institutional Review Board Policy (I-LIB/CME-009) with revised 2018 Common Rule Regulations

By Patricia D. Moore, PhD, RN and Celina Makowski, DHA, MBA, CHCP

2023

Objectives

At the conclusion of this educational activity, participants will be able to:

- Identify one historical key triggering event that led to the establishment of ethics in research.
- Explain the purpose of an Institutional Review Board (IRB).
- Define key changes incorporated in the Revised Common Rule.
- Describe the importance of Informed Consent.

Ethics in Research: Historical Background

- **Historical Key Triggering Events**:
  - **Nazi Experiments in Concentration Camps (1939-1944)[1]**
    - Prisoners kept in tanks of ice water, wounds intentionally infected
  - **Tuskegee Syphilis Study (1932-1972)[2]**
    - Impoverished black men with syphilis denied penicillin
  - **Research at Willowbrook State School, New York (1963-1975)[3]**
    - Intellectually disabled children exposed to hepatitis

1. Nazi Medical Expericments (n.d.). *The United States Holocaust Museum*. Retrieved from https://encyclopedia.ushmm.org/content/en/article/nazi-medical-experiments
2. 2.U.S. Public Health Service Syphilis Study at Tuskegee (2015). *CDC*. Retrieved from https://www.cdc.gov/tuskegee/
3. Willowbrook State School – A voice behind the wall. (n.d). Retrieved from http://willowbrookstateschool.blogspot.com/p/history.html

Ethics in Research: Historical Background

- Ethical Principles
  - The **Nuremberg Code (1947)** resulted from Nuremberg Trials (prosecution of Nazi Germany leadership). Includes the following criteria:
    - Researcher must inform study subjects about the research study and be qualified to conduct research
    - Research must be for the good of society; be based on results of animal experimentation and a knowledge of the natural history of a disease; and avoid all unnecessary physical, and mental suffering, and injury to research subjects
    - Subjects and/or researchers can stop a study at any time

Ethical Codes & Research Standards Ethical Codes. (n.d.). *Office of Human Research Protections*. Retrieved from https://www.hhs.gov/ohrp/international/ethical-codes-and-research-standards/index.html

Ethics in Research: Historical Background

- **Declaration of Helsinki (1964)[1]**
  - The World Medical Association's ethical principles for medical research involving human subjects.
- **National Research Act (1974)[2]**
  - Developed the National Commission for the Protection of Human Subjects of Biomedical And Behavioral Research that created the Belmont Report establishing ethical principles that govern all research supported by the U.S. government
  - Established the modern Institutional Review Board (IRB) system for regulating research involving human subjects
- **Declaration of Helsinki Revision (1975)[3]**
  - Supported the concept of Institutional Review Boards in the United States and Ethical Committees/Review Boards globally

1. Ethical Codes & Research Standards Ethical Codes. (n.d.). *Office of Human Research Protections*. Retrieved from https://www.hhs.gov/ohrp/international/ethical-codes-and-research-standards/index.html
2. The President's Council on Bioethics. (n.d.). Retrieved from https://bioethicsarchive.georgetown.edu/pcbe/reports/past_commissions/
3. Declaration of Helsinki 1975. *World Medical Association.* Retrieved from https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/doh-oct1975/

Ethics in Research: Historical Background

- **Belmont Report**
  - Created by the National Commission for the Protection of Human Subjects of Biomedical And Behavioral Research
    - Issued September 30,1978 and published in the Federal Register April 18,1979
  - Ethical principles that govern all research supported by the U.S. government. Basis for subsequent regulations designed to ensure protection of human subjects in research incorporating the following:
    - **Respect for Persons**-treat individuals as ***autonomous agents***; don't use people as a means to an end; allow people to ***choose for themselves***; provide ***extra protections*** for those with diminished autonomy (prisoners, children, cognitively impaired)
    - **Beneficence**-do ***no harm***; maximize possible benefits and ***minimize risks***
    - **Justice**-treat people ***fairly***, fair ***sharing of burdens and benefits*** of the research
- Watch Belmont Report Video (test questions associated) at https://www.youtube.com/watch?v=M6AKIIhoFn4&feature=youtu.be

Breaches in Research Ethics: Current Headlines

Facebook

Facebook emotion study breached ethical guidelines, researchers say

Lack of 'informed consent' means that Facebook experiment on nearly 700,000 news feeds broke rules on tests on human subjects, say scientists

Poll: Facebook's secret mood experiment: have you lost trust in the social network?

Charles Arthur

@charlesarthur

Mon 30 Jun 2014 04.51 EDT

10,858 371

This article is over 4 years old

The New York Times

An N.Y.U. Study Gone Wrong, and a Top Researcher Dismissed

Diane Ruffcorn, of Seattle, was a participant in the N.Y.U. study who said she had been sexually abused as a child. "I was given this drug, and all these tests, and then it was goodbye, I was on my own," she said. "There was no follow-up." Ruth Fremson/The New York Times

By Benedict Carey

June 27, 2016

KHN KAISER HEALTH NEWS

CONNECT WITH US:

HEALTH LAW | AGING | INDUSTRY | PHARMA | INVESTIGATIONS | MORE TOPICS | DATA & DOCS | Search

INVESTIGATION

University Under Fire For Off-The-Grid Herpes Vaccine Experiments

By Marisa Taylor

JANUARY 23, 2018

REPUBLISH THIS STORY

News Articles About Breaches in Research Ethics

1998

- *Study or Human Experiment? Face-Lift Project Stirs Ethical Concerns* by Philip J. Hilts
  - https://www.nytimes.com/1998/06/21/nyregion/study-or-human-experiment-face-lift-project-stirs-ethical-concerns.html

2001

- *Scholar Sets Off Gastronomic False Alarm* by John Kifner
  - https://www.nytimes.com/2001/09/08/nyregion/scholar-sets-off-gastronomic-false-alarm.html

2013

- *HHS-Funded Experiment Exposed Babies to Risk of Death and Blindness Without Informing Parents*
  - *https://www.citizen.org/media/press-releases/hhs-funded-experiment-exposed-babies-risk-death-and-blindness-without-informing*

2017

- *University could lose millions from "unethical" research backed by Peter Thiel* by Beth Mole
  - https://arstechnica.com/science/2017/11/university-could-lose-millions-from-unethical-research-backed-by-peter-thiel/

2018

- *The Homeless as Human Subjects* by *The Ethics and Society Blog*
  - *http://www.bioethics.net/2018/05/the-homeless-as-human-subjects/*

2022

- *Anti-Pesticide Researchers May Have Committed Serious Ethics Breaches*
  - *https://www.realclearscience.com/articles/2022/04/13/anti-pesticide_researchers_may_have_committed_serious_ethics_breaches_826830.html*

Breaches in Research Ethics: Professional Impact

10/16/2018 Harvard and the Brigham call for 31 retractions of cardiac stem cell research - STAT

STAT

Harvard and the Brigham call for more than 30 retractions of cardiac stem cell research

By Ivan Oransky @ivanoransky and Adam Marcus @armarcus

October 14, 2018

Brigham and Women's Hospital in Boston. *Aram Boy*

The New York Times

Harvard Calls for Retraction of Dozens of Studies by Noted Cardiac Researcher

Some 31 studies by Dr. Piero Anversa contain fabricated or falsified data, officials concluded. Dr. Anversa popularized the idea of stem cell treatment for damaged hearts.

By Gina Kolata

Oct. 15, 2018

JAMA Network

For The Media

News releases & journal articles from the JAMA Network

Post-Embargo News Releases Videos FAQ Contact Us Apply For Access

Post-Embargo News Releases > Our Embargo Policy Print

JAMA Network Retracts 6 Articles That Included Dr. Brian Wansink as Author

FOR IMMEDIATE RELEASE: SEPTEMBER 19, 2018

Media advisory: To contact JAMA Network Media Relations email mediarelations@jamanetwork.org.

CHICAGO – *JAMA*, *JAMA Internal Medicine* and *JAMA Pediatrics* have retracted six articles that included Brian Wansink, Ph.D., of Cornell University, Ithaca, New York, as author. Below is the notice of retraction published online today by *JAMA*, which references the retracted articles (see references 4-9). Similar notices were published online today in *JAMA Internal Medicine* and *JAMA Pediatrics*.

EDITORIAL

Notice of Retraction: Wansink B, Cheney MM. Super Bowls: Serving Bowl Size and Food Consumption. *JAMA*. 2005;293(14):1727-1728.

Howard Bauchner, MD

On May 8, 2018, notices of Expression of Concern[1-3] were published regarding articles published in *JAMA*[4] and the JAMA Network journals[5-9] that included Brian Wansink, PhD, as author. At that time, Cornell University was contacted and was requested to conduct an independent evaluation of the articles to determine whether the results are valid.

Cornell University has notified *JAMA* that based on its investigation they are unable to provide assurances regarding the scientific validity of the 6 studies. Their response states: "We regret that, because we do not have access to the original data, we cannot assure you that the results of the studies are valid." Therefore, the 6 articles reporting the results of these studies that were published in JAMA,[4] *JAMA Internal Medicine*,[5-7] and *JAMA Pediatrics*[8,9] are hereby retracted.

ARTICLE INFORMATION

Author Affiliation: *JAMA* and the JAMA Network, Chicago, Illinois.

Corresponding Author: Howard Bauchner, MD, Editor in Chief, *JAMA* and the JAMA Network, 330 N Wabash Ave, Chicago, IL 60611 (howard.bauchner@jamanetwork.org).

Published Online: September 19, 2018. doi:10.1001/jama.2018.14249

REFERENCES

First and Vegetables Last," "Hungry Grocery Shoppers Buy More Calories, Not More Food," and "Watch What You Eat: Action-Related Television Content Increases Food Intake" by Brian Wansink. *JAMA Intern Med*. 2018;178(8):1015. doi:10.1001/jamainternmed.2018.1986

3. Bauchner H. Expression of Concern: "Consequences of Belonging to the 'Clean Plate Club'" and "Preordering School Lunch Encourages Better Food Choices by Children" by Brian Wansink. *JAMA Pediatr*. 2018;172(6):522. doi:10.1001/jamapediatrics.2018.0940

6. Tal A, Wansink B. Fattening fasting: hungry grocery shoppers buy more calories, not more food. *JAMA Intern Med*. 2013;173(12):1146-1148. doi:10.1001/jamainternmed.2013.650

7. Tal A, Zuckerman S, Wansink B. Watch what you eat: action-related television content increases food intake. *JAMA Intern Med*. 2014;174(11):1842-1843. doi:10.1001/jamainternmed.2014.4098

8. Wansink B, Payne C, Werle C. Consequences of belonging to the "clean plate club". *Arch Pediatr Adolesc Med*. 2008;162(10):994-995. doi:10.1001

Laws and Regulations for Research

- All research, ***including research at Flagler Hospital, Inc***., is governed by national, state, and local laws.
- The "Common Rule" (Federal Regulations 45 CFR 46) *Office of Human Research Protection of the Department of Health and Human Services* (OHRP): ensures compliance with the principles of the Belmont Report and **establishes Institutional Review Boards and informed consent.**
  - Flagler Hospital, Inc. has assured the Office of Human Research Protection that all human subject research activities within Flagler Hospital, Inc. will be guided by the Belmont Report, will comply with the Common Rule, and any other applicable regulations. In return, Flagler Hospital, Inc. is issued a Federal Wide Assurance (FWA) number, which allows Flagler Hospital, Inc. to conduct research.
  - **Note: There are various laws that may pertain to particular research studies (example FDA); however, these laws are always in addition to the Common Rule.**

History of Federal Policy for the Protection of Human Subjects ("Common Rule")

- The current U.S. system of protection for human research subjects is heavily influenced by the Belmont Report, written in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. As previously mentioned, the Belmont Report outlines basic ethical principles in research involving human subjects. In 1981, with the Belmont report as foundational background, Health and Human Services (HHS) and the Food and Drug Administration, in conjunction with their respective statutory authorities, revised their existing human subjects research regulations.

- In 1991, the Federal Policy for the Protection of Human Subjects or the "Common Rule" was published and codified by 15 Federal departments and agencies. The HHS regulations, 45 CFR part 46, include four subparts: subpart A, also known as the Federal Policy or the "Common Rule"; subpart B, additional protections for pregnant women, human fetuses, and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children.

Revised Common Rule

- The ***Revised Common Rule*** was published by Office for Human Research Protections (OHRP) in July 2018 and made effective as of January 21, 2019.
- Key Changes:
  - Clarification of research definition and other key terms
  - Revisions in vulnerable population definition
  - Definition of Limited IRB Review and clarification of Types of Review processes
  - Clarification of Informed consent requirements including changes in alteration and waiver criteria for informed consent
  - Revision in elements of continuing review process for research
  - New requirement to post IRB approved informed consent form for each clinical trial conducted and/or supported by a federal department or agency
  - Effective in 2020: Any multiple site federally funded research study requiring an IRB approval, will be required to have a single IRB oversee the study

Key Terms from "Revised Common Rule"

- **Clinical trial**: a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
- **Human subject**: a living individual about whom an investigator (whether professional or student) conducting research:
  - (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  - (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Identifiable private information**: private information for which the identity of the research subject is or may readily be ascertained by the researcher and/or the identity of the research subject is directly associated with the information.
- **Intervention**: includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of research subjects or their environment that are performed for research purposes.
- **Minimal risk**: indicates that the probability and magnitude of harm and/or discomfort anticipated in research studies are not greater in and of themselves than those ordinarily encountered in daily life or during performance of routine physical/psychological examinations and/or tests.

Key Terms from "Revised Common Rule"

- **Private information**: includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place. Further more, when an individual provides information for specific purposes like research, he/she can reasonably expect that the information will not be made public (e.g., a medical record). However:
  - (i) Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the researcher and/or identity of the subject is directly associated with the information.
  - (ii) An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the researcher and/or identity of the subject is directly associated with the biospecimen.
- **Research**: a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
- **Vulnerable Populations**: Per OHRP, vulnerable populations are "individuals with impaired decision-making ability". When some or all research subjects are likely to be vulnerable to coercion or undue influence (such as children, prisoners, individuals with impaired decision-making capacity, economically or educationally disadvantaged persons) additional safeguards have been included in the research study to protect the rights and welfare of vulnerable populations participating in research.

Institutional Review Board (IRB) at Flagler Hospital, Inc.

- The Flagler Hospital, Inc. IRB is a **multidisciplinary group of individuals,** who are responsible to the Flagler Hospital, Inc. Governing Board for the review, approval, modification, or disapproval of all investigational research performed on human subjects at Flagler Hospital, Inc.
- **At all times**, the primary purpose of the Flagler Hospital, Inc. IRB research review process is to: **ensure informed consent, protect the rights and welfare of human subjects from undue research risk, and ensure research subjects' confidentiality and privacy.**

Flagler Hospital, Inc. IRB Membership

- The Flagler Hospital, Inc. IRB shall consist of at least eleven (11) members, appointed by the IRB Chair, and should include:
  - Three physicians
  - EVP & Chief Physician Executive
  - VP/Chief Nursing Officer
  - Administrator of Pharmacy & Support Services
  - Director of Risk Management
  - Two Nursing Administrators
  - Two members of the community, one not otherwise associated with Flagler Hospital, Inc. and who is not a member of the immediate family of a person who is affiliated with Flagler Hospital, Inc., and one with PhD-level education.

- The aforementioned membership should include one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.

NOTE: Flagler Hospital, Inc. IRB members' titles may have changed since publication of this presentation.

Reference Flagler Hospital, Inc. Institutional Review Board (IRB) Policy: I-LIB/CME-009

Flagler Hospital, Inc. IRB Submission Requirements

In compliance with the Flagler Hospital, Inc. IRB policy (PRE-009), the Principal Investigator (PI) is required to complete Flagler Hospital, Inc. Institutional Review Board (IRB) Research Application Form including all required information delineated in #5 IRB Submission Checklist, and submit all required information in the entirety to: flaglerhospitalIRB@flaglerhospital.org.

No research study may be conducted at Flagler Hospital, Inc. unless approved by Flagler Hospital, Inc. IRB.

Criteria for Flagler Hospital, Inc. IRB Approval

For approval of a proposed research study, as per Policy (PRE-009) the Flagler Hospital, Inc. IRB shall determine that all of the following requirements are satisfied:

1. The risks to human subjects are minimized. In assessing such risks, the IRB shall consider, among other factors, the following:

a. Whether risk(s) to the human subject(s) is so outweighed by the benefits to the human subject(s) and the importance of knowledge to be gained as to warrant a decision to approve the research and thereby allow the subject(s) to accept the risks (The risk to human subjects is reasonable in relationship to the anticipate benefits.).

b. Whether the rights and safety of the human subjects will be adequately protected.

c. Whether the informed consent will be obtained by adequate and appropriate methods.

d. Whether the proposed research will be or is being reviewed by the sponsor and/or the IRB as appropriate at intervals appropriate to the degree of the perceived risk.

2. The selection of human subjects is equitable.

3. A process has been established for obtaining informed consent from each prospective human subject or the subject's legal representative, in accordance with and to the extent required by FDA regulations and the policies of the state and the hospital.

4. A process has been established for documenting informed consent.

5. A procedure has been established to monitor data collected to ensure safety of human subjects.

6. The investigational research plan adequately provides protection of human subjects' privacy including maintenance of their data confidentiality.

LIMITED IRB REVIEW

A Limited IRB Review of research applications shall be performed by the IRB Chair or by one or more experienced members of the IRB, as designated by the IRB Chair. A Limited IRB Review can occur on an expedited basis and does not require consideration by a full convened board.

- Designated IRB reviewers may require modifications to the research application prior to approval.
- If a Limited IRB Review does not result in approval under the exempt categories, the designated IRB reviewers must evaluate whether or approval is appropriate under one of the expedited categories.
- Disapprovals of research applications must be made by the full convened IRB board.

Types of IRB Review

Note: The Flagler Hospital, Inc. IRB utilizes the *Office of Human Research Protections Human Subject Regulations Decision Charts* to determine the appropriate type of IRB review from among the following:

- **EXEMPT** – Determination of exempt review shall be performed by the IRB Chair or by one or more experienced members of the IRB, as designated by the IRB Chair.
  - A review may be performed by an IRB on research applications exempt from federal regulatory requirements and from the need for written informed consent. The Principal Investigator should indicate that the research study is potentially exempt. In addition to the usual requirement for approval by the IRB, Principal Investigators who seek approval for research applications involving use of hospital records shall conform to the policies and procedures of the hospital for use of medical records. Confidentiality and privacy must be maintained. *Reference 46.104(d)(1-8) for exempt categories.*

Office for Human Research Protection. (n.d.) HHS.gov. Retrieved from https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html

Types of IRB Review continued

- **EXPEDITED** – Expedited review may be performed by the IRB Chair or by one or more experienced members of the IRB, as designated by the IRB Chair.
  - No research application shall be disapproved by expedited review. If questions arise, the research application must be submitted for a full convened IRB review.
  - Guidelines for expedited reviews include research for minimal risk as listed in the FDA published list of *research* categories that may be reviewed by an expedited process.
  - Research that has been approved with contingencies through a full convened IRB review may undergo expedited review once minor changes have been made.

Expedited research must meet all the approval criteria under *45 CFR 46.111*, including all categories of consent (i.e. informed or waived).

What are the different types of clinical research? (2019, January 4). *U.S. Food & Drug Administration.* Retrieved from https://www.fda.gov/ForPatients/ClinicalTrials/Types/default.htm

Types of IRB Review continued

- **EMERGENCY USE EXEMPTION** – "Emergency Use" shall mean use of an unapproved or investigational drug or device (test article) on a human subject in a life threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. ***Emergency use is not considered research.***
  - The term ***test article*** refers to any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections *351 or 354-360F of the Public Health Service Act*.
  - An emergency use exemption can only be used in a life-threatening situation or with serious diseases or conditions when there is no available alternative and no time to obtain FDA approval.
  - The emergency use exemption allows for one emergency use of a test article without prospective full IRB review. Any subsequent use of the investigational test article should have prospective full IRB review and approval, unless the IRB is unable to convene a meeting prior to a second individual requiring an emergency treatment.

Types of IRB Review continued

- **EMERGENCY USE EXEMPTION** continued
  - In emergency use situations, informed consent must be obtained from either the patient or the patient's legally authorized representative. If obtaining informed consent is not possible, both the treating physician and an independent physician who is not otherwise participating in the clinical investigation must certify in writing the following information:
    - The subject is confronted by a life-threatening situation necessitating use of the test article.
    - Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
    - Time is not sufficient to obtain consent from the subject's legal representative.
    - No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
    - If, in the treating physician's opinion, immediate use of the research drug(s) and/or equipment is required to preserve the human subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the treating physician should make the determination and, within five (5) working days after use of the drug and/or device, have the determination reviewed and evaluated in writing by an independent physician who is not participating in the associated clinical investigation.

***NOTE*: Any emergency use exemption at Flagler Hospital, Inc. must be reported to the Flagler Hospital, Inc. IRB flaglerhospitalIRB@flaglerhospital.org by the treating physician within five (5) working days of the emergency use.**

Types of IRB Review continued

- **HUMANITARIAN DEVICE EXEMPTION (HDE)** --- A humanitarian device exemption is a special approval given by the FDA that allows marketing a device that is designed to treat or diagnose a condition that affects fewer than 4,000 individuals per year. An HDE is given even though the efficacy of the device has not been tested or proven, because it is not financially feasible to do the usual clinical testing when so few individuals are affected.
- With the exception of emergency use, the FDA requires IRB approval prior for use of a Humanitarian Use Device (HUD), even though the use is *not considered research*. A Humanitarian Use Device (HUD) can be approved in any of the following ways:
  - For general use (applies to future patients who are deemed appropriate),
  - For a specific group of patients who are identified and meet specific criteria,
  - Or on an individual patient basis.

Types of IRB Review continued

- **HUMANITARIAN DEVICE EXEMPTION (HDE) continued**
- A physician who is seeking IRB approval for a HUD must submit a letter to the IRB, including the following information:
  - type of approval being requested (general, group of patients, individual patient),
  - description of the HUD,
  - type of patient(s) who qualify for the HUD,
  - likelihood that the HUD is appropriate for the patient's condition/disease state.
- **NOTE**: For initial review of a HUD, a full convened Flagler Hospital, Inc. IRB meeting is required. The Flagler Hospital, Inc. IRB may use the expedited review process to address the continuing review request. The physician and/or designated administrator must request continuing review of the approved HUD from the Flagler Hospital, Inc. IRB **flaglerhospitalIRB@flaglerhospital.org**.

Types of IRB Review continued

- **CONTINUING REVIEW** – The Flagler Hospital, Inc. IRB shall conduct continuing review of research, regardless of degree of risk, not less than once per year.
- The intervals for continuing review shall be established by the Flagler Hospital, Inc. IRB at the time the research application including consent form is initially approved.
- As part of the continuing review process, the Flagler Hospital, Inc. IRB shall also determine intervals for submission of progress reports and document as appropriate.
- The Principal Investigator shall be required to promptly submit interim reports of any services and/or unexpected adverse drug reactions, irrespective of the regular progress report schedule, to the Flagler Hospital, Inc. IRB.

***NOTE*: Failure of the Principal Investigator to submit required reports in a timely manner, as specified by Flagler Hospital, Inc. IRB may result in withdrawal of Flagler Hospital, Inc. IRB approval**.

Informed Consent in Research

- All potential research study participants have a right to know what will happen to them prior to signing an informed consent for their participation in a research study, just as all patients entering a hospital have the right to know what will happen to them before signing a consent form for all procedures.
- Protection of research participants "right to know" revolves around the concept of informed consent.
- Informed consent is:
  - *Required* prior to any research study
  - *Documented* (usually with a signature on a written form)
  - *An initial and ongoing discussion between researcher and subject/participant* that provides new information that may impact a subject's/participant's willingness to continue in the research study

Refer to Office of Human Research Protection (OHRP) Basic Elements of Consent 46.116(b) and Flagler Hospital, Inc. Institutional Review Board (IRB) Policy: I-LIB/CME-009 Informed Consent (Addendum E).

Informed Consent in Research

- Key elements of Informed consent:
  - *type of information needed* by all research subjects/participants
  - *degree of understanding* required of all research subjects/participants in order to give consent
  - *free choice in giving consent* for all research subjects/participants.

- According to the Revised Common Rule, the following five factors must be included at the *beginning* of the informed consent process (including consent form):
  - Informed Consent is being sought for research and participation is voluntary
  - The purpose of research, expected duration of participation in research, research methodology
  - Foreseeable risks and/or discomforts to research participants
  - Benefits reasonably expected from research results to research participants or others
  - Appropriate alternative procedures or course of treatments

Refer to *Research Study Informed Consent Form*, Appendix E of Flagler Hospital, Inc. Institutional Review Board (IRB) Policy: I-LIB/CME-009

Informed Consent: Risks and Benefits of Research

- Principal Investigators must discuss the risks and benefits of research as part of the Informed Consent process in order to minimize the possibility that research participants have misconceptions about effects of research interventions

- Principal Investigators must explain to research participants, funding agencies, and the IRB why the potential benefits of research outweigh the risks of participating in a research study.

- The principle of beneficence also requires that Principal Investigators consider the condition of ***equipoise*** for clinical trials and other types of research requiring interventions to research participants

Informed Consent: Equipoise in Research

- **Equipoise**: “The principle of equipoise states that, when there is uncertainty or conflicting expert opinion about the relative merits of diagnostic, prevention, or treatment options, allocating interventions to individuals in a manner that allows the generation of new knowledge (eg, randomization) is ethically permissible. The principle of equipoise reconciles two potentially conflicting ethical imperatives: to ensure that research involving human participants generates scientifically sound and clinically relevant information while demonstrating proper respect and concern for the rights and interests of study participants.”[1]

- There should be a condition of equipoise in research studies that may pose risks to participants involving clinical trials or other types of interventions (i.e. teaching strategies). If the effects (results) of a research intervention in a particular study are already known (not new knowledge), then it is not ethical to expose participants in that research study to the risks that may be associated with the study when new knowledge cannot be gained. **A condition of equipoise is essential for gaining new knowledge through research.**

NOTE: Therefore, as emphasized in the revised Common Rule, a thorough discussion of risks and benefits is required in the beginning of the informed consent process to ensure that research participants do not have any misconceptions about research interventions and fully understand and accept the risks and benefits of their participation in a research study.

1. London, A. J. (2017). Equipoise in research: integrating ethics and science in human research. *JAMA, 317*(5), 525-526. doi:10.1001/jama.2017.0016

Breaches of Informed Consent in Research Studies

EINSTEIN
Albert Einstein College of Medicine

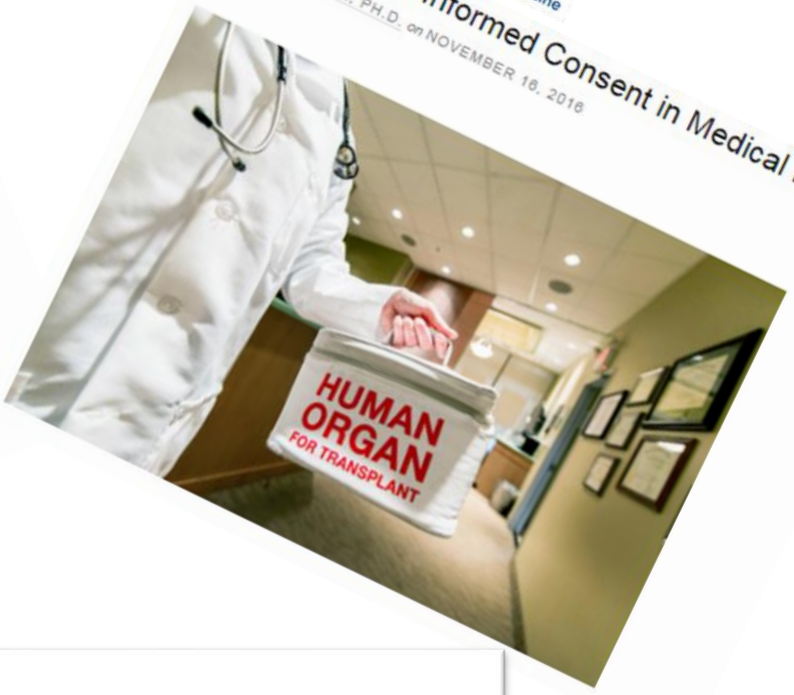
Informed Consent in Infant Research: Ethical Problems Remain

by RUTH MACKLIN, PH.D. on APRIL 18, 2013

EINSTEIN
Albert Einstein College of Medicine

The Erosion of Informed Consent in Medical Research

by RUTH MACKLIN, PH.D. on NOVEMBER 16, 2016



MINNEAPOLIS

Patients sedated by ketamine were enrolled in Hennepin Healthcare study

Forced sedation in their best interest, hospital says.

By Andy Mannix Star Tribune | JUNE 23, 2018 — 7:51PM

"Egregious and shocking deficiencies in the informed-consent process"


The Crux

« Archivists Want AI to Help Save, Analyze Everything Trump Says
The Frog Tongue's Sticky Secrets Revealed »

You Might Be in a Medical Experiment and Not Even Know It

By Alice Dreger | January 31, 2017 12:34 pm


VA HEALTHCARE

Portland VA: Human Experiments Unethical, No Consent

By Benjamin Krause - April 27, 2016

Facebook Twitter LinkedIn Email Print

Welcome to the
Portland VA Medical Center

HHS-Funded Experiment Exposed Babies to Risk of Death and Blindness Without Informing Parents

- "…as documented in a March 7, 2013, letter from the Office for Human Research Protections (OHRP) in the Department of Health and Human Services (HHS) to the University of Alabama at Birmingham, one of the lead institutions for the SUPPORT study, the consent forms for the study did not disclose to the babies' parents any of the risks of the experimental oxygen management interventions, including risks of severe retinal damage, possible blindness, neurologic injury and death. The consent forms also failed to address two other critically important pieces of information:

• That one purpose of the research was to determine whether extremely premature infants were more likely to die if treated with the higher versus lower oxygen target; and

• An explanation of how the infants would be treated if they weren't in the study compared to how they would be treated by participating in the study.

Dreger. A. (2017). You might be in a medical experiment and not even know it. The Crux.Retrieved from http://blogs.discovermagazine.com/crux/2017/01/31/medical-experiment-informed-consent/#.XHb_UMBKjRY

HHS-Funded experiment exposed babies to risk and death and blindness without informing parents. (2013, April 10). Retrieved from https://www.citizen.org/media/press-releases/hhs-funded-experiment-exposed-babies-risk-death-and-blindness-without-informing

Krause, B. (2016) Portland VA: human experiments unethical, no consent. Retrieved from https://www.disabledveterans.org/2016/04/27/portland-va-human-experiments-unethical-no-consent/

Informed Consent: Alteration and Waiver Criteria

- Under some conditions, elements of informed consent may be altered or waived. It is the Principal Investigator's responsibility to request alterations or waivers of informed consent, and to ensure that in doing so, the rights and welfare of research participants are adequately protected. The Principal Investigator is required to submit a written request incorporating the appropriate criteria elements referenced in following slide that justifies his/her written request.

Informed Consent: Alteration and Waiver Criteria

45 CFR 46.116(c) and (d) –Alteration or Waiver of Informed Consent Criteria

The Common Rule permits an IRB to approve the conduct of research without meeting all of the required elements of informed consent. Requests to alter or waive the consent process may be granted under the following conditions:

1. Government Program Evaluation Research

a. The research is an evaluation of a public program of services, is subject to governmental approval, and is evaluating procedures for obtaining benefits, changes in the program, or methods or levels of payment to be made under the program, AND

b. The research cannot practicably be carried out without the alteration or waiver

2. Other Research

a. The research involves no more than minimal risk,

b. The alteration or waiver will not adversely affect the rights and welfare of the subject,

c. The research cannot practicably* be carried out without the alteration or waiver; AND

d. The subjects will be provided with additional pertinent information, if appropriate, after participation.

<u>*NOTE</u>: In interpreting the meaning of *practicability* the standard to be met goes beyond inconvenience of the Principal Investigator. There must be reasons that make it inadvisable or infeasible to obtain altered or waived elements of informed consent, for the IRB to approve a request to alter or waive elements of an informed consent.

Informed Consent: Alteration and Waiver Criteria

- **45 CFR 46.117 – Waiving Documentation of Informed Consent Criteria**
- Informed consent pertains to a process. It is possible to obtain informed consent without documenting the process (i.e. consent form), and this may be advisable in some settings. However, waiver of documentation is not the same as waiver of informed consent requirements.
- Requests to waive the requirement to obtain a consent form may be granted when:
  - The consent form is the only record linking the participant and the research, and the principal risk to the participant would be potential harm resulting from a breach of confidentiality. Participants will be asked if they want documentation linking them to the Principal Investigator, and the participants' wishes shall govern.

    OR
  - The research presents no more than minimal risk and involves no procedures for which written consent would be required outside of the research context (e.g. drawing a blood sample, or asking shoppers in a mall about the ambient lighting or temperature).

NOTE: When submitting a request for waiver of documentation of consent, the request must be accompanied by a script of the information to be given orally.

Office for Human Research Protection. (n.d.) Retrieved from http://www.hhs.gov/ohrp/regulations-and-policy/decision-trees/#c10

Broad Consent: Relationship to Informed Consent

Broad Consent Defined

- Under the revised Common Rule, *Broad Consent* is an (optional) alternative informed consent process for use only for the storage, maintenance, and secondary use of identifiable private information or identifiable biospecimens for future, yet-to-be-specified research. To utilize *Broad Consent* the researcher responsible for the storage of the identifiable data/biospecimens is required to:
  - identify the types of research that may be conducted with the data/biospecimens,
  - record and track who has agreed to or refused consent, and
  - track the terms of consent to determine whether proposed future secondary research use falls within the scope of the identified types of research

NOTE: ***At this time, Flagler Hospital, Inc. IRB, will not mandate or implement use of Broad Consent due to lack of an extensive and seamless IT research management system for tracking purposes, including exemption categories 7 and 8, which rely on Broad Consent (*Reference 46.104(d)(1-8) for exempt categories).**

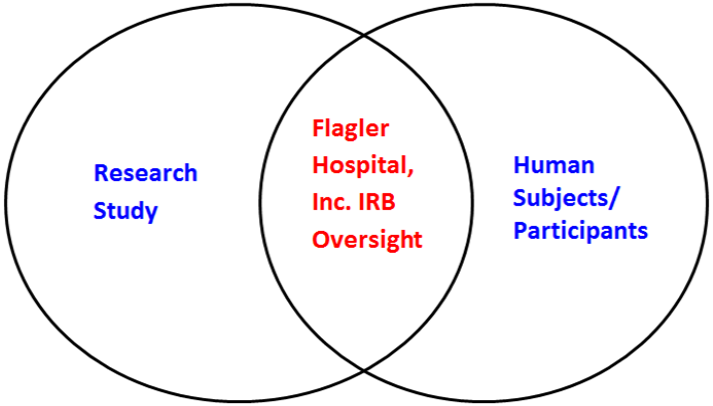
For more information pertaining to ***Recommendations for Broad Consent,*** *refer to* https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-august-2-2017/index.html

Revised Common Rule Key Change with Multi-Site Research

Effective as of 2020

- Any multiple-site federally funded research study requiring IRB approval, will be required to have a single IRB oversee the research study.

<u>Nevertheless, remember that all proposed research at Flagler Hospital, Inc. must always be submitted to the Flagler Hospital, Inc. Institutional Review Board (IRB) Policy: I-LIB/CME-009</u>



Remember:

No research study may be conducted at Flagler Hospital, Inc. unless approved by Flagler Hospital, Inc. IRB.

Submit all research applications to **flaglerhospitalIRB@flaglerhospital.org**.