STFM 2018 Annual Spring Meeting

The Institutional Review Board (IRB): Everything You Wanted to Know But Were Afraid to Ask

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Workshop Objectives

- Review basic guidelines regarding the ethical conduct of research
- Review the history of human subject protection
- Discuss issues of informed consent
- Discuss the ethics of and use of incentives for recruitment and participation of human subjects in research studies
- Discuss QI vs Evaluation vs Human Subjects Research
- STFM Connect: IRB Determination Template
- **Examples for Attendee Participation**

Direct and Indirect Needs for Human Subjects Protection

- There are a number of challenges to ethical conduct in research!
- Whether conducted in an academic setting or a healthcare institution/agency/organization, research involving human subjects often raises ethical concerns as study participants may experience risks and inconveniences primarily to benefit others by advancing knowledge.
- Ethical questions may arise at any time during the research process – from the design phase to subject recruitment to data collection to analyses and dissemination of study results.

Direct and Indirect Needs for Human Subjects Protection

- Institutions engaged in research using human subjects are required to provide written assurance of compliance with regulations (including documentation that the IRB reviewed the research project) to funding sources.
- There may be times when multiple IRBs must approve the study (e.g., for multi-center trials, for collaborative projects between two agencies, etc.). Studies conducted at multiple sites may pose additional IRB concerns (e.g., maintaining confidentiality of data held at multiple sites; ensuring consistency of protocols between sites, etc).

The History of the Human Subjects Protection System

- The modern story of human subjects protections began with the *Nuremberg Code* (of 1947), developed for the Nuremberg Military Tribunal as the standard by which to judge the human experimentation conducted by the Germans.
- The Code captures many of what are now taken to be the basic principles governing the ethical conduct of research involving human subjects.
- The first provision of the Code states that "*the voluntary consent of the human subject is absolutely essential*."
- Freely given consent to participation in research is the *cornerstone* of ethical experimentation involving human subjects.

The History of the Human Subjects Protection System

- The Code provides details implied by such a requirement:
  - capacity to consent;
  - freedom from coercion; and
  - comprehension of the risks and benefits involved.
- Other provisions require:
  - the minimization of risk and harm;
  - a favorable risk / benefit ratio;
  - qualified investigators using appropriate research designs; and
  - freedom for the subject to withdraw at any time.

The History of the Human Subjects Protection System

- Similar recommendations were made by the World Medical Association in its *Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects* – first adopted in 1964.
- In the U.S., regulations protecting human subjects first became effective in 1974. The regulations established the IRB as one mechanism through which human subjects would be protected.

The History of the Human Subjects Protection System

- The National Research Act, passed in 1974, led to the issuance of reports and recommendations identifying the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and recommending guidelines to ensure that research is conducted in accordance with those principles – known as *The Belmont Report (submitted in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research – the commission established by the National Research Act)*.

The History of the Human Subjects Protection System

- The Belmont Report set forth the basic ethical principles of respect for persons, beneficence, and justice – *the quintessential requirements for the ethical conduct of research involving human subjects*.
- Respect for persons involves a recognition of the personal dignity and autonomy of individuals, and special protection of those persons with diminished autonomy. This principle underlies the need to obtain *informed consent*.

The History of the Human Subjects Protection System

- Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm. This principle underlies the need to engage in a risk / benefit analysis and to *minimize risks*.
- Justice requires that the benefits and burdens of research be distributed fairly. This principle requires that subjects be *fairly selected*.

Historical Consequences of Not Having IRB Oversight

- Tuskegee Study of untreated syphilis in African American men, 1932-1972
- Walter E. Fernald State School, 1946-1953
- Thalidomide, 1957-1961
- Jewish Chronic Disease Hospital, 1963
- Willowbrook Hepatitis Study, 1963-1966
- Holmesburg Prison, 1964-1968
- Stanford Prison Experiment, 1971
- Johns Hopkins Study of Lead Paint Hazards, 1990s - 2001

Institutional Review Board (IRB)

- The goal of the Institutional Review Board (IRB) (AKA: Human Subjects Committee or Committee for the Protection of Human Subjects Research) process is **to protect the rights and welfare of those individuals who contribute to the research process by participating as subjects**. In protecting the rights of subjects, the IRB also **protects the institution and the researcher from the potential consequences of an inadequate consent process or the exposure of the subject to a negative risk**.
- "The ultimate responsibility for protecting human subjects must be borne by the institutions that perform the research." (Shalala, D. Protecting research subjects - what must be done. New Engl J Med 2000;343:808-10)

Informed Consent

- Informed consent requires documentation ensuring that research subjects have voluntarily accepted to participate in the research and have been properly informed of each step in the research process.
- Informed consent should include: an invitation to participate in the research study; the purpose of the research; the selection criteria; the research procedures; the description of the benefits and risks; an alternative treatment if an experimental procedure is offered; the possibility to have questions answered by the study team; and an assurance of confidentiality.

Informed Consent

- Informed consent ensures the privacy (and sometimes the anonymity) of research subjects.
- Issues of informed consent are particularly important for vulnerable populations (e.g., the disabled, inmates, those with cognitive impairments or mental illness, children, pregnant women, and the elderly) where comprehending information and making voluntary choices isn't always possible.

Informed Consent

- Under federal guidelines, there are 2 circumstances in which informed consent is not required:
  - when the research is exempt from the regulations; and
  - when consent may be waived.
- Research involving surveys, interviews, or observation of pubic behavior, and research using existing records *may* be exempt from the federal regulations provided that data are recorded in such a way that the human subjects cannot be identified either directly or through linked identifiers.

Informed Consent

- Retrospective chart reviews (e.g., medical/school records) *may* also be conducted without individual consent, provided that identifying information is not recorded, directly or through identifiers linked to the subject.
- HOWEVER, individual IRBs may be more strict than federal regulations and may require IRB review and subsequent study subject consent.

Informed Consent

- Additionally, IRBs may no longer consider collection of some data (such as dates) as exempt if it includes any of the 18 identifiers specified in the federal privacy regulations mandated by the Health Insurance Portability and Accountability Act (HIPAA).
- Research that poses minimal risk but does not qualify as exempt may be eligible for review under the expedited process.

HIPAA

- HIPAA is the **Health Insurance Portability and Accountability Act**.
- It is a complex regulation that affects many researchers at all universities.
- HIPAA was designed to protect the use and disclosure of **Protected Health Information** (**PHI**).
- This regulation is applicable if your research study uses or will use PHI belonging to a provider/insurer of health services.

HIPAA

- The following 18 identifiers are considered Protected Health Information (PHI):
  - Names
  - Geographic subdivisions smaller than a state (addresses, zip codes, etc.)
  - Telephone numbers
  - Fax numbers
  - Email addresses
  - Social security numbers
  - Medical record numbers
  - Health plan beneficiary numbers
  - Account numbers
  - Certificate/license numbers
  - Vehicle identifiers and serial numbers (including license plate numbers)
  - Device identifiers and serial numbers
  - Web URLs
  - Internet protocol (IP) address numbers
  - Biometric identifiers (finger and voice prints)
  - Full face photographic images
  - Any other unique identifying number, characteristic or code

Incentives for Participation

- With many, many research projects, study subjects are often ‘paid’ for participating in research funded by federal bureaus, state agencies, private institutions, etc.
- Gone are the days when internal incentives – i.e., ‘wanting to help’, were sufficient to recruit subjects.
- In some cases, incentives are monetary.
- In other cases, ‘rewards’ are offered in lieu of money (e.g., free medical care, free medications, gift certificates to local stores, movie tickets, raffle ‘tickets’ – a chance to win a bigger prize, offers to donate money to a local charity, etc.).

Incentives for Participation

- Regardless of the external incentive, IRBs must consider whether 'paid' participants in research are recruited fairly, informed adequately, and reimbursed appropriately.
- Taking into consideration the subjects' medical, employment, and educational status, as well as their financial, emotional, and community resources, the IRB must determine whether incentives for participation in research constitute *undue inducements* or *coercion*.
- Federal regulations governing research with human subjects contain no specific guidance for IRB review of payment practices.

Incentives for Participation

- One of the primary responsibilities of the IRB is to ensure that a subject's decision to participate in research is truly *voluntary*.
- Clear cases of coercion may seem obvious, but 'undue inducement' is sometimes more difficult to recognize.
- Undue inducements may be problematic because:
  - Offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and
  - They may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling – or continuing – as participants in the research project.

The IRB Process

- The purpose of the IRB is to review research and determine if the rights and welfare of human subjects involved in research are adequately protected.
- It has the authority to approve, require modification, or disapprove all human subjects research activities.
- Research approved by the IRB may be subject to review/ approval or disapproval by officials of the institution.

The IRB Process

- Office for Human Research Protections (OHRP), overseen by the U.S. Department of Health and Human Services, oversees all IRB functions at academic institutions and performs periodic audits of these institutions and the IRB applications approved.
- **OHRP can halt ALL HUMAN SUBJECT RESEARCH at an institution found not to be in compliance.**

The IRB Process

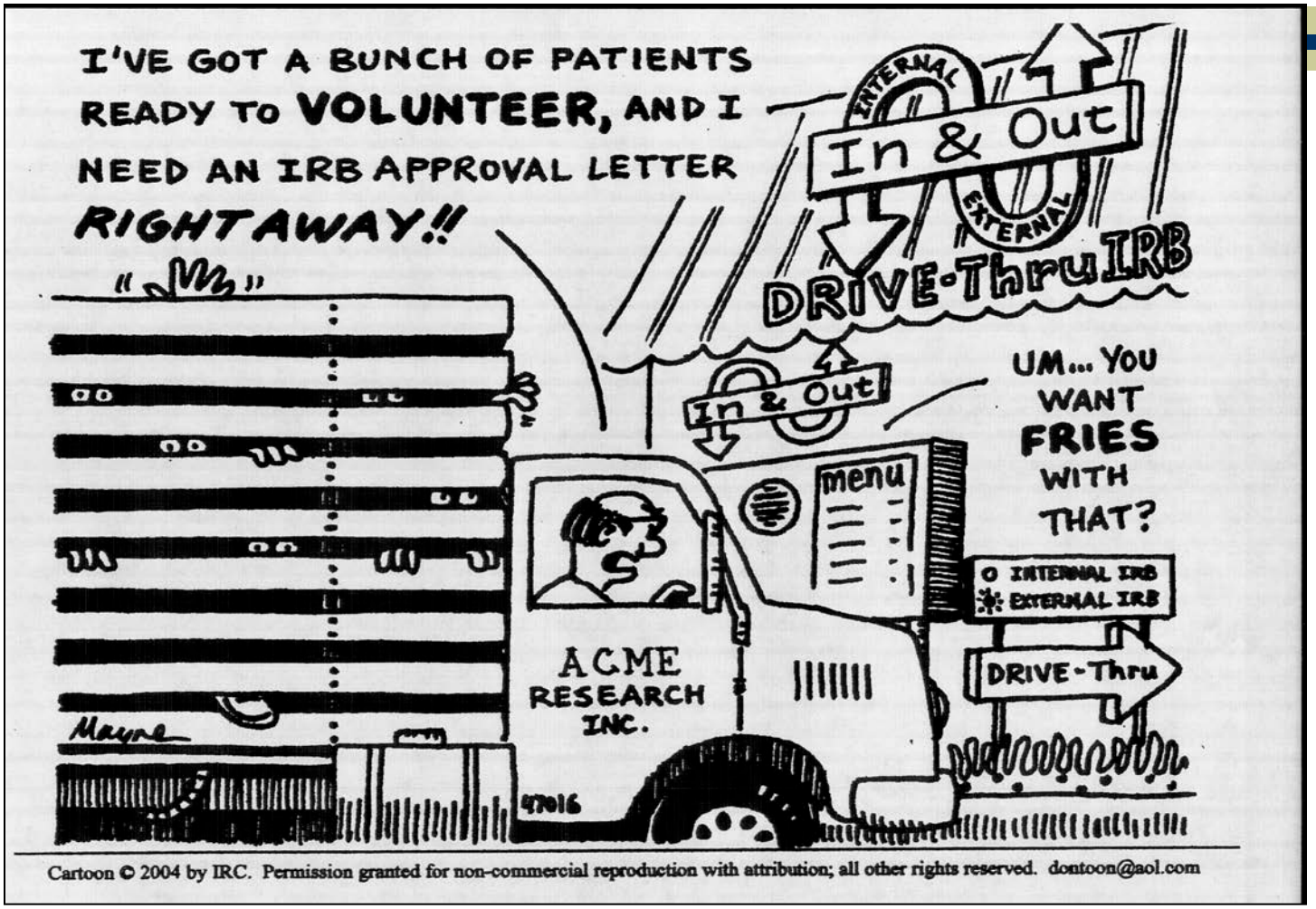
- The type of IRB review that is required typically depends on the level of risk presented by the study. The primary focus of IRBs is on the safety and well-being of research participants.
- The IRB office is typically a valuable resource in determining whether a research project requires a full or expedited review or whether the project may be exempt from review.

Types of Human Subject Reviews

- IRB reviews are qualified as one of three types: full, expedited, or exempt.
- **The IRB office** determines which level of review is needed.

- Full IRB Reviews:
  - Studies that include drug and device trials, vulnerable populations (children, prisoners, pregnant women), and high risk studies.

Expedited Reviews – Not…



Types of Human Subject Reviews

- Expedited Reviews:
  - Expedited review does not mean “fast”. It means that the study qualifies as minimal risk and does not need the approval of the entire review board.
  - Research involving data, documents, records or specimens that have been collected or will be collected solely for **nonresearch** purposes (e.g., medical/school record reviews, discarded tissue from surgical/pathology procedure, registry studies).

Types of Human Subject Reviews

- Expedited Reviews (continued):
  - Research on individual or group characteristics and behavior or research using surveys, interviews, focus groups, program evaluations, and quality assurance methodologies (see additional handouts on QI projects and program evaluations).
  - Collection of data through noninvasive procedures routinely employed in the clinical practice, excluding procedures involving x-rays (e.g., sensors attached to the skin, body composition assessment, moderate exercise).

Types of Human Subject Reviews

- Reviews receiving Exempt status:
  - Research involving prisoners does not qualify for exemption, nor can a project be exempt if the funding agency prohibits this.
  - Research conducted in an established or commonly accepted educational setting, involving normal education practices such as instructional strategies, research on effectiveness, or comparison among instructional techniques, curricula or classroom management.

Types of Human Subject Reviews

- Reviews receiving Exempt status (continued):
  - Research involving the use of educational tests, survey procedures, interview procedures or observation of public behavior as long as the information obtained is recorded such that the human subject cannot be identified directly or through identifiers linked to the subjects.
  - However, if there's a possibility that any disclosure of human subjects' responses outside of the research could reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation, the study will not qualify for an exemption.

Types of Human Subject Reviews

- Reviews receiving Exempt status (continued):
  - Research that involves only the collection or study of **existing** data, documents, records, pathological specimens, or diagnostic specimens. Existing means existing before the research is proposed or initiated; existing at the time of request. The data, documents, records, etc., to be used must be publicly available OR recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Types of Human Subject Reviews

- Reviews receiving Exempt status (continued):
  - Exemption from regulations does not necessarily mean that there is no IRB oversight. Many IRBs do not allow investigators to determine exempt status themselves (though this *is* allowed by federal guidelines); rather, there is a formal process for making such a determination.
  - Because journals are increasingly requiring evidence of IRB approval, it would be wise to consult with the IRB about exempt status, even if the project does not require formal review.

The IRB CITI Process

- The Collaborative IRB Training Initiative (CITI) program is the vehicle for ensuring comprehensive education in bioethics and human subjects protection.
- The CITI program is a 13-module program created by 'IRB experts' and is used by many academic health centers across the country. Certification via the CITI exam can be transferred to another academic institution.
- The complete set of modules may take up to 4 hours to complete, but they *do not* have to be completed at one sitting. Recertification is required every three (3) years.

Is IRB Oversight Required?

- In order for a project to require IRB review, it must involve human subjects and qualify as research.
- A *Human Subject* is defined as "A living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information." (45 CFR 46, subpart A, section 46.102)

Is IRB Oversight Required?

- *Research* is defined as “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.” (45 CFR 46, subpart A, section 46.102)
- **NOTE**: Intent to publish, by itself, is *not* a reason to go to the IRB for review/oversight. It must be human subjects research (HSR) at the start of the study.

Is IRB Oversight Required?

The IRB asks: Is it HSR?

If yes, does it meet any of the exemption categories?

If no, does it meet any of the expedited review categories?

If no, requires full Committee review

Is IRB Oversight Required?

- Quality Improvement Activities FAQs: http://answers.hhs.gov/ohrp/categories/1569
  - What is the purpose of the activity? Is it research?
  - Are you using QI data to answer a research question?
  - Remember: Intent to publish isn't, by itself, a rationale for IRB review – it must be human subjects research at the start of the study.
- How to Distinguish Research from Quality Improvement. J of Empirical Research on Human Research Ethics 2015; 19(2):209-201

Is IRB Oversight Required?

- Program Evaluations:
  - http://oregonstate.edu/research/irb/does-evaluation-require-irb-review
    - When does evaluation require IRB review?
  - https://compliance.vpr.okstate.edu/IRB/documents/IRB_toolbox/Program_Evaluation.pdf
    - Program Evaluation: When is it Research?

Is IRB Oversight Required? New Tool to Help Determination

STFM Connect / Member Forum: April 3, 2018

- Marjorie Bowman, MD, MPH and Rose Maxwell, PhD, MBA – Wright State University Boonshoft School of Medicine
- IRB Rules – Guided Project Analysis https://redcap.wright.edu/surveys/index.php?s=EEAC49MY4D or…
- https://is.gd/GuidedPorjectAnalysis_IRBRules
- Designed to help analyze research projects according to the Human Research Subjects Protections regulations that Institutional Review Boards must follow.

Is IRB Oversight Required? New Tool to Help Determination

STFM Connect / Member Forum: April 3, 2018

- Based on current OHRP Human Subjects Decision Charts.
- Provides a user-friendly evaluation of an investigator's specific project according to Decision Charts. Requirements may change as OHRP provides new information for the new Common Rule.
- Helps investigators determine whether their project meets the definition for ‘Research’ – informs you on whether IRB review is likely required.
- If ‘Research’, determines whether the project likely meets criteria for Exempt status or qualifies for Expedited Review.
- Includes information on requirements for vulnerable populations and for waiver/alteration of consent.

New Common Rule

Changes to the Federal Code of Regulations for the Protection of Human Subjects

- Original roll-out: January 19, 2018 (did not happen)
- New roll-out: July 19, 2018 (may be stalled)
- Potential new roll-out: January 21, 2019

- Some changes are specific to research that is FDA-regulated or funded/supported by the Department of Justice.

New Common Rule

Changes to the Federal Code of Regulations for the Protection of Human Subjects

- Examples of some upcoming changes:
  - New definition of ‘human subjects’
  - New consent template
    - Provides information a reasonable person would want to know, creating opportunity to discuss
    - Begins with concise and focused presentation of key information most likely to aid in understanding why someone might or might not want to participate
    - Indicates whether clinically relevant research results - including at the individual level - will be disclosed, and if so, under what conditions

New Common Rule

Changes to the Federal Code of Regulations for the Protection of Human Subjects

- Examples of some upcoming changes (continued):
  - Additional exemption categories that do not require Continuing Review
    - Uses of secondary data and biospecimens that are already subject to HIPAA
    - Research involving benign behavioral interventions with adults
    - Research that only includes interactions involving educational tests, survey procedures, interview procedures, or observation of public behavior, even if identifiers are recorded and disclosure may pose a confidentiality risk to research participants

New Common Rule

Changes to the Federal Code of Regulations for the Protection of Human Subjects

- Examples of some upcoming changes (continued):
  - New periodicity for some expedited research
  - Annual reminders from eIRB of investigator obligations
  - Automatic Certificate of Confidentiality (for NIH funded studies with identifiable sensitive information)
  - Public posting of clinical trial consent forms (for studies conducted/supported by federal agencies)
  - Changes to criteria for waiver of informed consent

What Type of Review is Needed?

Case 1:

- Is more health policy education needed within the medical school curriculum?
- One-time anonymous survey of 3rd year medical students prior to a one-day interclerkship on the health care system.
- What do they know about health care reform and the current health care system? Where have they learned this: inside and/or outside of medical school courses and experiences? What should be taught? Where should it be taught?
- Is this research? Does it need IRB review, and if so: what type of review?

What Type of Review is Needed?

Case 2:

- Does the addition of scribes in a primary care FM practice influence work/life balance and provider satisfaction – ultimately influencing recruitment and retention of providers?
- One FM health center; residency training site; 6 attendings; 2 FTE scribes (4 part-time scribes); 6-month pilot study
- Data collection: Attending time tracking patient care and summary documentation; provider surveys on satisfaction; patient surveys on acceptance of scribes; administrative data on number of visits pre/post scribes (ROI data for clinical system); focus group with scribes; focus group with nurses
- Is this research? Does it need IRB review, and if so: what type of review?

What Type of Review is Needed?

Case 3:

- Evaluation of service models to enhance screening and treatment of HCV in primary care settings – conducted on behalf of the MA Dept. of Public Health
- Mixed methods study (chart review and site visits with interviews and focus groups) to evaluate process of care and patient outcomes of current HCV screening and treatment among young IDUs at 2 MA FQHCs.
- Goal: evaluate existing service delivery models and generate information to inform development of a pilot intervention program to enhance HCV screening and treatment.
- Is this research? Does it need IRB review, and if so: what type of review?

What Type of Review is Needed?

Case 4:

- Behavioral health screening among children covered by Medicaid: assessing screening prevalence and outcomes following screening – new screening mandate in MA.
- 2000 chart reviews for each of 3 years: baseline and 2 follow-up periods; administrative encounter data of health care utilization following screening.
- Work conducted for MassHealth (MA Medicaid); stratified random sample of statewide charts by age group.
- Is this research? Does it need IRB review, and if so: what type of review?

What Type of Review is Needed?

Case 5:

- Evaluating the integration of oral health and primary care training
- HRSA funded; collaborators: UMass, Harvard Medical School, and Harvard Dental School
- 14 nationwide anonymous surveys (medical/dental schools; primary care residencies and fellowships; NP/PA/CNM programs, etc.) to describe current OH education offered to trainees; identifying barriers and facilitators to implementing an OH curriculum; results to facilitate development of a consensus document for a standardized set of OH competencies.
- Is this research? Does it need IRB review, and if so: what type of review?

What Type of Review is Needed?

Case 6:

- Negative pressure wound therapy (NPWT) for accelerated secondary wound closure versus primary closure (standard of care) in vascular surgery patients with groin incisions
- Departmental funding; goal – to determine whether secondary wound closure with NPWT will decrease rate of SSI and/or incision complications when compared to primary wound closure in vascular patients with groin incisions.
- Prospectively enrolling 10 patients undergoing an index vascular surgery procedure requiring groin incision(s) to a randomized controlled trial comparing primary closure and closure by secondary intention with NPWT.
- Is this research? Does it need IRB review, and if so: what type of review?

Selected Bibliography and Contact Information

- DHHS.gov web site: http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm. NOTE: This website has an abundance of historical information about conducting research using human subjects, plus dozens of useful and interesting references and links to other pertinent information.
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