

Research Ethics:

The Protection of Human Subjects

The Regulations and the Roles of the Researcher and the IRB

Presented by

Sinclair Community College

Institutional Review Board

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Research Ethics: The Protection of Human Subjects



A Historical Perspective

1947: Nuremberg Trials

- Twenty-six Nazi physicians are tried at Nuremberg, Germany, for research atrocities performed on prisoners of war
- Nazi War Crimes Tribunal issues first internationally recognized code of research ethics

Nuremberg Code

- Basic principles of voluntary consent
 - Capacity of subjects to consent
 - Freedom of subjects from coercion
 - Comprehensive analysis of risks and benefits
 - Minimization of risk and harm to subjects
 - Favorable risk/benefit ratio
 - Qualified investigators
 - Appropriate research design
 - Freedom of subjects to withdraw at any time

1940s: Tuskegee Studies

- Study of natural history of untreated syphilis in Tuskegee, Alabama
- Poor, black males uninformed about presence of disease and denied a treatment discovered in 1947
- Abuses revealed in 1972

1962: Kefauver-Harris Bill

- Ensured greater drug safety in the U.S. after thalidomide found to be the cause of severe birth defects in thousands of babies in Western Europe

1964: Declaration of Helsinki

- Recommendations guiding medical doctors in biomedical research involving human subjects
 - Similar principles to Nuremberg Code
 - Distinguishes therapeutic from non-therapeutic research
- Adopted by 18th World Medical Assembly

1974: National Commission Established and Act Passed

- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research established
- National Research Act passed by Congress
 - Established IRBs and required review of federally funded research involving human subjects

1979: The Belmont Report

- Issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research as a guide for U.S. research with human subjects
- Principles for Human Subject Research
 - Autonomy
 - Beneficence
 - Justice

Autonomy

- Give respect, time, and opportunity to subjects to make own decisions
- No pressure to participate
- Protection for potentially vulnerable populations such as
 - Children
 - Elderly
 - Cognitive or emotionally impaired
 - Prisoners

Beneficence

- Obligation to secure well-being of research participants
- Protection of subjects from harm
- Maximization of benefits
- Careful balancing of risks and benefits

Justice

- Distribute benefits and burdens of research fairly and without bias
- Selection of subjects not based on
 - convenience
 - subject availability
 - compromised position of subjects
 - subject manipulability
 - language barrier

Subject Selection Considerations

- Do not base on gender, class, race, or socioeconomic status
(unless justified by study objectives)
- Be aware of perception of inequality of roles and/or potential for coercion
 - Counselor-client relationship
 - Teacher-student relationship
 - Employer-employee relationship

1980s: Federal Regulations

- FDA codified regulations in 1980
(For new drugs and devices)
21 CFR 50 and 21 CFR 56
- DHHS codified regulations in 1981
(45 CFR 46)
 - Various revisions over the years
 - Most recent revision (expedited review criteria) in November 1998

1990s: Federal Regulations

- “Common Rule” adopted in 1991
 - Based on 45 CFR 46, Subpart A
 - Adopted by 16 Federal Agencies including:

DOE	NASA	USAID	HUD
DOJ	DOD	DOEd	EPA
NSF	DOT	DHHS	
 - Various revisions over the years
 - Most recent revision (of expedited review criteria) on November 9, 1998

1990s: Other Happenings

- 1993: *Albuquerque Tribune* publicizes 1940s secret radiation experiments
 - indigent patients and mentally retarded children deceived about the nature of their treatment
 - received plutonium injections

1990s: Other Happenings

- 1994: National Bioethics Advisory Commission (NBAC) created
- 1995: President's Advisory Committee on Human Radiation Experiments concludes some of the 1940s radiation experiments were unethical

1990s: Other Happenings

- 1997: Formal presidential apology to subjects of Tuskegee syphilis experiments
- NBAC continues investigation into genetics, consent, and privacy

2000 and Beyond

- 2000: U.S. Public Health Service mandates training for all researchers using human subjects
- 2000: U.S. Public Health Service proposes mandate for training of all researchers in “Responsible Conduct of Research”

Federal Regulations

- Code of Federal Regulations Title 45
 - Part 46 - Protection of Human Subjects
 - Subpart A - Basic DHHS Policy
 - Subpart B - Fetuses, Pregnant Women, and Human *in vitro* Fertilization
 - Subpart C - Prisoners as Subjects
 - Subpart D - Children as Subjects

Research Ethics: The Protection of Human Subjects



The Institutional Review Board

Federally Mandated IRB Responsibilities

- To safeguard the rights and welfare of human subjects
 - Review research protocols
 - Require protocol modifications
 - Approve or disapprove protocols
 - Ensure or waive informed consent
 - Conduct continuing review of research

Additional Responsibilities of the IRB

- To safeguard the rights and welfare of students and staff being recruited on-campus by researchers not affiliated with Sinclair Community College
 - Review research protocol applications and approvals from other IRBs
 - Require protocol modifications
 - Grant or deny permission to recruit on campus

The Authority of the IRB

The IRB's decision to deny approval of a protocol (or to deny permission to recruit subjects on-campus) *cannot* be overridden.

The IRB's decision is *FINAL*.

IRB Membership

- At least five members
- Members with varying backgrounds
- Diverse membership (gender, race, cultural background)
- Sensitivity to issues such as community attitudes

IRB Membership

- Knowledgeable in standards of professional conduct and practice
- Not all members of one profession
- At least one scientist
- At least one non-scientist
- At least one member not affiliated with Sinclair Community College

IRB Meeting Issues

- Member with conflicting interest may not participate in initial or continuing review
- Outside consultants may be used
- IRB must review certain protocols at convened meetings
 - Majority of members must be present
 - At least one must be non-scientist
 - Majority of those present must approve

IRB Review Criteria

- Risks to subjects are minimized
- risks to subjects are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent
 - is sought from each prospective participant or legally authorized representative
 - is documented
- Adequate preparation is taken to protect privacy and confidentiality of subjects
- Adequate provision are made for ongoing monitoring of subjects welfare

Research Ethics: The Protection of Human Subjects



Definitions

What Must be Reviewed?

- Research that will be conducted by
 - a faculty member
 - a staff member **or**
 - a student
- from Sinclair Community College that involves
 - humans subjects
 - records gathered on human subjects
- and that will take place
 - at Sinclair Community College
 - at another institution
 - in a community setting

Who is a “human subject?”

- A *living* individual about whom the investigator obtains
 - Data through *intervention* or *interaction* with the individual *and/or*
 - *Identifiable* private information

What is “research?”

- A *systematic investigation*
 - Research development
 - Testing
 - Evaluation

which is intended to develop or contribute to *generalizable knowledge*

What is “intervention?”

- Physical procedures
 - Specimen collection
 - Physical measurements
- Manipulation of the subject
- Manipulation of the subject’s environment

What is “interaction?”

- Communication
 - Interviewing
- Interpersonal contact
 - Surveying

What is “private information?”

- Information about behavior that the subject can reasonably expect is not being observed or recorded
- Information provided by the subject that he/she reasonably expects will not be made public

What is “private information?”

- Must be readily identifiable
 - Subject’s identity can be readily ascertained by investigator **or**
 - Subject’s identity can be associated with the information

What is “minimal risk?”

...when 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 performance of routine physical or psychological examinations or tests

Research Ethics: The Protection of Human Subjects



Informed Consent

Informed Consent

- Required Elements
 - Identification and affiliation of researcher
 - Statement that study involves research
 - Explanation of purpose of research
 - Expected duration of subject's participation
 - Description of procedures
 - Identification of experimental procedures

Informed Consent

- Required Elements
 - Description of reasonably foreseeable risks or discomforts to subject
 - minimal
 - more than minimal
 - Description of any benefits which may reasonably be expected
 - for subject
 - for society

Informed Consent

- Required Elements
 - Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
 - Statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

Informed Consent

- Required Elements
 - An explanation of any costs associated with participation
 - An explanation of any compensation for participation
 - For research involving more than minimal risk...
 - An explanation of any medical treatments available if injury occurs
 - What treatments consist of
 - Where to obtain further information

Informed Consent

- Required Elements
 - Statement that...
 - Participation is voluntary
 - Refusal to participate will involve no penalty or loss of benefits to which subject is otherwise entitled
 - Subject may discontinue participation at any time without penalty or loss of benefits to which he/she is otherwise entitled

Informed Consent

- Required Elements
 - Name of contact person to...
 - Provide answers to questions about the research
 - Provide information about research subjects' rights
 - Inform about research-related injuries

Additional Elements of Consent

- As appropriate...
 - Statement that there may be unforeseeable risks to subject and/or embryo or fetus
 - Anticipated circumstances under which subject may be terminated from the study without regard to his/her consent

Additional Elements of Consent

- As appropriate...
 - Any additional costs to the subject that may result from participation
 - Consequences of a subject's decision to withdraw from the research
 - Procedures for orderly termination of participation by the subject

Additional Elements of Consent

- As appropriate...
 - Statement that significant new findings during the study which may relate to subject's willingness to continue participation will be provided
 - Approximate number of subjects involved in the study

Informed Consent

- Is an educational process
- Is about people's understanding and willingness to participate in the research study
- Is more than a signed form
- Is ongoing
- Is respectful

Informed Consent

- Begins with non-coercive subject identification and recruitment
- Involves a proxy for subjects who are not of legal age or who are deemed incompetent
- Involves full disclosure about the study

Informed Consent

- Involves disclosure of researcher conflict of interest
- Gives subject adequate time to consider participation
- Uses understandable language
- Gives the participant the opportunity to ask questions and reflect

Suggested Consent Process

- Obtain IRB approval
- Present prospective participant with consent document
- Read document together
 - explain significant or difficult points
 - answer questions
 - address all elements of consent

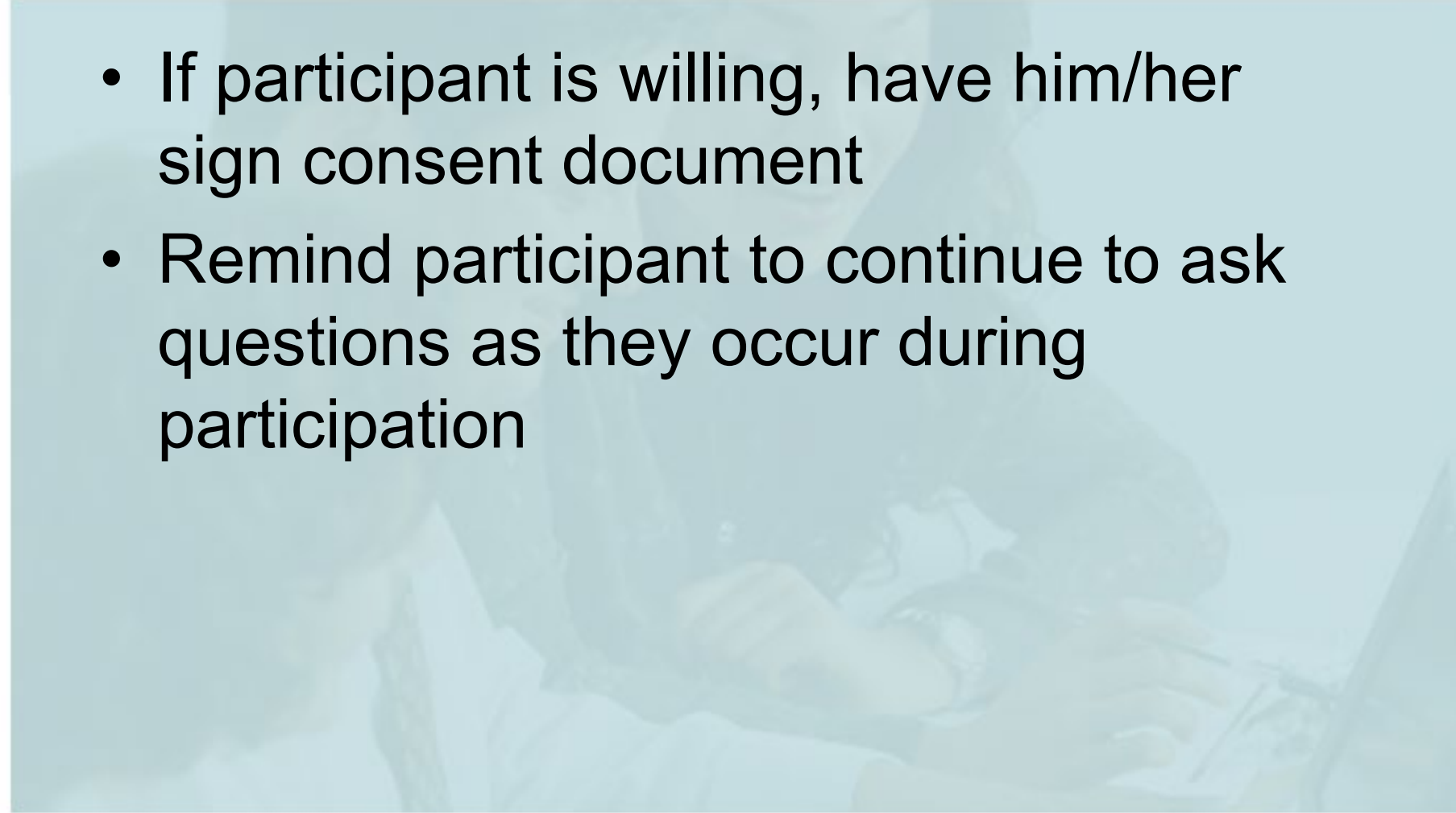
Suggested Consent Process

- Give prospective participant a copy of the consent document
- Allow him/her to take the document home for review with family and friends
- Meet him/her again

Suggested Consent Process

- Ask open-ended questions about nature of study and participation to ensure understanding
 - “Describe in your own words the purpose of this study.”
 - “What more would you like to know?”
 - “Would you please explain to me what you think I’m going to ask you to do.”
 - “What are your concerns??”

Suggested Consent Process

- If participant is willing, have him/her sign consent document
 - Remind participant to continue to ask questions as they occur during participation
- 
- A faded, light blue background image showing a person's hands signing a document. The person is wearing a white lab coat and a watch. The document is held in their left hand, and their right hand is writing on it with a pen. The background is slightly out of focus, emphasizing the action of signing.

Documentation of Consent

- Must be written
- Must be signed by subject or his/her legally authorized representative
- Subject must receive a copy
- Must contain all elements **or**
- Must indicate all elements given orally with witness present

Documentation of Consent

- If subject is a minor and...
 - Is too young to agree or refuse to participate in the research
 - Get parent/guardian consent
 - Is old enough to agree or refuse to participate in the research
 - Get parent/guardian permission **and**
 - Get child's assent (written or verbal)

Documentation of Consent

- Other Considerations
 - Sinclair Community College IRB requires documentation of IRB approval on consent forms given to subjects

IRB Waiver of Written Consent

- When the consent form is the only record linking the subject to the research and potential harm could result from breach of confidentiality **or**
- When the research presents no more than minimal risk and involves no procedures for which written consent is normally required outside the research context

(Written statement regarding the research may be required to be given to subjects)

IRB Consent Options

- May approve consent procedure which alters some or all of the required and additional elements

or

- May waive requirement for informed consent

if...

IRB Consent Options

- The study is conducted or approved by the government and examines a public service/benefit program
- The research could not practicably be carried out without waiver or alteration of informed consent
- The research involves no more than minimal risk

IRB Consent Options

- The waiver or alteration will not adversely affect rights and welfare of subjects
- The subjects will be provided with additional pertinent information after participation, as appropriate
- The waiver does not conflict with other federal, state, or local laws

Comparison: APA Ethical Principles for Dispensing with Informed Consent

- Informed consent is **not** required for
 - Anonymous questionnaires
 - Naturalistic observations
 - Some kinds of archival research
- **unless** required by
 - Governmental regulations
 - IRB requirements

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Exemption from IRB Review

Federal Exemption Category 1

- Research conducted in established or commonly accepted educational settings, involving educational practices, such as
 - Research on regular and special education instructional strategies
 - Research on effectiveness of, or comparison among,
 - Instructional techniques
 - Curricula
 - Classroom management methods

Federal Exemption Category 2

- Research involving
 - educational tests (cognitive, diagnostic, aptitude, achievement)
 - survey procedures
 - interview procedures **or**
 - observation of public behavior
- unless**
- information is recorded in such a way that subjects can be identified directly or through identifiers **and**
 - disclosure could reasonably
 - place subject at risk of criminal or civil liability **or**
 - be damaging to financial standing, employability, or reputation

Federal Exemption Category 2

Note:

- Exemption for survey and interview procedures does *not* apply to research involving children.
- Exemption for observation of public behavior does not apply to research involving children except when the investigator does *not* participate in the activities being observed.

Federal Exemption Category 3

- Research involving
 - educational tests (cognitive, diagnostic, aptitude, achievement)
 - survey procedures
 - interview procedures **or**
 - observation of public behavior
- that is not exempt under Category 2 **if**
- subjects are elected or appointed public officials or candidates for public office **or**
 - federal statute requires without exception that confidentiality of the personally identifiable information be maintained throughout the research and thereafter

Federal Exemption Category 4

- Research involving collection or study of existing
 - data
 - documents
 - records
 - pathological or diagnostic specimens

if

 - sources are publicly available **or**
 - information is recorded by the investigator in such a manner that subjects cannot be identified
 - directly **or**
 - through identifiers linked to the subjects

Federal Exemption Category 5

- Research and demonstration projects
 - conducted by, or subject to, approval of a federal department or agency
 - that are designed to study, evaluate, or examine
 - public benefit or service programs
 - procedures for obtaining benefits or services under those programs
 - possible changes in, or alternatives to, benefit or service programs or procedures **or**
 - possible changes in methods or levels of payment for benefits or services under these programs

Federal Exemption Category 6

- Taste and food quality evaluation and consumer acceptance studies **if**
 - wholesome, additive-free foods are consumed **or**
 - if a food is consumed that
 - contains an ingredient at or below the level, and for a use, found to be safe **or**
 - contains an agricultural chemical or environmental contaminant at or below the level found to safeby the FDA or approved by the EPA or the USDA

Other Exempt Research

- Student Research
 - A normal part of student's coursework
 - Supervised by a faculty member
 - Primary purpose is to develop student's research skills
 - Presents no more than minimal risk to subjects or the student investigator
 - Does not deal with issues of a sensitive nature **and**
 - Is not genuine research expected to result in publication or dissemination

Non-Exempt Student Research

- Research to satisfy requirements for the following is NOT automatically exempt:
 - Independent Study
- Review by the IRB is required unless the protocol meets federal exemption criteria

Important Notes About Exemptions

- Written informed consent is not required for exempt protocols
- If written consent is desired by the investigator, the IRB provides specific wording to be used
- Applications for exemption are acted on in 10 working days.

Research Ethics: The Protection of Human Subjects



Expedited Review

Expedited Review

- Must be minimal risk research
- Must meet federal criteria for expediting
- Cannot include request for waiver of written informed consent
- Review is done by expediting team
(IRB Chair may expedite in emergency)
- Approval subject to full IRB concurrence at next convened meeting
- Expediter may recommend convened review

Expedited Review Category 1

- Clinical studies of drugs and medical devices only when
 - the investigational device exemption application is not required **or**
 - the medical device is cleared/approved for marketing and is being used in accordance with its cleared/approved labeling

Expedited Review Category 2

- Collection of blood samples by finger stick, heel stick, or venipuncture from
 - healthy, non-pregnant adults
 - weighing at least 110 poundsfor whom
 - amounts drawn do not exceed 550 ml in an eight-week period **and**
 - collection is not more frequent than two times per week

Expedited Review Category 2 (Cont'd.)

or

- other adults and children for whom, considering age, weight, health, and collection procedures,
 - the amount to be collected does not exceed the lesser of 50 ml or 3 ml per kg in an eight-week period **and**
 - collection does not occur more frequently than twice per week

Expedited Review Category 3

- Prospective collection of biological specimens by non-invasive means, including, but not limited to,
 - hair and nail clippings (in a non-disfiguring manner)
 - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction
 - permanent teeth if routine patient care indicates need for extraction
 - Collection of excreta and external secretions
 - sweat

Expedited Review Category 3 (Cont'd.)

- excreta and external secretions (including sweat)
- uncannulated saliva collected in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying dilute citric solution to the tongue
- placenta removed at time of delivery
- amniotic fluid at time of rupture prior to or during labor

Expedited Review Category 3 (Cont'd.)

- supra- and subgingival dental plaque and calculus, provided
 - collection procedure is not more invasive than routine prophylactic scaling of teeth **and**
 - process is in accordance with accepted prophylactic techniques
- mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings
- sputum collected after saline mist nebulization

Expedited Review Category 4

- Collection of data through non-invasive procedures
 - not involving general anesthesia or sedation
 - routinely employed in clinical practice
 - excluding procedures involving x-rays or microwaves
 - including, but not limited to...
 - physical sensors applied to the body surface or at a distance that do not involve
 - input of significant amounts of energy into the subject **or**
 - invasion of the subject's privacy

Expedited Review Category 4 (Cont'd.)

- weighing or testing sensory acuity
- magnetic resonance imaging
- electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography
- moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate, given the age, weight, and health of the subject

(Note: Where medical devices are employed, they must be cleared/approved for marketing.)

Expedited Review Category 5

- Research involving materials such as
 - data
 - documents
 - records
 - specimens

that have been collected--or will be collected--solely for non-research purposes, such as

- medical treatment
- diagnosis

Expedited Review Category 6

- Collection of data from
 - voice recordings
 - video recordings
 - digital recordings
 - image recordingsmade for research purposes

Expedited Review Category 7

- Research on individual or group characteristics or behavior, including, but not limited to, research on
 - perception
 - cognition
 - motivation
 - identity
 - language
 - communication
 - cultural beliefs or practices
 - social behavior

Expedited Review Category 7 (Cont'd.)

or

- Research employing the following methodologies:
 - survey
 - interview
 - oral history
 - focus group
 - program evaluation
 - human factors evaluation
 - quality assurance

Expedited Review Category 8

- Continuing review of research previously approved by the convened IRB where
 - the research is permanently closed to enrollment of new subjects,
 - all subjects have completed all research-related interventions, **and**
 - the research remains active only for long-term follow-up of subjects

Expedited Review Category 8 (Cont'd.)

or

- where no subjects have been enrolled and no additional risks have been identified

or

- where the remaining research activities are limited to data analysis

Expedited Review Category 9

- Continuing review of research
 - not conducted under an investigational new drug application or an investigational device exemption
 - where Categories 2 through 8 do not apply
 - but the IRB has determined and documented at a convened meeting that
 - the research involves no greater than minimal risk **and**
 - no additional risks have been identified

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Miscellaneous...

Required Review Time

(Assuming complete application)

– Exemptions

- 1-5 working days
- Done by Director of IRB Chair

– Expedited Review

- 5-10 working days
- Done by IRB Chair

Required Review Time

– Full Review

- Must be submitted by posted deadline (10 calendar days before meeting)
- Reviewed quarterly regular meeting
 - May be conducted by telephone
- Notification in 1-5 working days after IRB meeting

Failing to Follow the Rules

The IRB has the authority to suspend or terminate approval of research and destroy data that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to subjects.

Failure to follow the rules may result in charges of scientific misconduct!

IRB Information...

Go to

<<http://www.sinclair.edu/departments/grants/?????>
?????>

- IRB policies and procedures
- IRB meeting schedule
- Application for exemption
- Application for expedited or convened review
- Model consent form (mandatory format)
- Protocol modification/continuing review/ final report form
- This presentation

Other Information Sources

- Office of Protection from Research Risks (OPRR)
 - http://www.nih.gov/grants/oprr/library_human.htm