Human Subjects Research: The DePaul IRB Process and Protocol Preparation Guidance

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Note

- The information in today's talk reflects the revised human subjects regulations at 45 CFR 46 (the Common Rule), which became effective January 21, 2019.

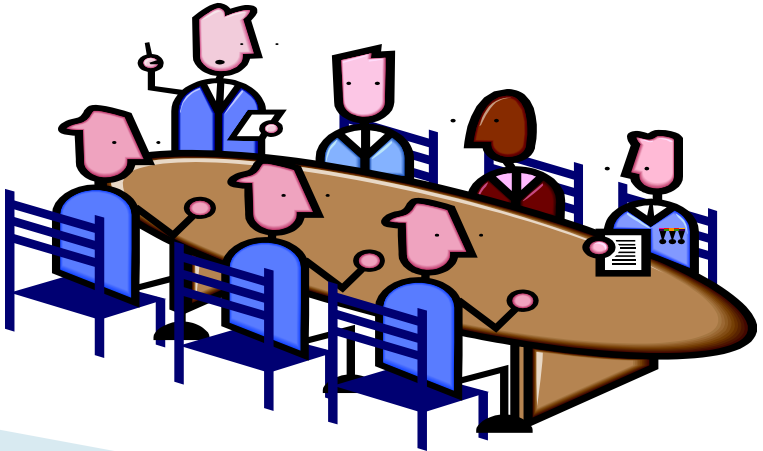
Topics

- Purpose of IRB
- History of the IRB
- What Requires Review
- Levels of Review
  - Non-Reviewable
  - Exempt
    - Limited IRB Review
    - Broad Consent
  - Expedited
  - Full
- Short Summary of DePaul Process
- Guidelines for submission
- eProtocol Online Submission System
- Common General Problems
- Common IRB Concerns
- Consent Principles and Concerns
- Contact Information
- Q &A

The Purpose of the IRB

- A committee that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects.

- Has authority to approve, require modifications, or disapprove research



The IRB and the Human Subject Protections Program

Human Subjects Protection Program

FWA Institution

Office of Research Services

Institutional Review Board

Researchers

Separate Scientific Review processes (i.e., Departmental Review)

Support Offices

- ORS-Grants and Contracts
- Compliance
- Billing
- General Counsel

What Requires IRB Review?

- All human subject research conducted by DePaul faculty, staff, or students, whether conducted at DePaul or in other locations.
  - Activities must meet the definition of research contained in the Federal regulations.
  - Activities must involve human subjects as defined in the federal regulations.

IRB History & Evolution

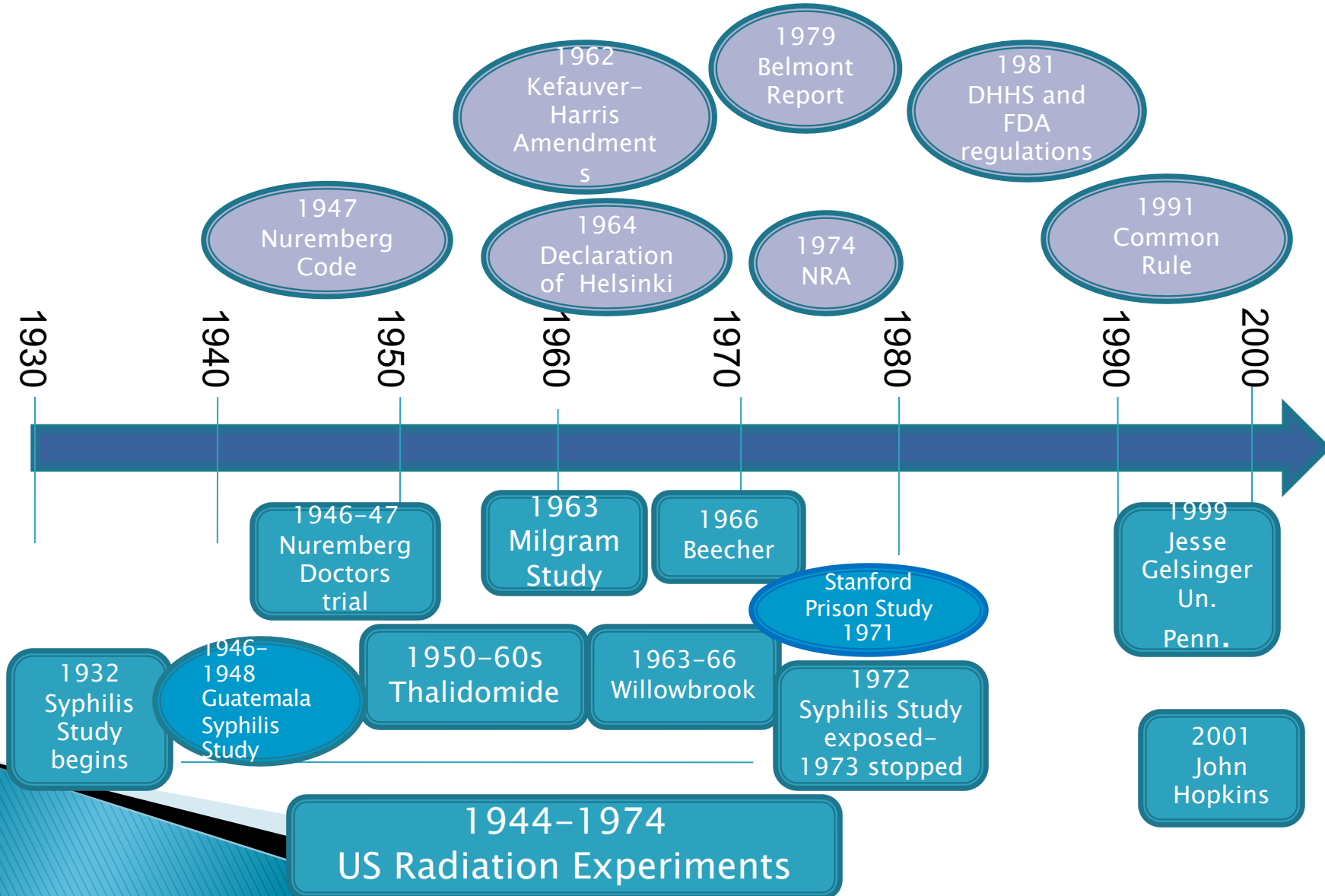
- Nuremberg Code (1947)
- "This is the legacy of the Nuremberg Tribunal and the Nuremberg Code. The respect for human rights in human experimentation demands that we see persons as unique, as ends in themselves . . . we must not see any person as an abstraction." – Elie Wiesel
- Nazi Doctors Trial (1946-1947)

- Milgram Study – Yale (1963)
  - Studied obedience and response to authority.
  - Use of deception.

IRB History & Evolution

- Willowbrook – 1956 –1970
- Mentally disabled children were given hepatitis in an attempt to track development of the viral infection at the Willowbrook State School in Staten Island.
- Thalidomide Drug Use & Birth Defects 1950-1960
- Stanford Prison Experiment – 1971
- U.S.P.H.S. Syphilis Study (Tuskegee) – 1932
- Cambridge Analytica – 2015

Timeline of Events



Where to Start?

- Is what I am doing research?
  - Does this activity involve a systematic investigation designed to develop or contribute to generalizable knowledge?
    - Am I using a systematic approach, such as scientific methods, to collect and analyze data?
    - Is the primary goal or intent to disseminate the information or apply it to persons outside the individual or group involved in the activity?
    - Will the activity result in knowledge expressed in theories, principles, and statements of relationships that can be applied to others' experiences?

Revised Regulations–What is not research

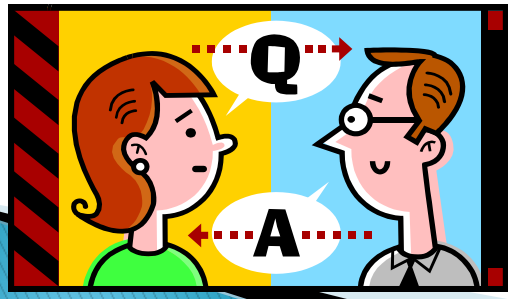
- (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- (2) Public health surveillance, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.

Revised Regulations– What is not research (cont.)

- (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes
- (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

If it is "Research," What's Next?

- Does my research involve Human Subjects?
  - *Human subject* means a **living individual** about whom an investigator 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.



Levels of Review

- Non-Reviewable
  - Not research
  - Not involving human subjects
  - Activity does not engage DePaul or DePaul personnel
- Exempt
- Expedited
- Convened or Full
- Resources
  - DePaul website: Levels of review https://offices.depaul.edu/ors/research-protections/irb/Pages/default.aspx

  OHRP decision trees http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

What changes do the revised regulations bring?

- Slightly revised definitions of research and human subject
- Revised and new categories of exempt research
  - New concept of limited IRB review
  - New concept of broad consent
- Elimination of continuing review for most expedited research
- New required elements of consent and consent format
- Changes to the waiver of consent and waiver of documentation of consent requirements
- No longer requiring a waiver or alteration of consent for screening subjects or determining eligibility
- IRB no longer required to review grant applications
- Other changes specific to some research, i.e., clinical trials
- Other smaller changes summarized in tables available from multiple sources

What research is non-reviewable?

- Activities that do not engage DePaul or DePaul personnel in the conduct of research
- Projects that do not involve "research" and/or "human subjects"
  - Non-generalizable survey/interview research, such as:
    - Surveys/interviews for internal program evaluation
    - Surveys/interviews conducted by students for a class project & that will not be used outside of the class
  - Any of the types of research specifically noted as not research, i.e., journalism, oral history, legal, etc.
  - Research utilizing information about deceased persons
  - Research using archival or currently existing data or biospecimens, when:
    - Data accessed or used by the researcher are permanently de-identified or coded and the PI will not have the key to link the data to the person

Non-Reviewable Determination Process

- Submit protocol through the eProtocol system at https://researchcompliance.depaul.edu
  - Receive a letter with Non-Reviewable Determination

- Why might you want this?
  - Funding agency
  - Journal publication
  - Personal records
  - Organizations where subjects are recruited request it

Exemption Determinations

- Little or no risk to the subject
- The **only** involvement of human subjects will meet the criteria for one or more of the (8) exemption categories
- Pregnant women (Subpart B) allowed
- Prisoners (Subpart C) not allowed unless the research is looking at a broader subject population that only incidentally includes prisoners
- Children (Subpart D) allowed for categories 1, 4, 5, 6, 7, and 8, but not 2 (i) and (ii) educational tests or observation of public behavior when the investigator(s) do not participate in the activities being observed, and not allowed for 2 (iii).
- Must be someone with institutional authority that makes the exemption determination as defined in institutional policy

Exempt from What?

- In-depth IRB review
  - May be reviewed administratively
- Informed consent with all elements of consent
  - DePaul requires an information sheet or process- some new required content for use of deception and confidentiality
  - New regulations also bring in a new concept of Broad Consent for categories 7 and 8
- Continuing Review

Exempt Category 1

1. Research conducted in established or commonly accepted educational settings, that specifically involves **normal educational practices** that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exempt Category 2

- Research that **only** includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recordings) if at least one of the following criteria is met:
  - (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
  - (ii) Any disclosures of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, educational advancement, or reputation; or
  - (iii) The information obtained is recorded by the investigator in such a manner that the identity of human subjects can readily be ascertained directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determinations required by 45 CFR 46.111 (a) (7).
    - There are adequate provisions to protect the privacy of the subjects and to maintain the confidentiality of data.

Exempt Category 3

3 (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recordings if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

- (A) The information obtained is recorded by the investigator in such a manner that the identity of the subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
- (B) Any disclosures of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, educational advancement, or reputation; or
- (C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determinations required by 45 CFR 46.111 (a) (7).
  - There are adequate provisions to protect the privacy of the subjects and to maintain the confidentiality of data.

Exemption 3 (cont.)

- (ii) benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.
  - Examples; playing an online game, having subjects solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.
- (iii) If the research involves deceiving the subjects regarding the nature or purpose of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Exemption Category 4

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
   - (i) The identifiable private information or identifiable biospecimens are publicly available;
   - (ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
   - (iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR Parts 160 and 164 (HIPAA) or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
   - (iv) The research is conducted by, or on the behalf or, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 2089\(b) of the e-Government Act of 2002, 44 U.S.C. 3501…

Exemption Category 5

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs and procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

Examples: Internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants

- Each Federal department or agency must post a list of such projects on a publically accessible Federal web site and publication must occur before the research begins.

Exemption category 6

- 6. Taste and food quality evaluation and consumer acceptance studies:
- (i) If wholesome foods without additives are consumed, or
- If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the EPA or the Food and Safety Inspection Service of the U.S. Department of Agriculture.

Exempt Category 7

- 7. Storage or maintenance for secondary research for which broad consent is required: storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by 45 CFR 46.111(a)(8).

Category 7 and 8- Limited IRB review

- (i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of 45 CFR 46.116 (a) (1)-(4), (a)(6), and (d);
- (ii) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with 45 CFR 46.117; and
- (iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Exempt Category 8

- 8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use if the following criteria are met:
  - (i) Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d);
  - (ii) documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117;
  - (iii) An IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and
  - (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent investigators from abiding by any legal requirements to return individual research results.

Expedited Review

- Initial Review
  - Does not mean fast review
  - Minimal risk-i.e., probability and magnitude…not greater than daily life …or routine examinations
  - Reviewed by one or more IRB members
  - Specific categories (7 initial, 2 for continuing review)-will be revised at some point
  - In the past, expedited protocols were assigned an approval period most often 364 days, but under revised regulations expedited review research no longer requires annual continuing review unless the IRB specifically requires it, and documents the rationale for doing so.
    - Some protocols staying under the older regulations will still have continuing review requirements. Protocols reviewed and approved before January 21, 2019 are grandfathered under the old regulations.
  - Still need to submit amendments and get them approved before the changes are implemented

- Other items that may be reviewed under expedited review procedures:
  - Continuing review applications, if required
  - Amendments
  - Final reports
  - Unanticipated problems/adverse events

Expedited Categories

- OHRP Guidance documents
- http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html

Expedited Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met. (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Expedited Categories (Cont.)

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; **or**

from other adults and children [2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

Expedited Categories (Cont.)

- 3. Prospective collection of biological specimens for research purposes by noninvasive means.
  Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

Expedited Categories (Cont.)

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

Expedited Categories (Cont.)

5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

(6) Collection of data from voice, video, digital, or image recordings for research purposes.

(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, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Expedited Continuing Review Categories

(8) Continuing review of research previously approved by the convened IRB as follows:

- a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- b) where no subjects have been enrolled and no additional risks have been identified; or
- c) where the remaining research activities are limited to data analysis.

Note: Under revised regulations IRB may now close studies that meet 8 (a) or (c), if the study is fully transitioned to new regulations.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (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.

Convened or Full Review

- Greater than minimal risk or minimal risk research that doesn't fit into one or more of the expedited categories
  - Protocol receives a review by the convened Board, rather than a subcommittee review
  - Is assigned an approval period, usually 364 days, but can be different as determined by the IRB
  - No categories

Summary of DePaul Process

- PI submits protocol through eProtocol online submission system.
- IRB subcommittee reviews materials and asks for revisions
- PI completes revisions and sends revised materials back to IRB through eProtocol system.
- IRB reviews the materials and approves the research or may ask for additional revisions
- If there are more revisions, the PI completes revisions and sends revised materials back to the IRB
- IRB reviews the materials and approves the research. PI receives approval notification via email with the formal approval letter within the eProtocol system.

How Much Time Does this Take

- IRB tries to provide comments in 7-10 working days, with 15 business days being the outside limit for number of days.
- If revisions are requested, then the total amount of time depends upon how long the PI takes to respond to the IRB's request
  - Additional 7-10 days for the IRB review of revisions.

Guidelines for Submission

Materials Required for Exempt Projects	Materials Required for Expedited or Full Projects
Exempt application	Expedited/full application
Exempt info sheet or process	Consent, parent/guardian permission, assent forms, as appropriate
Measures or data collection tools	Measures or data collection tools
Recruitment materials (e.g., scripts, flyers, emails, letters)	Recruitment materials (e.g., scripts, flyers, emails, letters)
Collaborative IRB approval*	Collaborative IRB approval*
Letters of collaboration or support*	Letters of collaboration or support*
Grant application, if requested by IRB	Grant application, if requested by IRB
CITI training completion for PI and Faculty Sponsor- hard copy not needed except for external collaborators	CITI training completion for PI and Faculty Sponsor-hard copy not needed except for external collaborators

eProtocol System

DePaul University

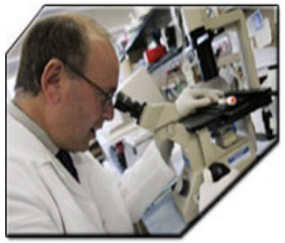
Key Solutions
Comprehensive IT for Research

version 2.7.56.7

ePROTOCOL

Welcome to DePaul University's eprotocol portal. The portal will allow you to submit, manage, and update your Institutional Review Board (IRB), Institutional Animal Care and Use Commitee (IACUC) and Institutional Biosafety Committee (IBC) protocols online without using paper forms. Almost all activity related to your protocol will occur online through the information system. So that means you will have access to up to date status information for each protocol submission, which means fewer phone calls or emails to ORS to determine the status of a submission. The information system also means better tracking of education and training for personnel listed on a protocol. Over the next several months, we will begin training everyone on how to use the system. The Research Protections team is here to assist you with working within the system. We hope that we can create a smooth transition to our paperless protocol submission process.

Office of Research Services, Research Protections Team

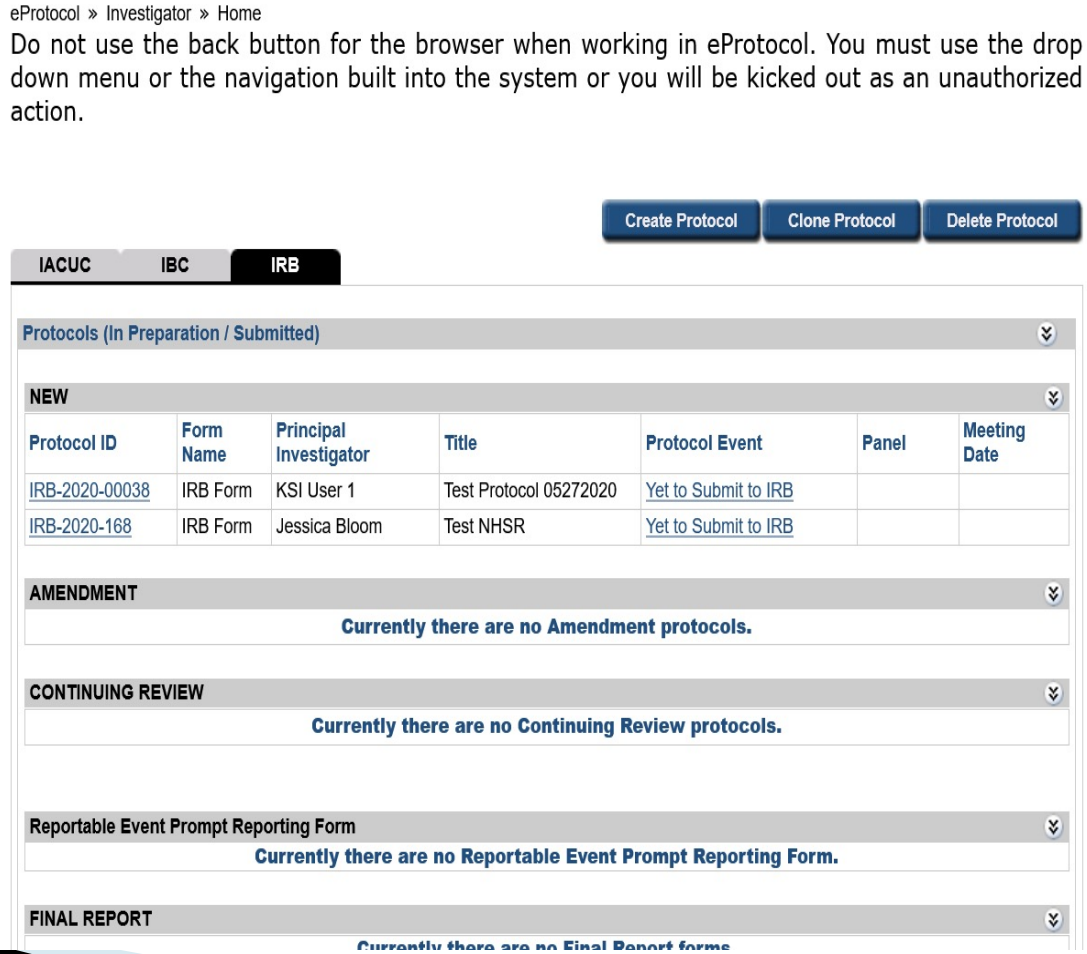


User ID

Password

Login

eProtocol System for Investigators



Common General Problems

- Before beginning the IRB process–PLAN YOUR RESEARCH PROTOCOL!
- Proof read your materials for typos, incoherent or confusing language, and inconsistencies
- Avoid scientific jargon, write as if explaining to someone not in your field of study (i.e., lay or everyday language)
- Ensure the application matches the consent documents/recruitment materials regarding risks, benefits, and limits of confidentiality, etc.
- Make sure the info sheets or consent documents are written at a 6^{th}–8^{th} grade reading level, or at a level appropriate for the target population
- More information is better than too little

Common IRB Concerns

- Recruitment
  - Snowball recruitment
  - Privacy issues
  - How contact information is obtained
  - Engagement of others
  - How it is used, in final format
- Online surveys
  - When and how is the information sheet or consent presented to subjects?
  - Active consent or agreement process?
  - Can they skip questions?
  - Will payment be offered? If so how is contact information gathered?
  - Anonymous or confidential?

Common IRB Concerns

- Data collection
  - How is data recorded?
    - De-identified, coded, with identifiers.
  - What procedures or method of data collection will be used?
    - Surveys (anonymous or confidential), questionnaires, interviews, audio or video recording interviews, review of private records, collection of artifacts.
    - Measures to protect confidentiality of data once collected
    - What happens to data when research is completed?
- Audio or video recording
  - How will these be used in the research?
  - Will they be used outside of the research?
    - Archived, documentary, teaching/training
  - Is appropriate language included in the consent or information sheet?
  - When are these destroyed?
  - State law (see guidance document)

General Principles of Consent

- Consent process
  - Is a process, it is not about signing a form.
    - Involves providing information in an understandable way, assessment of understanding through discussion with the subject, obtaining voluntary consent (verbal or written), and in some instances, ongoing assessment and affirmation (longitudinal studies).
  - Begins with initial contact with the participant (recruitment).
  - Can be written, verbal, or elements or the entire process can be altered or waived.

Common Consent Concerns

- During IRB review:
  - Missing elements or information
  - Inaccurate or incomplete information
  - Reading level and vocabulary
  - Age appropriate assent
  - Does the subject have the capacity to provide consent?
- During conduct of the research:
  - Not obtaining signatures
  - Not obtaining appropriate Legal Guardian permission
  - Not using the currently approved document(s)

Responsible Conduct of Human Subject Research

- Conducting research with human subjects is a privilege, not a right
- Follow the approved protocol
- Submit amendments before changes are initiated
- Follow the PI responsibilities on the form
- When applicable, ensure an adequate consent process.
- Keep and maintain the research records during and for 3 years after the research is completed.
- Submit a Final Closure Report

Contact Information

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IRB Webpage: https://offices.depaul.edu/ors/research-protections/irb/Pages/default.aspx

eProtocol online submission system: https://researchcompliance.depaul.edu

Q and A

- Questions?