Institutional Review Board (IRB)

Overview for Medical, Behavioral and Educational Research

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DISCUSSION POINTS

- Regulatory Oversight
- What is Research?
- Levels of IRB Review
- Qualifications and Training
- Application Process
- Investigator Responsibilities
Oversight of all Investigator Human research activities:
- Provide assistance and guidance to investigators
- Ensure ethical conduct and compliance in performance of human research in the following areas:
  - Human subject protection
    - Adults, Children and Prisoners (Vulnerable Populations)
  - Promote responsible conduct of Human research
    - Consideration for subject safety, ethics, and integrity
  - Oversight of Behavioral, Educational and Medical research
  - Conflict of Interest (determination and avoidance)
Operate in accordance to all Federal, State, local regulations

- Office for Human Research Protections (OHRP) guidelines
  45 CFR 46
  HHS/NIH supported clinical and non-clinical research

- Food and Drug Administration (FDA) Code of Federal Regulations
  (21 CFR Part 50, 54, 56, 312 and 812)
  Drug, Devices, Biologicals, Radiological

- Health Insurance Portability and Accountability Act (HIPAA)
  Protection of personal, identifiable health information

- University or Institution specific policies and IRB guidelines
  Encompass all areas of research
Consequences of Improper Conduct

- Physical or emotional injury of subjects
- Reputational damage to
  - Research focus and advancing research
  - Researcher and their institution = financial hardship (loss of funding, etc.)
- Litigation
- Regulatory sanctions
- Fundamentally unethical
What Is Research?

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

HHS regulations define research at 45 CFR 46.102(d)
Types of Research Requiring IRB Review

STUDIES INVOLVING:

- Human subjects or information derived from human subjects that is about that subject (sensitive surveys/questionnaires with identifiers)
- Human tissues and specimens specifically, and prospectively collected for purposes of research
- Data and confidential information from human subjects which is identifiable and/or linked to the subject
- Research that may place the subject at minimal to more than minimal risk
- Studies involving vulnerable populations
  - Prisoners, pregnant women and fetuses, children, emotionally challenged or deficient.
Who decides whether an IRB review and approval is required?

- OHRP has recommended that investigators not be given the authority to make an independent determination that research does not involve human subjects.
  - IRB members/staff and Investigators may reference SOP HRP-310 “Human Research Determination” worksheet.

- All investigators irrespective of whether their study involves human subjects or not, should contact HRP/IRB for a determination as to whether the proposed study is research and whether it involves humans subjects.

- Individuals who are authorized to make this decision within an Institution or University are:
  - IRB Chairs or Chair’s designees
  - Director, Human Research Protection
What is an IRB?

- IRBs ensure that human subjects are protected from harm or injury, that research is conducted in accordance with all applicable regulations, and that the rights of subjects are protected.

- An administrative board which has the authority to approve, request modifications to, or disapprove research involving human subjects or the use of identifiable information derived from human subjects.

- Drexel University’s IRBs are comprised of affiliated and unaffiliated members whose background, training and areas of expertise allows them to evaluate human research proposals for risks of physical or emotional harm to human subjects. The members are scientists and non-scientists of varying backgrounds, academic faculty and staff as well as child and prisoner advocates.
IRB Review Considers Belmont Principles

Respect for Persons
- Research subjects are treated as autonomous agents, making independent decisions to enter into research.

Beneficence
- Maximize benefits and minimize risks of harm from research, evaluate risks
  - Risk may be either
    - A) No more than minimal; equivalent to risks of usual daily activities of the subjects
    - B) More than minimal risk; beyond the risks of usually daily activities of the subjects
IRB Review Considers Belmont Principles

Justice

- Fair distribution of risks and benefits of participation in research, no one group of subjects should be exposed to greater risk or benefit of the research than any other group of subjects.
IRB Review of Research
Involving Human Subjects

DHHS require eight specific criteria to be satisfied before an IRB can approve research (45 CFR 46.111)

1. Risks to subjects are minimized using procedures consistent with sound research design and do not unnecessarily expose subjects to risk.

2. Risks to subjects are reasonable relative to (1) anticipated benefits and (2) the importance of the knowledge that may reasonably be expected to result.

3. Selection of subjects is equitable; participants have equal/fair chance of research participation, no one group is specifically selected to benefit or suffer consequences from participation in research.
IRB Review of Research
Involving Human Subjects

4. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative.

5. Informed consent is appropriately documented in accordance with appropriate regulations and institutional policy.

6. Adequate provisions to protect the privacy of subjects and confidentiality of data collected.

7. Adequate provisions for monitoring the data collected to ensure protection of subjects.

8. When subjects are likely to be vulnerable to pressure or coercion, additional safeguards are included to protect subjects.
Drexel University IRB Committees

DU research oversight is registered with DHHS under an Assurance for Drexel University

Five separate IRBs:

IRB #1- Adult Medical/Psychological Trials
IRB #3- Adult Behavioral/Educational/Social
IRB #4- Children Medical/Psychological Trials
Western IRB (WIRB)- Multicenter Industry Sponsored Clinical Trials
National Cancer Institute’s Central IRB (CIRB)
Meeting Dates

Drexel University IRB’s

- IRB #1 meets every 2nd Monday of each month, at Hahnemann University Hospital/NCB.

- IRB# 3 meets every 3rd Thursday of each month scheduled at Drexel University and 1601 Cherry St.

- IRB#4 meets every 3rd Wednesday of each month at St. Christopher’s Hospital for Children.

- WIRB meets weekly

- NCI CIRB (as determined by NCI)
Meeting dates and deadlines for submission to the full board meetings are posted on Human Research Protection Website:

www.drexel.edu/research/administration/compliance/humanSubjects/irb/calendars/

There are NO deadlines for Exempt and Expedited review applications.

WIRB deadlines: Contact WIRB directly at:

www.WIRB.com
Levels of Review

Study may fall within the guidelines of one of the following levels of review:

- Letter of Reliance
- Letter of Determination
- Case study or case report
- Exempt from IRB review (essentially no risk)
- Expedited review (minimal risk)
- Full review (more than minimal risk) requiring rigorous review of risks and benefits by convened IRB
Levels of Review

Letter of Reliance (LOR or IRB Authorization Agreement)

- An agreement between two or more IRBs where one IRB agrees to be recognized as the IRB of record for each participating site/investigator (Ex: multicenter trials)
- Agreement executed for multisite research, cooperative research b/w investigators from unaffiliated sites
- IRB of record is usually the institution hosting the enrollment or treatment of the subjects or owner of the data/specimens studied
- LOR agreements are encouraged by OHRP, institutions can opt out or decline entering into the LOR
- Execution of the agreement is conducted b/w IRB offices not the PIs.
- Contact DU Human Research Protection (HRP) for directions and guidance 215-255-7857
Levels of Review

Letter of Determination

- Administrative review and approval of protocols determined to NOT involve human subjects or identifiable information/specimens about human subjects

- Examples:
  - Secondary analysis of an already existing deidentified data set to which the PI has no access to any code or links that may be used to re-identify the subjects.
  - Program evaluations and improvements; use of an agency’s or health clinic’s records, data sets or employees to evaluate services provided, customer satisfaction or in general quality improvement. Data results are provided to the agency or health clinic only, data would not be made available as “generalizable knowledge”.
  - Contact DU HRP for directions and guidance 215-255-7857
Levels of Review

Case study and Case reports
- Three or fewer patients/subjects, are prepared for the purpose of illustrating some points in the care of a patient, to educate and formulate new research questions which may eventually lead to generalizable knowledge.

Examples:
- Uncommon observations
- Report of a new condition, treatment and follow up
- Report of a familial condition with a proposed mode of inheritance
- Questions regarding a new theory
- Unusual combination of conditions or events that cause confusion
- Adverse responses to therapies
Levels of Review

Exempt: Categories 1-6

- Category 1: Research involving normal educational practices
  - May involve children
- Category 2: Educational tests, surveys, questionnaires
- Category 3: Survey and interview of public officials
- Category 4: Use of existing records/data/biological samples
  - PI does not retain a link or code to re-identify subjects
- Category 5: Evaluation of public service programs
- Category 6: Taste and food quality evaluations

- Rarely will involve consent of subject, may require use of HIPAA waiver of authorization (biologic samples/specimens)
Levels of Review

Expedited Review

- No more than minimal risk to the human subjects,
  
  - "minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
  
  - "Minimal Risk" does not include administration of medication or use of any device placed inside the body.

HHS 45 CFR Part 46.102i,
Levels of Review

Types of Expedited Review:

- Retrospective chart review with waiver of consent and HIPAA authorization waiver, and retention of a “code key” linking source document and data collection tool/spreadsheet.
- Prospective collection of health information with informed consent inclusive of HIPAA authorization.
- Minimally invasive collection of human specimens (venipuncture, prospective collections of discardable tissue).
- Questionnaires and surveys of a sensitive/private nature with identifiers linked to the subjects.
Levels of Review

**Full IRB review:**

- Projects for which the level of **risk** is determined by the IRB to be **greater than minimal**.
  - The probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination(s) or test(s)

- Examples: projects which involve deception, use of drugs or significant risk devices, evaluation/observation of illegal behavior, or legally incompetent persons

- Investigational New Drugs (IND)
- Investigational Device Exemptions (IDE)
QUALIFICATIONS AND TRAINING

Who can be a PI?

– Policy may vary and is Institution specific, (Someone sufficiently qualified by training and/or expertise)

– Policy at DU requires a PI to be
  - Attending Physician
  - Faculty
  - Staff

Who can be a sub-investigator?

- Fellows
- Residents
- Students
- Research assistants
Human Research Training

- Every Investigator, faculty member, staff or student directly involved in the proposed research activity must complete the appropriate Collaborative Institutional Training Initiative (CITI) training modules before a research protocol is approved.

- CITI training is required regardless of the type or level of IRB review and approval.

- Approval letters for new applications to the IRB, Periodic renewals for continued enrollment or data analysis, and amendments to protocol to add new personnel will not be released until the necessary CITI training modules are complete.
CITI Training Courses

DU offers four (4) CITI training courses

1. CITI Human Subject Research (HSR) Training
   • (All Investigators/Key Personnel)
2. CITI Good Clinical Practice (GCP)
   • (drug, device or conducting clinical trials)
3. CITI Responsible Conduct of Research (RCR)
   • (required for applicants to National Science Foundation)
4. CITI Health Information Privacy and Security (HIPS)
   • (Investigators and key personnel accessing PHI)

All applicable CITI training courses require recertification every three (3) years.
The required CITI training courses may be found at:

- [http://www.drexel.edu/research/administration/compliance/humanSubjects/humansubjectstraining/](http://www.drexel.edu/research/administration/compliance/humanSubjects/humansubjectstraining/) or
- [www.citiprogram.org](http://www.citiprogram.org)

Personnel with CITI training certificates completed at non-DU institutions will be honored, though additional modules may be required, and be renewed every three (3) years.
Drexel Core Training Modules

Additional training courses may be required depending upon:

- Use or access to Protected Health Information (PHI)
  - HIPAA I & II from the Drexel Core Modules web site (no re-cert)
- Use of surrogate/substitute or proxy consent process
  - Substituted consent training from the Drexel Core Modules web site (no re-cert)
- Collection and processing of human specimens/tissues,
  - Bloodborne pathogen/laboratory safety training from Dept. Health and Safety
- Shipping of human or animal specimens/tissues off campus,
  - Infectious Substances Packaging training from the Drexel Core Modules web site (annual re-cert)

Drexel Core training modules may be found at https://apps.research.drexel.edu/train/login.asp

Drexel University Dept. of Health and Safety http://www.drexel.edu/facilities/healthSafety/training/
The Process

Who can Assist you?

– Each committee has a specifically assigned IRB Coordinator

Human Research Protection

http://www.drexel.edu/research/hrp

Phone: 215 255-7857

HRPP@drexel.edu

Address: 1601 Cherry Street, 3 Parkway Bldg., Suite 10-444 Philadelphia, Pa 19102
Working with the IRB

- Pre-submission questions
  - Set up an appointment with HRP
  - Request for departmental meeting
  - Obtain information on levels of review
  - Obtain information on how to complete forms

- Once you have applied review study status and follow up for assistance with your IRB Coordinator
What does an IRB expect of an application?

- **Consideration** of how the substantive issues & methods fit with ethical guidelines & IRB requirements
- **Clarity** in statement of problem, Research Questions & Methods of data collection
- **Consistency** in content of all documents
- **Completeness** of all materials
What Forms Do I Submit?

Letter of Determination: (1 copy Electronically)

- Letter of Determination application,
- Permission letter for access to privately held data (as applicable),
- Data collection tools, surveys, questionnaires

http://drexel.edu/research/administration/compliance/humanSubjects/irb/applications/
What Forms Do I Submit?

Case Study: (1 copy Electronically)

- Case Study application,
- HIPAA authorization waiver,
- Copy of the final Case Study

http://drexel.edu/research/administration/compliance/humanSubjects/irb/applications/
What Forms Do I Submit?

Exempt, Expedited and Full Standard Applications

Each application will use the same minimum documents as part of the initial application

- HRP 201 Contact Information
- HRP 211 Application for Initial Review
  - link for financial conflict of interest form found within this document, all personnel must complete a FCOI disclosure form
- HRP 503 Template Protocol
- Written proposal/Grant/thesis
What Forms Do I Submit?

Exempt, Expedited and Full Standard Applications

As Applicable documents to submit

- HRP 502 Template Consent form
- Surveys/questionnaires
- Advertisements/flyers
- Letters of permission to access privately held data, specimens or populations of subjects
- Phone scripts
- HRP-432 Good Clinical Practice (completed when protocol requires PI to follow ICH-GCP standards)

http://drexel.edu/research/administration/compliance/humanSubjects/irb/applications/
Electronic Submission Process

1. IRB/WIRB application documents that require signatures will be printed, signed, then scanned and saved, while word docs or PDFs, such as consent forms, written protocols or investigator brochures, etc. that do not require a signature may be saved directly to your PC/MAC without need for scanning.

2. Each individual document type is scanned or saved and individually named; ex: ([ICF word doc. Investigator 12345]; [written protocol PDF, Investigator 12345]; [investigator brochure PDF, Investigator 12345]; [WIRB Initial Review form word doc, Investigator 12345…]). (DO NOT USE ANY CHARACTERS IN THE WORD DOC/PDF FILE NAME)
Electronic Submission Process

3. 20 MBs is the maximum size in total of all attachments that an email is capable of sending or receiving. Each document is attached to the email as an individual word doc/PDF document and titled appropriately.

4. If the MB size of all documents in total exceeds 20 MBs you have the following options:
   A. compress the attachments into a Zip file and attach to the email,
   B. save the application to a CD/DVD and mail/drop off at the ORRC, or
   C. send the application in multiple separate emails however you must label each email in the “subject” box as PI name, brief title and also note email as 1 of 2; 1 of 3, etc.
Electronic Submission Process

5. New applications as well other forms of action with the IRB, such as Continuing Reviews, Adverse Event reports, Amendments, etc.; are to be emailed to HRPP@drexel.edu and Cc’d to the primary IRB coordinator for the applicable IRB committee (#1, #3, #4 or WIRB).

Medical Adult IRB
#1: Exempt/Expedited applications: Barbara Ferrigno bf34@drexel.edu
#1: Full application:

Social/Behavioral IRB
#3: All applications: Teresa Hinton tch47@drexel.edu

Medical Pediatric IRB
#4: All applications: Linda Tate lmt43@drexel.edu

WIRB All applications: Lois Carpenter lac87@drexel.edu
How Long Does IRB Approval Take?

- **IT DEPENDS** upon the level of review and the investigator’s responses to IRB conditions.
- Exempt and Expedited reviews generally take less time than Full board reviews.
- In general, turnaround time may be improved if investigators responds to IRB questions quickly.
- Need assistance in responding to questions or clarifications on questions, contact your IRB coordinator to help you resolve any questions.
WHEN CAN I BEGIN MY RESEARCH?

NO RESEARCH ACTIVITIES MAY COMMENCE UNTIL:

- YOU HAVE RECEIVED YOUR IRB LETTER OF APPROVAL, AND IF APPLICABLE,
- YOUR APPROVED AND STAMPED CONSENT FORM
WHO CAN ASSIST WITH MY RESEARCH ACTIVITIES AND CONSENTING OF SUBJECTS?

Only investigators, sub-investigators and research coordinators or assistants who have been approved by the IRB for the study, and have completed all relevant training requirements.
WHO IS PERMITTED TO OBTAIN A RESEARCH SUBJECT’S CONSENT?

ONLY THOSE QUALIFIED INDIVIDUALS WHO:

– HAVE COMPLETED THEIR HUMAN SUBJECTS RESEARCH TRAINING,
– HAVE SIGNED A CONFLICT OF INTEREST STATEMENT,
– HAVE BEEN APPROVED BY THE IRB, AND
– HAVE BEEN NOTED IN FORM HRP 211 AS BEING INVOLVED IN THE CONSENT PROCESS.
WHO IS RESPONSIBLE OF FOR THE RESEARCH ACTIVITIES AND OUTCOMES?

- The Principal Investigator is responsible for all actions and activities of all individuals who contribute to the study.

- Any misconduct, failure to follow the approved protocol or failure in compliance and reporting is the PI’s responsibility!
What happens after initial Approval?

How can I change the protocol after it is approved?

- Researcher submits for review all modifications, if any and however trivial they may be, using form HRP-213 “Modification of Approved Human Research”
- Directions are located with HRP-213

Examples:
- Change in research procedure or intervention, data collection method or tools, advertisements or phone scripts.
  - Include as applicable; revised form HRP-503 Template Protocol, HRP 502 Template Consent, questionnaires/surveys and any document being modified
What happens after initial Approval?

Continuing Reviews and Annual Reporting

Every Expedited, Full and Letter of Reliance project is approved for the duration of one year;

Annual (at minimum) **IRB review** for continued enrollment, follow up of subjects, or data analysis only is required for the continuation of the research for all Expedited Full and Letter of Reliance protocols.

Continuing/final reviews are submitted using form HRP-212 “Continuing Review Progress Report”

Continuing review deadline calendar may be found at [http://drexel.edu/research/administration/compliance/humanSubjects/irb/calendars](http://drexel.edu/research/administration/compliance/humanSubjects/irb/calendars) /
What happens after initial Approval?

- Protocol Expiration: 364 Days after date of approval for all Full and Expedited and Letter of Reliance protocols
  - Exempt categories, Letters of Determination and Case reports do not have an expiration date.

- If continuing review is not done, the project expires on the expiration date, no new subjects may be enrolled into the study, reporting obligations to the IRB remain.

- Expired protocols for reactivation requires a brand new application and review by the IRB.

- A Final Report is to be provided to the IRB for protocols approved as letter of reliance, Exempt, Expedited or Full.
New Reportable Information

Report any of the following using form HRP-214 “Reportable New Information”

- New or increased risk and/or safety issues
- Harm experienced by a subject or other individual that are unexpected and probably related to the research procedures
- Non-compliance with applicable regulations, IRB determinations or allegations of non-compliance
- Audit, inspection or inquiry by a federal agency
- Written reports of study monitors
- Failure to follow protocol due to action or inaction of PI or staff
- Breach of confidentiality
- Change in protocol without advance IRB approval
- Complaint of a subject PI is unable to resolve
- Premature suspension or termination of research by PI, sponsor or institution.
- Unanticipated adverse device effect
What happens after initial Approval?

**Accurate record keeping is critical**
- all documents related to the study must be kept in the regulatory binder
- IRB documents are kept a minimum of 3 years from study closure
- Documents related to HIPAA/PHI are kept a minimum of 7 years from study closure
- Data/PHI collected from children are kept for a minimum of 7 years beyond a child’s 18th birthday
- Data retention policy and retention schedule
  - [http://www.drexel.edu/generalcounsel/drexelpolicies/OGC-6/](http://www.drexel.edu/generalcounsel/drexelpolicies/OGC-6/)
  - [http://www.drexel.edu/~media/Files/GeneralCounsel/RecordRetentionProgramMasterSchedule5282013.ashx](http://www.drexel.edu/~media/Files/GeneralCounsel/RecordRetentionProgramMasterSchedule5282013.ashx)
Non-compliance Consequences

- **Serious Noncompliance**
  Human subject research being carried out without IRB review and approval by institution’s IRB. Serious noncompliance also includes substantive modifications to IRB-approved research without IRB approval.

- **Continuous Noncompliance**
  This involves a principal investigator making the same mistake several times repeatedly, particularly after an IRB has informed him or her and his/her team member(s) of the problem. Continuous noncompliance also includes if the principal investigator has multiple problems with noncompliance over a long period of time or has a problem with multiple projects.

- **Suspension or Termination**
  The IRB, Signatory Official and the Humans Subject Protection Administrator have the authority to suspend or terminate approval of human subject research that is not being conducted in accordance with the IRB’s requirements.
In Summary

- When in doubt, ask questions; seek help
- Remember: consideration for clarity, consistency, completeness
- On-going process – keep dialogue open
- All committees use “reasonable person” standard to ensure high standards of ethical research
- These committees help facilitate responsible conduct of research
Questions?

Contact Human Research Protection at

215-255-7857

http://www.drexel.edu/research/hrp