Tips to Prepare an IRB Protocol for a Timely Approval

Susan L. Pocotte, Ph.D.

Professor, CON

Chair, Biomedical Institutional Review Board

susan.pocotte@utoledo.edu

Tip 1:

Keep the primary concern in your mind at all times.

It does not minimize the work, but it motivates us to put our best effort forward from the beginning and work together for the best interests of human subjects in research.

susan.pocotte@utoledo.edu

The protection of Human subjects, their biospecimens and their private data is the primary concern.

All other concerns are secondary.

susan.pocotte@utoledo.edu

Federal Regulations

- Based on the three Belmont principles
  - Respect for Persons- Individual allowed to choose participation.
  - Beneficence- Max. benefits and minimum risk; “do no harm”
  - Justice- No group should bear the risks when the benefits apply broadly.
- Two parallel sets of regulations were written and enacted in 1981.
  - Department of Health and Human Services (DHHS)
  - Food and Drug Administration (FDA) – regulated drug, devices
- Common rule/Final rule

The Common Rule

- A general set of regulatory provisions governing human subjects protections.
- Important aspects of the Common Rule:
  - Requirements for compliance by research institutions.
  - Requirements for IRB memberships, responsibilities, functions, review of research, and record-keeping.
  - Requirements for obtaining and documenting informed consent.
  - Recognizes there are additional requirements for the protection of vulnerable subjects –vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

susan.pocotte@utoledo.edu

Why an IRB?

- Federal law and regulations require such review.
- Research ethics require independent review.
- Past abuses demonstrate that researchers cannot determine benefits/risks.

susan.pocotte@utoledo.edu

TIP 2:

Understand the UToledo processes for IRB approval of Human Subject Research.

HRPP staff will keep up to date with the Federal Regulations and incorporate them into our policies and procedures.

We are here to help- not hinder.

susan.pocotte@utoledo.edu

Two primary groups work with the IRB Applications via a 2 Step Process

1. Human Research Protections Program (HRPP)
2. Institutional Review Board (IRB)

- Additionally, many Human Subject Clinical Research Protocols require input from other stakeholders at UTMC, UToledo Compliance, or UToledo Research Sponsored Programs.

UToledo Policy: 3364-70-05 Protection of human subjects in research

Human Research Protection Program (HRPP)

- Provides support to UToledo IRBs.
- Provides educational activities.
- Serves as a resource for faculty, staff and student researchers.
- Recommends and implements policies and regulations for the protection of human subjects in research.
- Ensures compliance with relevant laws, regulations, and ethical standards while addressing the needs and concerns of investigators who conduct research with human subjects.

susan.pocotte@utoledo.edu

HRPP Processes IRB Applications **before** IRBs Review/Approve

- Initial point of contact for researcher's questions.
- Receive submission and conduct pre-review.
- Check training completion.
- Check for electronic signatures.
- Check application is complete and documents consistent.
- Determine level of review. IRB can change level.
- Determine that a certain application is not human subject research.
- Communicate with researcher regarding needed corrections.
- Assign for IRB review.

Human Research Protection Program (HRPP)

Mahesh Pillai, MD, PhD
Manager
Research Compliance
R1 1020A
419-383-4251

Nicole Lederer, MEd
Analyst
SBE IRB
R1 1020D-1
419-530-6167

Marina Muchnik, BS
Associate Analyst
Biomedical IRB
R1 1020E
419-383-6903

Madison Rowe, BSE
Associate Analyst
IRB
R1 1020D-3
419-383-6904

Gabrielle McMunn, MS
Associate Analyst
IRB
R1 1020D-4
419- 383-6902

HRPP Staff

- 2 are certified IRB Professional (CIP) through PRIM&R, others in training
- Report to Assoc Vice President for Research, Dr. Schall

- Public Responsibility in Medicine and Research (PRIM&R) is a 501(c)(3) nonprofit, that works to ensure the highest ethical standards in research by providing education, membership, and other professional resources to the research and research oversight community, including those who work with human subjects protections programs (HRPPs), institutional review boards (IRBs), animal care and use programs, and institutional animal care and use committees (IACUCs).

UToledo Policy: 3364-70-05 Protection of human subjects in research

- All UToledo-related research involving human subjects must be reviewed and approved by the appropriate UToledo IRB or a UToledo-authorized external IRB prior to beginning the research, and at intervals specified by the reviewing IRB.
- UToledo Biomedical IRB may approve clinical research performed at UToledo-affiliated practice sites or sites where the university is formally authorized to review research.
- The UToledo IRBs have the authority to determine the appropriate course of action with respect to study deviations and adverse events depending on the degree of risk to subjects or affected individuals and previous deviations by the investigator.

UToledo Policy: 3364-70-05 Protection of human subjects in research

- Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

What does the IRB do with Applications?

- Conducts initial reviews and continuing reviews of research involving human subjects.
- Conducts reviews of proposed changes to approved research involving human subjects.
- Follows up on issues related to research involving human subjects such as:
  - Subject complaints or concerns
  - Suspected violations of federal or state regulations
  - Suspected violations of UT policies
- Only the IRB can approve the modification or waiver of informed consent.
- Final determination level, and risk.
- Final approval and signatory for Human Subject research.

susan.pocotte@utoledo.edu

Who is the IRB?

- A group of individuals charged with protecting the rights and welfare of human research subjects.
  - faculty and staff appointed by the Institutional Official (IO)
  - community members and nonscientists appointed by the (IO)
- Responsibilities of the Board given directly by the federal government.
- IRB is separate from UToledo administration and shared governance.
- The Board does NOT make regulations.
- Volunteer

susan.pocotte@utoledo.edu

Institutional Review Boards

Biomedical IRB

Interventions including therapies (e.g., drugs, diet, exercise, surgical interventions, or medical devices), diagnostic procedures (e.g., CAT scans), preventive measures, and review of medical records.

Social, Behavioral & Educational (SBE) IRB

Questionnaires, observations, studies of existing data (no PHI), and non-biomedical interventions.

- Submit to the most appropriate IRB, regardless of which campus you are on.
- Only faculty and staff can serve as PI. This does include residents and community based clinical or research faculty.

BIOMEDICAL IRB

Member	Scientific	Affiliated UToledo	Role and Specialization
Batts, Gary	No	No	Community Member
Baum, Caitlin Emily Ph.D.	Yes	Yes	Member (Pathology)
Federman, Douglas M.D.	Yes	Yes	Vice Chair (Internal Medicine)
Honisko, Marcia E. Pharm.D.	Yes	No	Member (Promedica clinical oncology Pharmacy)
Hoyt, Alastair M.D.	Yes	Yes	Member (Neurosurgery)
Hunter, Kimberly E. Ph.D.	Yes	Yes	Member (Psychiatry)
Khuder, Sadik Ph.D.	Yes	Yes	Member (Biostatistics)
Koffman, Boyd M.D., Ph.D.	Yes	Yes	Member (Neurology)
Linker, David	No	No	Community Member
McLuckie, Rachel Elizabeth PharmD	Yes	Yes	Chair Designee (Investigational Drug and Patient Safety)
Miller, Jolene MLS, BS, AHIP	No	Yes	Member (Mulford Library)
Palmer, Anthony C. M.D.	Yes	No	Member (Pediatric Oncology)
Peseckis, Steven M. Ph.D.	Yes	Yes	Vice Chair (Medicinal Chemistry)
Pillai, Mahesh R M.D., Ph.D.	Yes	Yes	Member (Biological Sciences, IRB Admin)
Pocotte, Susan Ph.D.	Yes	Yes	Chair (Pharmacology, Pathophysiology)
Stein, Dagmar T. M.D., Ph.D.	Yes	No	Member (Pediatric Oncology)
Taylor, Colleen Y. PhD, RN, FNP-BC CRG	Yes	Yes	Member (Nursing Practice)

Social, Behavioral & Educational IRB Members

Member (voting)	Specialization
Patricia Case, PhD (*Chair*)	Sociology and Anthropology
Sarah Alberts, MSW	Community Member
Wesley Bullock, PhD	Psychology
Shelley Cavalieri, JD (*Vice Chair*)	Law
Nicole Lederer, MEd, CIP	Mental Health, IRB Admin
Alexia Metz, PhD	Occupational Therapy
Mahesh Pillai, MD, PhD, CIP	Biological Sciences, IRB Admin
Jason Rose, PhD	Psychology
Nilgun Sezginis, PhD, RHIA, CCS (*Chair Designee*)	Health Information Administration

TIP 3:

Know the location of the policies, procedures, IRB application documents.

Essential to due process:

- HRPP Written Procedures
- Policy 3364-70-05: Protection of human subjects in research

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Where can you get information?

Web site - http://www.utoledo.edu/research/rsp/irb/ , under “Research”

- Policies and procedures, Regulations
- Guidance documents, consent form templates, answers to FAQs

IRB Manager - https://utoledo.my.irbmanager.com/

- xForms
- Study documents

Mahesh Pillai, M.D., Ph.D. – Manager, Research Compliance

Human Research Protection Program (R1 Building)

Telephone – 419-383-6796

E-mail – irb.biomed@utoledo.edu

Geez- Can’t we speed up the Approval Process?

susan.pocotte@utoledo.edu

HRPP and IRBs are committed to:

1. improving our processes;
and
2. reducing the time between submission and approval.

HRPP and the IRBs are committed to:

1. Advocating on behalf of the researchers to other groups for improved processes.

2. Helping the researchers learn and more efficiently navigate what can appear to be a mysterious system of procedures.

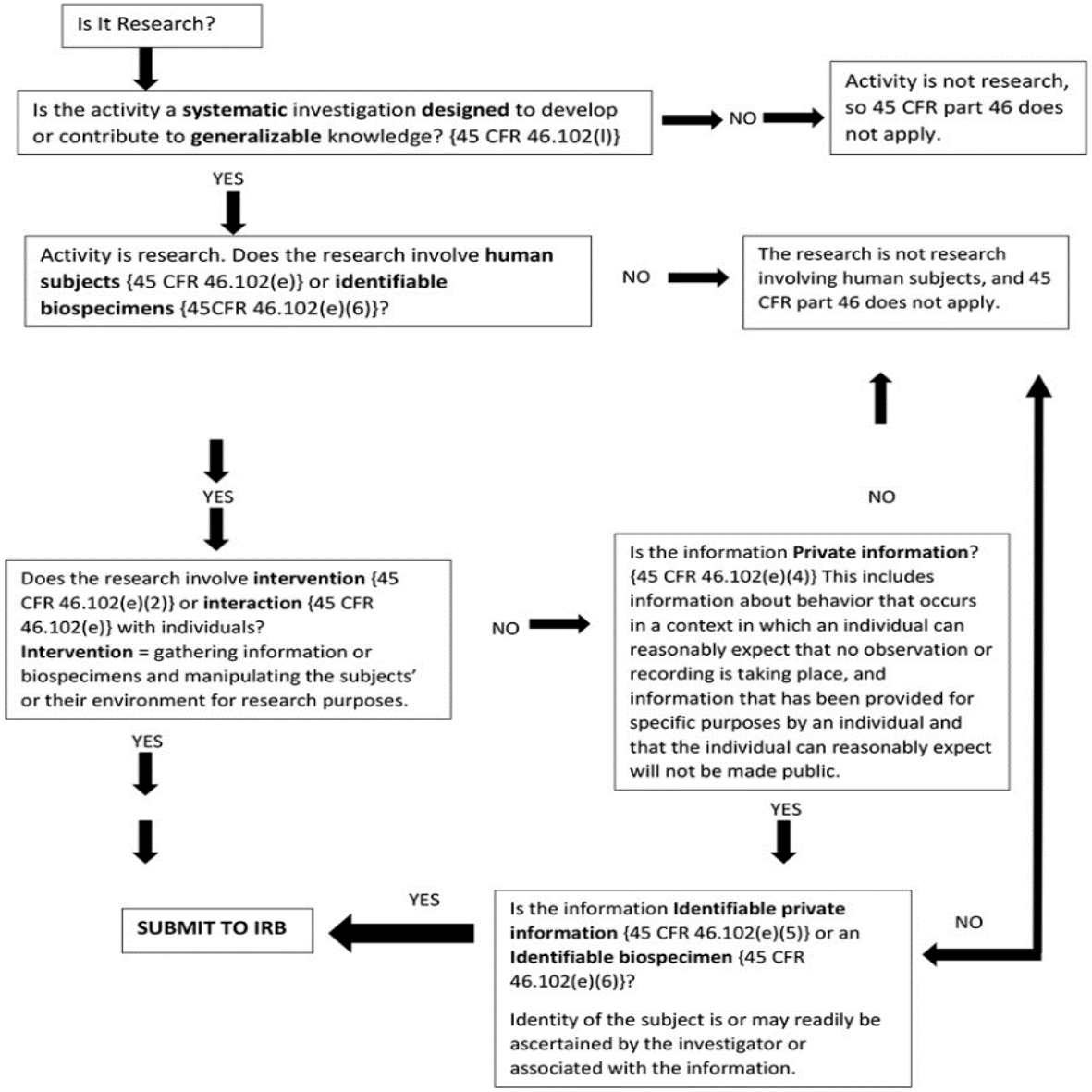
TIP 4:
Initial preparation steps for Researcher(s) to speed up the Pre-Review.

Make your “to do” list before submission of your IRB application.

UToledo HRPP and Biomed IRB (1/24/2023)
susan.pocotte@utoledo.edu

Step A.

Does my project need IRB Review?



Not sure?

Contact HRPP.

IRB Jurisdiction

- Human Subject:
  - Living individuals, about whom an investigator (whether professional or student) conducting research:
    - (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
    - (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
  - Recording heart beat, blood draw, survey, interview
  - Secondary data with identifying information attached

IRB Jurisdiction

- Systematic investigation - well-defined question(s) and organized data collection
- Research development, testing and evaluation - “Pilot" activities are considered to be research and require IRB review
- Generalizable knowledge - Add to the overall body of knowledge. Typically, by publication or presentation.
- Retrospective Chart Review
- Central IRB applications
- Humanitarian Use Devices (HUD)

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Not Usually IRB Jurisdiction

- The IRB has always said that case reports – up to 3 cases – did not meet the regulatory requirements for IRB review, because the reports are not **generalizable**. Federal Regulations define research as "**a systematic investigation, including development, testing, and**. **evaluation, designed to develop or contribute to generalizable knowledge**1 " (45CFR46.102(d)).

- Many internal quality improvement projects are not subject to IRB review. However, please check with HRPP especially if it is part of Student Scholarly Work that is intended for publication, not part of the student's employee responsibilities, and/or includes interventions that are not standard of care.

- If you need verification, HRPP can provide a *Not Human Subjects Research* application.

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Levels of Review

- Not Human Subjects Research
- Exempt, Expedited, Full Board
  - Exempt - least invasive and of minimal risk to subjects. UT policy requires that the HRPP makes the exempt determination
  - Expedited - Involves minimal risk, but potentially some
  - Full Board - Greater than minimal risk

* minimal risk means that 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 the performance of routine physical or psychological examinations or tests. (45 CFR 46.102(i))

Exempt Projects

- The use of educational tests, survey procedures, interview procedures or observation of public behavior
  - Participation is anonymous, or
  - Disclosure of responses outside the research would not place the subjects at risk

- The collection or study of existing data
  - If data are publically available, or
  - If the information is recorded by the investigator in such a way that subjects cannot be identified

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Expedited Projects

- Prospective collection of biological specimens for research purposes by noninvasive means. For example: deciduous/permanent teeth at the time of indicated extraction.
- Collection of data through noninvasive procedures routinely employed in clinical practice
- Research involving materials that were collected for non research purposes
- Retrospective Chart Reviews
- Surveys (not eligible for exempt)
- New/modified Intervention

Full Board Projects

- Some types of research automatically require full Board review:
  - Research with prisoners
  - Certain types of research with children (such as when a waiver of parental consent is requested by the researcher)
  - More than minimal risk to participants
- Research involving new drugs
- Research involving new devices

Step B.

Study Personnel Obtain and Maintain Appropriate Training

UToledo HRPP and Biomed IRB (1/24/2023)
susan.pocotte@utoledo.edu

Training for Human Subjects Research

CITI (Collaborative Institutional Training Initiative) training website at https://www.citiprogram.org.

- This training must be completed before an individual can be approved as a member of the research team.
- The appropriate Curriculum are: Biomedical Researchers & Students OR Social & Behavioral- Educations Researchers & Students. The Social & Behavioral- Educational Researcher IRB accepts Biomedical Researchers & Students CITI training.
- **There are two training courses:**
  - **BASIC** Basic training must be completed **before** completing refresher courses. Comparable basic training form other institutions may be considered by contacting the HRPP Office. BASIC training will expire **three** years
  - **REFRESHER-** complete every **three** years in the rotating cycle that your training expires. The system will direct you as to when another Basic course is due in your rotation cycle. Basic training is due once every 9 to 12 years (see below).
  - If you have a lapse in CITI training, you may be informed you are due for BASIC training when the rotation cycle would indicate Refresher training.

    BIOMEDICAL IRB study= BASIC → REFRESHER → REFRESHER → REFRESHER → BASIC

    SBE IRB study = BASIC → REFRESHER → REFRESHER → BASIC

IRB HIPAA Training Requirements

- All researchers that will access/view/analyze PHI on an IRB approved projects must complete UToledo's HIPAA compliance training. This training is completed annually.
- For additional information regarding HIPAA, please visit the Internal Audit and Compliance Office website (**https://www.utoledo.edu/offices/compliance/traiing.html**).

susan.pocotte@utoledo.edu

utoledo.my.irbmanager.com

- IRB Manager is the product used for the entire lifecycle of human subjects research, from the development and submission of protocol applications by researchers to the review of the applications by the Institutional Review Board through approval, amendment, renewal, and eventual closure.
- IRB Manager, despite its name, allows for the full suite of compliance processes to be handled in one system, and is the system used for IACUC and IBC protocol submission and review.
- Most people are able to navigate the application quite easily, but help with navigating the system overall will be provided by Human Research Protection staff, and through the short online videos linked above.

OPTIONAL HRPP PROGRAMING

- The HRPP is offering IRB trainings to support student, staff and faculty researchers who conduct research with human subjects. It is not mandatory but is encouraged if you are not familiar with the IRB process, federal regulations, UToledo policy, HRPP procedures, or best practices.
- The primary audience for the application training is those who have a clear research plan and need some guidance ensuring their procedures are in compliance with IRB approval procedure, providing the information in each application question that is needed for the IRB to make a determination, and general IRB Manager navigation. Please feel free to come with specific questions as this training is meant to not only provide a baseline understanding but to also help you in completing your application. *This training is NOT to learn the IRB Manager system*. Additionally, this is NOT the required human subjects training through CITI that all researchers who conduct research which human subjects must take. You may attend this training multiple times but class sizes are limited to ensure that we can give individualized attention where needed.
- The primary audience for the Q&A sessions are all faculty, staff, and student researchers that have general questions about IRB processes, human subject research regulations, and UT policies and procedures associated with conducting research with human subjects. These sessions are for both Biomedical and Social, Behavioral, and Educational research. The format for these sessions is unstructured.

To Schedule: Contact Mahesh Pillai, M.D., Ph.D. – Manager, Research Compliance E-mail – irb.biomed@utoledo.edu

Step C.

Principal Investigators- Please Train and Monitor your Study Personnel.

Please help your study coordinator or graduate student prepare the IRB application and documents.

susan.pocotte@utoledo.edu

Principal Investigator Assurance Statement

- *By electronically signing this submission with my UTAD and password, I certify that I am the person listed as PI of this study. Note that UT policy 3364-54-01, "Responsible technology use policy", states that accounts and passwords may not be shared with or used by other persons. Violations will be handled though university disciplinary procedures applicable to the relevant user.*
- *I certify that the information provided in this application is complete and accurate.*
- *I understand that as Principal Investigator, I have the ultimate responsibility for the protection of the rights and welfare of human subjects, and the strict adherence to any study-specific requirements imposed by the IRB.*
- *I agree to comply with all IRB and Institutional policies and procedures, as well as with all applicable Federal, State, and local laws and regulations regarding the protection of human subjects in research and the conduct of clinical research.*
- *I also agree to the following:*

1. to accept responsibility for the scientific and ethical conduct of this research study,
2. to obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent form, study sites or study personnel, recruitment procedures,
3. to immediately report to the IRB any serious adverse reactions and/or unanticipated effects on subjects which may occur as a result of this study,
4. to train study personnel in the proper conduct of human subjects research,
5. to assure that the personnel approved to explain and obtain consent have read the protocol, understand the study, and are fully knowledgeable of ALL details of the protocol and are able to answer ALL questions from research subjects such as risks and alternative treatments and therapies.
6. to complete the Continuing Review and Final Report Forms required by the UT IRB,
7. to adhere to the standards of Good Clinical Practice (GCP), developed by the International Conference on Harmonization (ICH).*

PI Responsibilities and Compliance Requirements

- Primary responsibility for the ethical conduct, which includes:
  - Training and supervising research assistants,
  - Ensuring the integrity and safeguarding of all data,
  - Following consent process,
  - Adhering to the research protocol,
  - Complying with the continuing review requirements,
  - Responding to HRPP requests for information,
  - Reporting all serious and unexpected adverse events as they occur,
  - Assuring compliance with all IRB and related UT policies,
  - Maintaining signed consent documents and related records for at least 5 years (6 years for studies with PHI) following the completion of the project. FDA regulated studies may have requirement for longer retention of records.

Step D.

Use the correct document templates for the IRB application.

First decide if you are using Biomedical or SBE IRB.

The templates are on the WebSite https://www.utoledo.edu/research/rsp/irb/

susan.pocotte@utoledo.edu

Consent Overview
It is a process, not just a document.

- Are all the elements of informed consent included?
  - Information - Is sufficient information given for potential subjects to make an informed decision about participation?
  - Comprehension - Is the information given in a way that potential subjects are likely to understand it?
  - Voluntariness - Do consent procedures ensure that potential subjects understand that they may choose whether to participate, free of coercion and undue influence?
- Is the consent procedure respectful and sensitive to subjects' vulnerabilities?
- How will subjects' agreement be documented?

susan.pocotte@utoledo.edu

Consent Templates

- Follow the directions on the templates.
  - Biomed or SBE
  - PHI or non PHI
- Language in 8th grade level
- Assent and parental consent documents if needed.
- Sample page next slide.

Consent: Key Information

Key Information:

{Be concise and focused in this section as you will elaborate on each key item later}.

- You are being invited to participate in a research study
- The purpose of the study is *{briefly sum up the research purpose}*.
- This research will take place *{where}*, will consist of *{survey, interview, etc.}*, and will take approximately *{minutes/hours}*.
- {If applicable, include alternative procedures, if not, delete}
- There are minimal risks, including loss of confidentiality *{briefly identify any other risks}*.
- You may benefit from your participation in this research by *{briefly identify any benefits to the participants}*.
- Your participation in this research is voluntary

Step E.

Provide sufficient details on xForm and all documents.

Do not be worried that we will say no to your research. We will delay and ask for clarifications.

It is Federal regulation that we are clear on the risk/benefit. Underrepresenting risk is a violation.

susan.pocotte@utoledo.edu

Risks and Benefits (Beneficence)

- Have both risks and anticipated benefits been clearly explained to the IRB?
- Have both risks and anticipated benefits been clearly explained to potential participants?
- Have all types of potential risks - physical, legal, financial, social, emotional - been considered?
- Have any risks to subjects been minimized (confidentiality)?
- Do the anticipated benefits of conducting the project outweigh the risks to subjects?

X

When data are primary source of risk

- What can you do to minimize the risk?
  - Collect data anonymously
  - Remove identifying information as soon as possible
  - Use codes for identifiers and keep the code list in a separate secure location.
  - Report data in aggregate or use pseudonyms
  - Store consent documents and data in a secure location
  - Limit who has access to data

X

susan.pocotte@utoledo.edu

TIP 5.

Lessons learned from common errors and required modifications.

susan.pocotte@utoledo.edu

Investigator Initiated and Sponsored Research

- Investigator Initiated
  - Provide sufficient information.
  - Use the Template “elements of a research protocol” for the attached document.
  - Provide track changes and clean documents for modifications.
- Sponsored research
  - For amendments: Please include a summary statement what has changed at the beginning of the textbox of xForm.
  - Use ICF UToledo Templates
  - The literature review of IB and research protocol can be used in place of preparing your own.

susan.pocotte@utoledo.edu

Adverse Events

- Did the event involve risks to subjects or others?
  - Includes adverse events, protocol deviations, other problems or events
  - May involve physical, psychological, social, legal or economic harms
- IF yes:
  - Do not delay in reporting!
  - Use the form please.
- IF no: then report at continuing review.

- This is part of human protections.

susan.pocotte@utoledo.edu

Deviations and Violations

- Flow chart on web site for guideline to report.
- Do not delay in reporting!
  - to the IRB within 10 working days after the deviation
- Single Subject Exception Request form can be submitted in advance of planned deviation.
- If Sponsor or FDA study, then it might require IO reporting.
- Device studies: deviations must be reported within 5 days
- This is part of human protections.

susan.pocotte@utoledo.edu

UToledo Policy: 3364-70-05 Protection of human subjects in research

- Submit final reports within thirty days following the expiration date of UToledo IRB approval or completion of data collection, analysis and cessationof all study activity (whichever comes first).
- If no expiration date is indicated, submit final reports within thirty days following the completion of data collection, analysis and cessation of all study activity.
- The UToledo IRB may withhold approval of subsequent research applications from an investigator who has not submitted a final report from previous research.

Common Issues that Delay Review/Approval because xForm returned to researcher.

- Typos, grammar, incomplete sentences on xForm
- Clarification on methods
- Incomplete or missing data collection tools
- More information about data security measures
- Provide all recruiting materials
- Clarification in consent document/provide required information- Consent is a process- not just a document.
- Consent language too complicated for the human subject.
- Old versions of required forms- ICF, assents

susan.pocotte@utoledo.edu

Common Issues that Delay Review/Approval because xForm returned to researcher.

- Documents don’t correspond/discrepancies
- Need to document approval from facility/school/organization
- Signed and updated CV for PI
- Lack of PI oversight, training, or editing of applications submitted by students. PI is responsible for mentoring.

susan.pocotte@utoledo.edu

Common Issues that Delay Review/Approval

- For unsponsored research: Digitally signed COI for all personnel
- Expired HIPAA
- Expired CITI
- Missed deadlines for convened meetings
- Missed deadlines for continuing review
- Continuing review applications with subject number discrepancies
- Delayed response to HRPP inquiries via the IRB manager or HRPP email system

Issues requiring other approval groups

- Funding contract reconciliation/approval on sponsored research.
- Revisions of ICFs on sponsored research.
- Missing Institutional Biosafety Committee (IBC) approval if applicable.
- Potential COI that requires review by COI committee.
- Privacy Officer approval for PHI access on patient charts.
- IT approval for other data retrieval needs.
- UTMC Clinical research resource utilization for all IN-PATIENT clinical trials.

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Where can I get additional information?

Web site - http://www.utoledo.edu/research/rsp/irb/ , under “Research”

- Policies and procedures, Regulations
- Guidance documents, consent form templates, answers to FAQs

IRB Manager - https://utoledo.my.irbmanager.com/

- xForms
- Study documents

Mahesh Pillai, M.D., Ph.D. – Manager, Research Compliance

Human Research Protection Program (R1 Building)

Telephone – 419-383-6796

E-mail – irb.biomed@utoledo.edu

UToledo HRPP and Biomed IRB (1/24/2023)
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QUESTIONS?

susan.pocotte@utoledo.edu