Good Clinical Practice (GCP)

- Kelly Dornin-Koss, Director, ECS-HSR
- Melissa Miklos, Associate Director, HRP
- Deb Montrose, PhD, Director, Research Operations, Department of Psychiatry
- Maggie Soncini, ECS-HSR Coordinator

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Objectives

- To provide an overview of Good Clinical Practice as they relate to:
  - GCP and the NIH adoption of GCPs
  - PI Responsibilities
  - Protocol Development and PittPRO
  - Informed Consent
  - Study Documentation

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What are GCPs?

- GCP is defined as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies

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What are the Foundations of GCPs?

- They are founded on:
  - Nuremburg Code
  - Belmont Report
  - The Declaration of Helsinki
  - Federal Regulations

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Why Do We Need GCPs in addition to the Regulations?

- The objective of the ICH is to provide a unified standard for the EU, Japan and US to facilitate the mutual acceptance of trial data
- They provide more details than our regulations
- They define and outline the responsibilities of key principles in clinical research, the IRB, the investigator, and the sponsor

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13 Principles of GCP

Conduct study ethically	Weigh risks to benefits	Protect subjects	Have adequate information to support proposed study
Protocol of sound design	Conduct study in accordance with IRB approved protocol	Care and decisions of subjects by qualified MD or dentist	Each person must be appropriately qualified
Freely given consent	Record and store data to permit accurate reporting	Respect the privacy and confidentiality of the subject	Assure quality of every aspect of the trial
	Investigational products produced according to GMP and used in accordance with the protocol		

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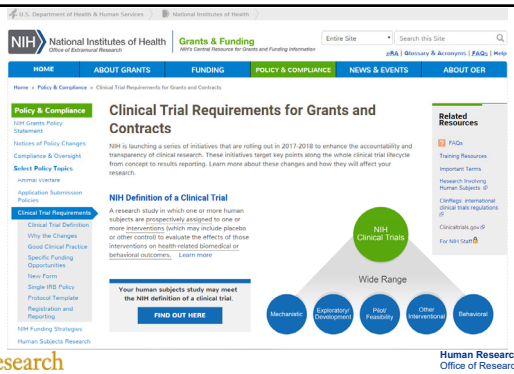

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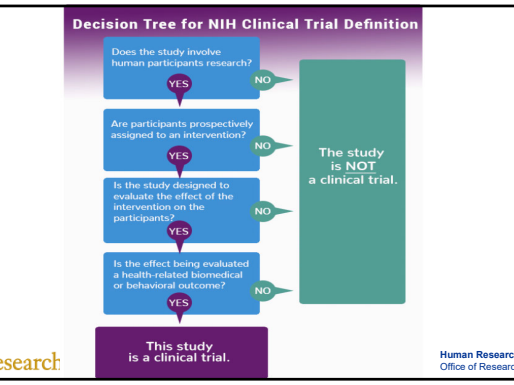

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Investigator Responsibilities

Deb Montrose, PhD, LSW

Director of Research Operations
UPMC Western Psychiatric Hospital
University of Pittsburgh Department of Psychiatry
Telephone: (412) 586-9020
Email: montrosedm@upmc.edu

1

PI Responsibilities

Ultimately responsible for ALL aspects of study conduct and for the study's RIGOR, REPRODUCIBILITY and RELIABILITY

- Ensure the study is conducted according to the approved protocol, signed agreements and regulations
- Ensure compliance with local, state, federal and international rules and regulations
- Control drugs, biological products and devices used in the study
- Any significant deviations from funded grant discussed with and approved by Program Officer, if applicable
- Protect the rights, safety and welfare of all individuals participating in the research (subjects, family members, community, research team) and minimize risks
- Evaluate, document and submit reportable new information
- Maintain adequate research records

Residents and Fellows can serve as PIs

- Must identify a faculty mentor

2

Delegation of Study Related Duties

Common practice for investigators to delegate certain study-related tasks to employees, colleagues, or other third parties (individuals or entities not under the direct supervision of the investigator)

When tasks are delegated, the investigator is responsible for providing adequate training and supervision of those to whom tasks are delegated

Investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study

3

Good Study Oversight Practices

- Maintain IRB approval and review protocol regularly to assess changes
- Review and update ClinicalTrials.gov
- Hold regular meetings with your research team, including data and safety monitoring
- Develop Manual of Operations
- Ensure proper training of your staff
- Obtain written consent from your study participants
- Document study procedures
- Review and report adverse events and unanticipated problems should they occur
- Oversight and audit of participant payments
- Implement ongoing quality assurance initiatives

4

Training Considerations for Clinical Researchers

- Who gets which training?
- Psychiatric symptom assessments
- Suicidality
  - Assessment
  - Action Plan
  - Tools (e.g., Columbia Suicide Severity Rating Scale, SAFE-T)

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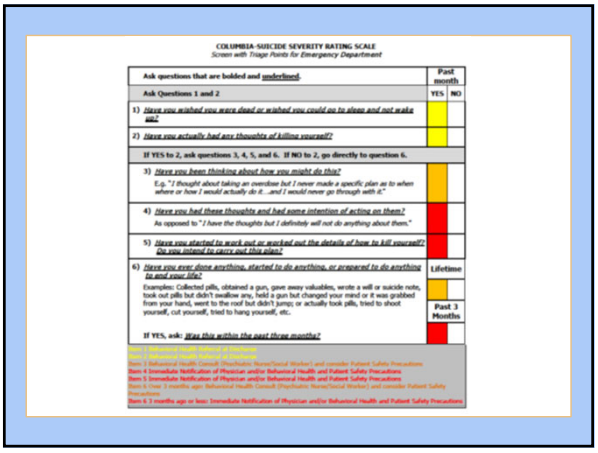

COLUMBIA-SUICIDE SEVERITY RATING SCALE

Screen with Triage Points for Emergency Department

Ask questions that are bolded and underlined.	Past month	
Ask Questions 1 and 2	**YES**	**NO**
1) **Have you wished you were dead or wished you could go to sleep and not wake up?**		
2) **Have you actually had any thoughts of killing yourself?**		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6.		
3) **Have you been thinking about how you might do this?** E.g., "I thought about taking an overdose but I never made a specific plan as to when where or how I would actually do it ...and I would never go through with it."		
4) **Have you had these thoughts and had some intention of acting on them?** As opposed to "I have the thoughts but I definitely will not do anything about them."		
5) **Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?**		
6) **Have you ever done anything, started to do anything, or prepared to do anything to end your life?** Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc.	Lifetime	
If YES, ask: Was this within the past three months?	Past 3 Months	

Item 1 Intervention Highly Advised if Positive

Item 2 Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions

Item 4 Immediate Notification of Physician and/or Behavioral Health and Patient Safety Precautions

Item 5 Immediate Notification of Physician and/or Behavioral Health and Patient Safety Precautions

Item 6 Over 3 months ago: Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions

Item 6 3 months ago or less: Immediate Notification of Physician and/or Behavioral Health and Patient Safety Precautions

6


SAFE-T
Suicide Assessment Five-step Evaluation and Triage
1
IDENTIFY RISK FACTORS
Note those that can be modified to reduce risk
2
IDENTIFY PROTECTIVE FACTORS
Note those that can be enhanced
3
CONDUCT SUICIDE INQUIRY
Suicidal thoughts, plans, behavior, and intent
4
DETERMINE RISK LEVEL/INTERVENTION
Determine risk. Choose appropriate intervention to address and reduce risk
5
DOCUMENT
Assessment of risk, rationale, intervention, and follow-up
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Substance Abuse and Mental Health Services Administration
www.samhsa.gov
Suicide assessments should be conducted at first contact, with any subsequent suicidal behavior, increased ideation, or pertinent clinical change, for inpatients, prior to increasing privileges and at discharge.
1. RISK FACTORS
Suicidal behavior: history of prior suicide attempts, aborted suicide attempts, or self-injurious behavior
Current/past psychiatric disorders: especially mood disorders, psychotic disorders, alcohol/substance abuse, ADHD, TBI, PTSD, Cluster B personality disorders, conduct disorders (antisocial behavior, aggression, impulsivity)
Co-morbidity and recent onset of illness: increase risk
Key symptoms: anhedonia, impulsivity, hopelessness, anxiety/panic, global insomnia, command hallucinations
Family history: of suicide, attempts, or more / psychiatric disorders requiring hospitalization
Precipitants/Stressors/Setting/arousal: triggering events leading to humiliation, shame, or despair (e.g. loss of relationship, financial or health status—real or anticipated). Ongoing medical illness (esp. CNS disorders, pain). Intoxication. Family turmoil/strain. History of physical or sexual abuse. Social isolation
Change in treatment: discharge from psychiatric hospital, provider or treatment change
Access to firearms
2. PROTECTIVE FACTORS Protective factors, even if present, may not counteract significant acute risk
Internal: ability to cope with stress, religious beliefs, frustration tolerance
External: responsibility to children or beloved pets, positive therapeutic relationships, social supports
3. SUICIDE INQUIRY Specific questioning about thoughts, plans, behaviors, intent
Ideation: frequency, intensity, duration – in last 48 hours, past month, and worst ever
Plan: timing, location, lethality, availability, preparatory acts
Behaviors: past attempts, aborted attempts, rehearsals (lying noose, loading gun) vs. non-suicidal self injurious actions
Intent: extent to which the patient (1) expects to carry out the plan and (2) believes the plan/act to be lethal vs. self-injurious. Explore ambivalence: reasons to die vs. reasons to live
*For youths: ask parent/guardian about evidence of suicidal thoughts, plans, or behaviors, and changes in mood, behaviors, or dispositions
Homicide-Suicide: when indicated, esp. in character disordered or paranoid males dealing with loss or humiliation. Inquire in four areas listed above
4. RISK LEVEL/INTERVENTION
Assessment of risk level is based on clinical judgment, after completing steps 1-3
Reassess as patient or environmental circumstances change
RISK LEVEL
RISK/PROTECTIVE FACTOR
SUICIDALITY
POSSIBLE INTERVENTIONS
High
Psychotic diagnosis with severe symptoms or acute precipitating event; protective factors not relevant
Nonlethal verbal suicide attempt or persistent ideation with strong intent or suicide rehearsal
Admission generally indicated unless a significant change reduces risk. Suicide precautions
Moderate
Multiple risk factors, few protective factors
Suicidal ideation with plan, but no intent or behavior
Admission may be necessary depending on risk factors. Develop crisis plan. Limit emergency/crisis contacts
Low
Modifiable risk factors, strong protective factors
Thoughts of death, no plan, intent, or behavior
Outpatient referral, symptom reduction. Give emergency/crisis numbers
(The chart is intended to represent a range of risk levels and interventions, not actual determinations.)
5. DOCUMENT Risk level and rationale; treatment plan to address/reduce current risk (e.g., medication, safety, psychotherapy, E.C.T., contact with significant others, consultation); firearms instructions, if relevant; follow-up plan. For youths, treatment plan should include roles for parent/guardian.

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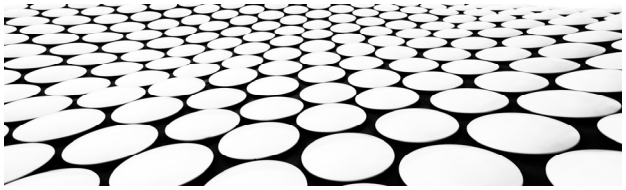
Tips for Protocol Development

Melissa Miklos, MSL, CIP – Associate Director, University of Pittsburgh Human Research Protection
December 7, 2021
mgm12@pitt.edu



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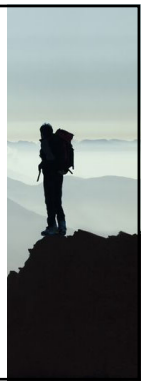
What you say, you must do



Start with a well-written protocol

- Do not repeat information in sections
- Review for consistency
- Ask if each procedures is necessary and realistic

2

GENERAL POINTS TO CONSIDER

- Write broadly, provide flexibility but be clear about procedures to be performed

- IRB needs to be able to determine risk/benefit, not be able to conduct the studies

- Consent forms are not required to follow a particular format. Templates are recommendations

3

Preparation is Key

- Staffing
- Training
- Materials
- Equipment
- Validated instruments
- Budget planning

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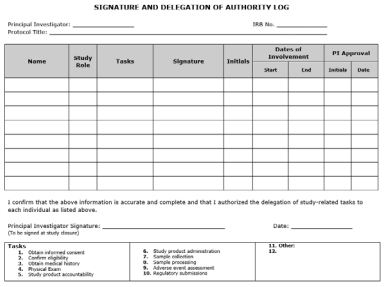
Study Conduct

- Train staff on SOPs
- Assign tasks
- Ensure understanding of performance of tasks
- Adequate credentials to perform task
- Adequate access to perform task



SIGNATURE AND DELEGATION OF AUTHORITY LOG

Principal Investigator: _____ IRB No. _____

Protocol Title: _____

Name	Study Role	Tasks	Signature	Initials	Dates of Involvement		PI Approval	
					Start	End	Initials	Date

I confirm that the above information is accurate and complete and that I authorized the delegation of study-related tasks to each individual as listed above.

Principal Investigator Signature: _____ Date: _____

(To be signed at study closure)

Tasks		
1. Obtain informed consent 2. Confirm eligibility 3. Medical/Social history 4. Physical Exam 5. Study product accountability	6. Study product administration 7. Conduct interviews 8. Sample processing 9. Adverse event assessment 10. Regulatory submissions	11. Other: 12.

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Study Con

- T
- A
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- Ade
perfor
- Adequate a
task

Questions?

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Recruitment and Advertisements

Direct Discussion: Face to Face interaction with a potential subject

Previous Subjects: Unless they explicitly declined further contact, previous subjects can be called

Mailings: Written info sent or given to subject from a known provider, clinic or program rep

Advertisements: Posted in public areas with instruction on how potential subject takes action

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Recruitment and Advertisements

Pitt+Me: Database of people who provide info and agree to be contacted for studies

Social Media: Can post ads, links other information. Restrictions apply for privacy protection

Community Outreach: Health fairs, community events, advocacy groups, schools, churches, etc

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Screening, Recruiting, Determining Eligibility §116(g)

An investigator can obtain information or biospecimens for screening, recruiting, or determining eligibility without informed consent:

- Information is obtained through oral or written communication with the prospective subject or LAR, or
- The investigator will obtain private identifiable information or identifiable biospecimens by accessing records or stored identifiable specimens

- Effectively eliminates the need for the IRB to grant waivers for screening and recruitment, consistent with FDA regulations and HIPAA
- **IRB must approve the procedure as a part of the recruitment plan**

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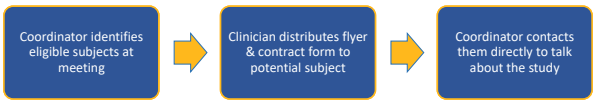
Provider Meeting Recruitment



- Waiver of Informed Consent must be justified
- No identifiable information can leave the meeting

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An investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative

Prior to the process, consider who should be present. While a specific person has to sign, others may participate in the process

- Healthy adult = self
- Child = parent
- Decisionally impaired adult = LAR
- Physically impaired adult = self

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Are they still "children" by definition?

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted 45 CFR 46.402(a)

Certain psychiatric research
Certain STD research
Certain contraceptive research
Certain pregnancy research

All of the research procedures must be something that the subject has the legal right to consent to under PA Law

CALL THE IRB for discussion

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Questions?
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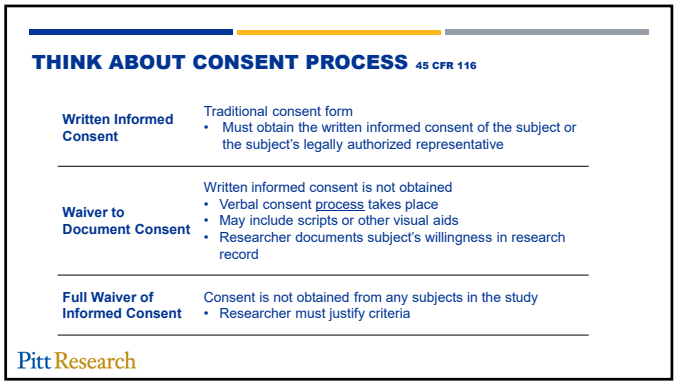
THINK ABOUT CONSENT PROCESS 45 CFR 116
Written Informed Consent
Traditional consent form
Must obtain the written informed consent of the subject or the subject's legally authorized representative
Waiver to Document Consent
Written informed consent is not obtained
Verbal consent process takes place
May include scripts or other visual aids
Researcher documents subject's willingness in research record
Full Waiver of Informed Consent
Consent is not obtained from any subjects in the study
Researcher must justify criteria
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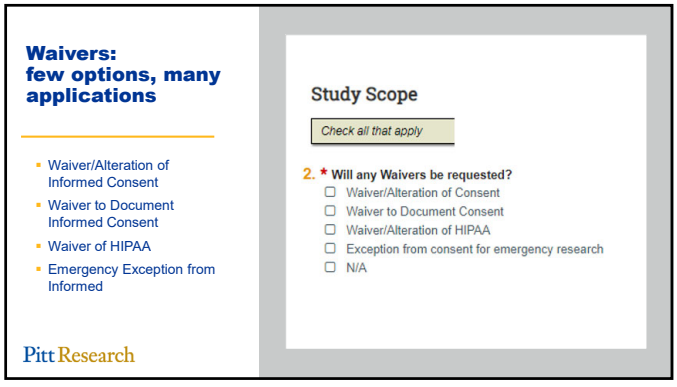
Waivers: few options, many applications
Waiver/Alteration of Informed Consent
Waiver to Document Informed Consent
Waiver of HIPAA
Emergency Exception from Informed
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Study Scope
Check all that apply
2. * Will any Waivers be requested?
Waiver/Alteration of Consent
Waiver to Document Consent
Waiver/Alteration of HIPAA
Exception from consent for emergency research
N/A

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Waiver of HIPAA

Accessing identifiable medical records for research requires a signed HIPAA Authorization or a waiver

- Exempt studies using PHI require authorization or waiver
- Verbal HIPAA authorization requires a waiver

- **RARELY** used on a full board study
- Not required when using medical records to identify subjects for recruitment (preparatory to research)
- Common on chart reviews

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OHRP eConsent Guidance

Electronic informed consent refers to the use of electronic systems and processes that may employ multiple electronic media, including text, graphics, audio, video, podcasts, passive and interactive Web sites, biological recognition devices, and card readers, to convey information related to the study and to obtain and document informed consent

- Method for providing copy to participant (does not have to be signed)
- Consistent for parental permission and assent
- Emphasis on process over form

https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-electronic-informed-consent-questions-and-answers/index.html

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21 CFR 11: Electronic Records; Electronic Signatures

- Generally applies to electronic records created, modified, maintained, archived, retrieved, or transmitted under an FDA regulated study
- For electronic signatures and their associated electronic records that meet this part, FDA will consider the electronic signatures equivalent to full handwritten signatures, initials, and other general signings as required by agency regulations
- Printed name of signer, date and time, responsibility

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What methods are there?

- Signature on electronic device
- Validated signature through password protection
- Exchange of traditional consent form through electronic means
- REDCap or Qualtrics
- DocuSign, Adobe

Be sure to discuss methods in Electronic Data Management

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Click to Continue

- Does not meet the definition of an eSignature
- Requires a waiver to document informed consent
  - Check "waiver to document consent: in Study Scope #2
  - Justify need and upload script on Waiver to Document page
  - Describe steps on Consent Process page
- **REMEMBER**: consent process still takes place. Only difference is no signature is obtained

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CONDUCTING CONSENT AND STUDY VISITS REMOTELY

Method depends on the sensitivity of the information to be disclosed during the visit and if it will be recorded

Pitt licensed versions:

- MS Teams
- Zoom (request HIPAA compliant version)
- Vidyo (UPMC)

Data Security:

- Recording storage
- Up-to-date anti-virus protection
- Storage in Pitt/UPMC cloud or University-managed server

NOT one size fits all approach!

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What about HIPAA?

HIPAA Authorization must be obtained prior to the access, use, or generation of past, present or future protected health information (PHI)

- Use of PHI requires written authorization
- Absence of written authorization requires alteration justification
- PHI is rarely exchanged during consent process (i.e. platform does not need to be HIPAA compliant)

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R

- If a
  sure it is
  process

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HOW DO I SUBMIT?

HSConnect

Set up HSConnect account with Pitt credentials when possible
(DO NOT use Gmail, etc. if you need to switch your account, contact HSConnect)

University of Pittsburgh
CITI Access Portal

Complete CITI training or link completed CITI training from another institution to Pitt account (https://www.citi.pitt.edu/)
- Responsible Conduct of Research
- Human Subjects Protection
- Good Clinical Practice

PittPRO Pitt Protocol Review Online

Build submission in PittPRO and submit for approval
(same username and password as HSConnect and CITI)

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Other Research Training

https://www.orp.pitt.edu/training-courses/training-table-list

(highlighted column is Human Subject Research)

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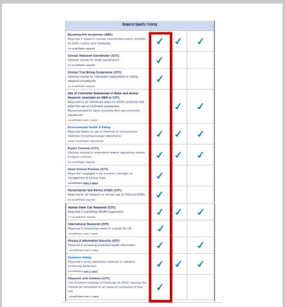

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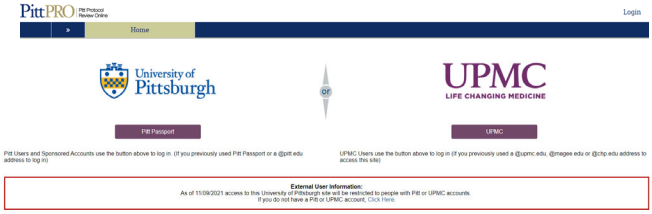
ACCESSING PITTPRO



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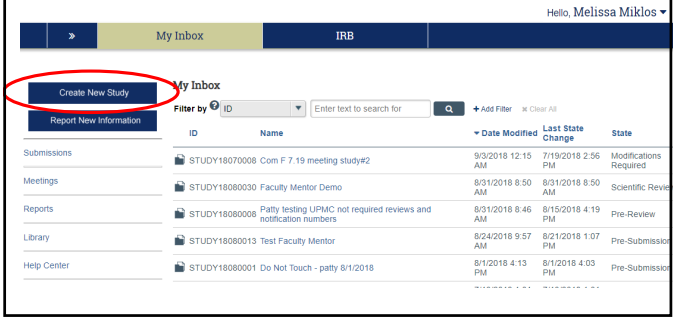
How do I create a study?



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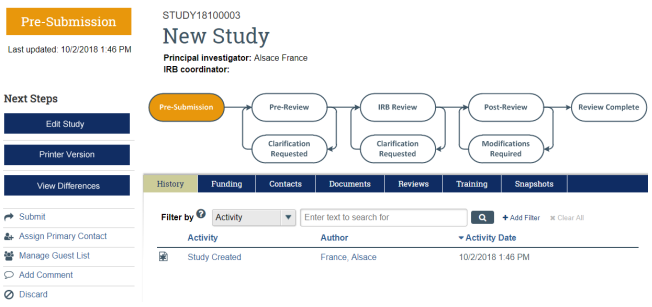
New Study Created



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Call us early and often

412-383-1480
Main IRB number

askirb@pitt.edu
General IRB questions

Irb.reliance@pitt.edu
Central IRB questions (aka sIRB)

orp@pitt.edu
Technical Issues

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Call us early and often

Questions?

Technical Issues

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Time for
a BREAK
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Informed Consent Process

Maggie Soncini

University of Pittsburgh

Office of Research Protections
Education and Compliance Support

mls130@pitt.edu

1

General Requirement for informed consent

Except as provided elsewhere in this policy:

(1) Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative.

DHHS Part 46, Subsection 116

2

Regulatory Resources

Food and Drug Administration	• 21 CRF 50
Department of Health & Human Services	• 45 CRF 46.116 • 45 CRF 46.117
International Conference on Harmonisation	• Section 4.8

3

Consent Process

Common Misconception

Although the consent document is an important part of the consent process

The consent process involves much more than obtaining a signature on a form

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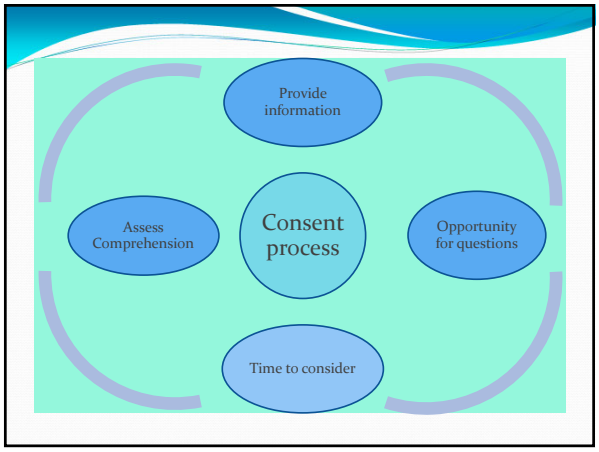

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Prior to completing any research procedures

Consent process must be undertaken

Written consent must be obtained

6

Consent Document

The federal regulations require the inclusion of **basic** and **additional** elements in the consent document

21 CFR 50.25 (a) / 45 CFR 46.116 (b)
21 CFR 50.25 (b) / 45 CFR 46.116 (c)

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Basic Elements

1) A statement that the study involves research
2) Description of potential risks or discomforts
3) Description of potential benefits
4) Alternatives that may be advantageous

8

Basic Elements

5) Confidentiality of records

6) Compensation or medical treatments in the event of a research-related injury

7) Explanation of who to contact:
   - Research-related questions
   - Rights of research subjects
   - Research-related injury
   - Emergency contact

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Basic Elements

8) Statement that participation is voluntary
- Right to refuse without loss of benefit
- Subject may discontinue at any time

9) Statement regarding identifiable private information or biospecimens

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Additional Elements

1) Statement regarding currently unforeseeable risks to subject (or to the embryo or fetus in the event the subject may become pregnant)

2) Circumstances leading to termination of subject's participation by investigator without regard to subject's consent

3) Consequences of subject's decision to withdrawal from research

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Additional Elements

4) Any additional costs to the subject incurred through participation

5) Approximate number of subjects expected to be enrolled

6) Statement that significant new findings will be provided to the subject

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Additional Elements

7) Biospecimens – Used for commercial profit?

8) Disclosure of clinically relevant research results

9) Whole genome sequencing

13

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Key Information

- Research / Voluntary Participation
- Purpose / Duration / Procedures
- Foreseeable Risks or Discomforts
- Reasonably Expected Benefits
- Alternative Procedures

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Building the Consent Document

Enhance comprehension by:

- Using charts or bulleted lists
- Avoid scientific/technical terms
- 6th grade reading level
- Spell check the document
- Copy/paste with care

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Building the Consent Document

- Always spell check your document
- Copy and paste from other documents with caution
- Identify member(s) of the research team to proofread the consent document

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Consent Process - Considerations

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Consent Process Considerations

- WHEN: Receive the consent document
- WHERE: Will the consent process take place
- WHO: Should be involved

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Consent Process
Principal Investigator

- Task can be delegated
- Qualified by training and experience
- Listed as an investigator or identified as being involved

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irb.pitt.edu

Policies & Procedures – Chapter 13 – Informed Consent

Policy – Greater than minimal risk study involving a drug, device or surgical procedure

A licensed physician investigator must obtain consent

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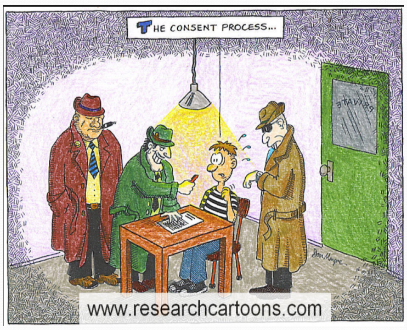

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Questions?

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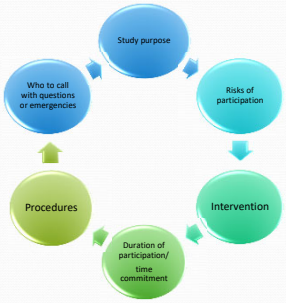
Assessing Comprehension

Evaluate subject's understanding of:



24

Teach Back Method

What is the purpose of the study?

What are some of the risks of study participation?

Consider asking the subject to define terms such as placebo-controlled or randomized

25

Written Consent

The current version of the consent document that has been approved by the IRB should be used to obtain written informed consent

Signatures should be recorded at the time of consent

Narrative note describing the consent process

26

Signatures

Federal regulations require that the subject (or legally authorized representative) sign the consent document

University of Pittsburgh requires that an investigator sign the consent document

Individuals must print their name and date their own signatures

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Signatures
Adult Participants

Pennsylvania –
Anyone 18 years or older may sign for themselves

Adults unable to provide consent because of an emergent situation or a decisional impairment, consent of a legally authorized representative is required (proxy consent)

28

Child Participants

Pennsylvania – anyone under the age of 18 years is considered a minor

Consent must be obtained from the biologic or adoptive parent(s) or from a legal guardian as established by the court

29

Child Participants

For greater than minimal risk research without direct benefit to the child, permission must be obtained from both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child (45 CRF 46.406)

Not reasonably available does not mean the absence of the second parent

30

Narrative Note of Consent

Food and Drug Administration requires documentation of informed consent in the subject's case history

Develop a template or include in a progress note

Document the specifics of the consent process

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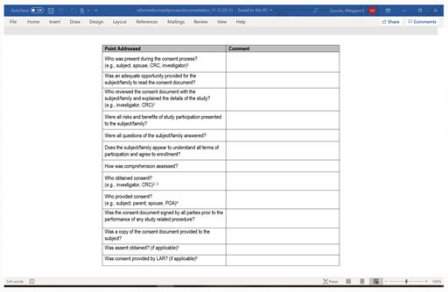
Consent Process Documentation

www.ecshsr.pitt.edu



Point Addressed	Comment
Who was present during the consent process? (e.g., subject, spouse, CRC, investigator)	
Was an adequate opportunity provided for the subject/family to read the consent document?	
Who reviewed the consent document with the subject/family and explained the details of the study? (e.g., investigator, CRC)?	
Were all risks and benefits of study participation presented to the subject/family?	
Were all questions of the subject/family answered?	
Does the subject/family appear to understand all terms of participation and agree to enrollment?	
How was comprehension assessed?	
Who obtained consent? (e.g., investigator, CRC)?	
Who provided consent? (e.g., subject, parent, spouse, POA)?	
Was the consent document signed by all parties prior to the performance of any study related procedure?	
Was a copy of the consent document provided to the subject?	
Was assent obtained? (if applicable)?	
Was consent provided by LAR? (if applicable)?	

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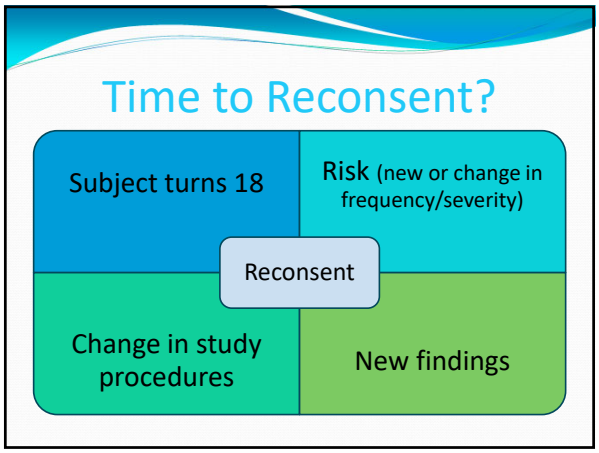
Original Consent Document

Maintain with research records

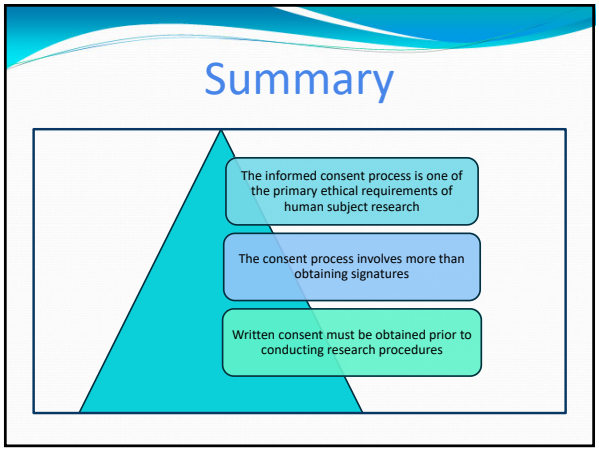
Should not be given to the subject

Should not be placed in the medical record

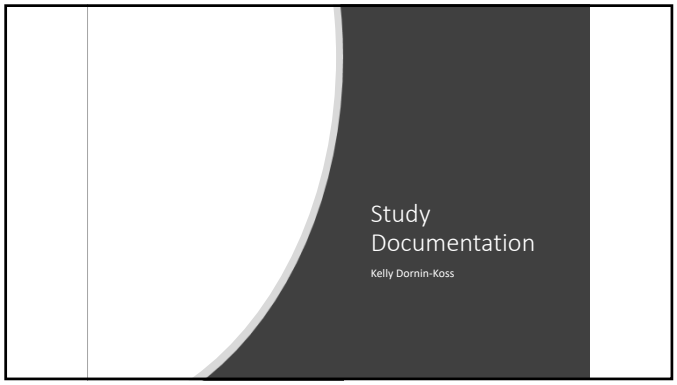
33


Time to Reconsent?
Subject turns 18
Risk (new or change in frequency/severity)
Reconsent
Change in study procedures
New findings

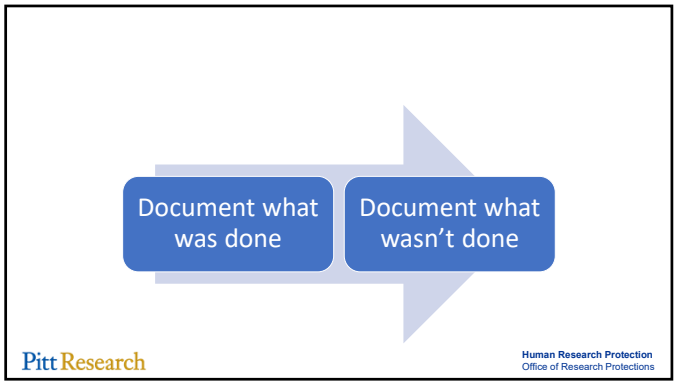
34


Summary
The informed consent process is one of the primary ethical requirements of human subject research
The consent process involves more than obtaining signatures
Written consent must be obtained prior to conducting research procedures

35


Study
Documentation
Kelly Dornin-Koss

10


Document what was done
Document what wasn't done
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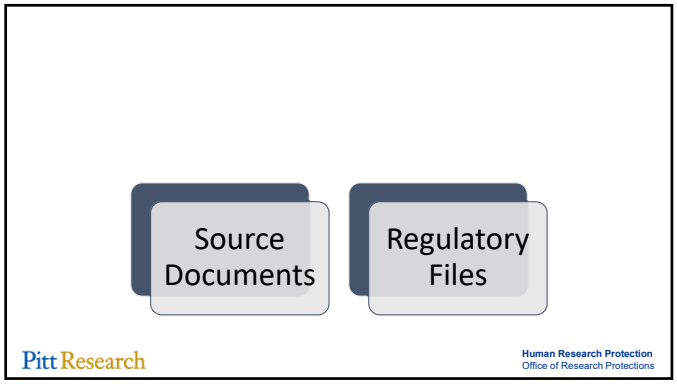
Source Documents
Regulatory Files
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Source documents are the original documents containing the first recording of information about a study subject during participation in a clinical trial.

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Source documents confirm:

- Completeness and accuracy of data collection, and,
- The study was conducted according to the protocol and ethically.

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Prior to enrollment:

REVIEW PROTOCOL THOROUGHLY

PREPARE DATA COLLECTION / CASE REPORT FORMS AND COMPARE TO PROTOCOL

15

Criteria	Comments	Met Y or N
Age 18-80 years		
Scheduled for surgery		
No history of alcohol abuse		
No alcohol in previous 24 hours		
No recreational drug use in last 6 months		
Not currently taking NSAIDS		
No history of renal failure (creatinine level < 1.3mg/dL)		
Not pregnant		
No significant medical history		

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Criteria	Assessment Instrument	Comments
Age 18-80 years	Phone Screen	
No history of alcohol abuse	SCID	
No alcohol in previous 24 hours	Self Report	
No recreational drug use in last 6 months	SCID	
Not currently taking NSAIDS	Demographic Form	
No history of renal failure (creatinine level < 1.3mg/dL)	Baseline labs	
Not pregnant	Urine test	

https://www.nimh.nih.gov/funding/clinical-research/nimh-clinical-research-education-support-and-training-crest-program.shtml

17

Maintain separate research records for each study subject

Maintain all study information in an organized manner

18

You should be able to *easily* reference all vital study information.

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Study Subject records organization

By visit with checklist and accompanying documents

By type of assessments

Separate sections for reports, adverse events, etc.

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Supportive Documentation should include:

- Original signed informed consent document
- Assessment tools – questionnaires, surveys, etc.
- Health records as applicable
  - Laboratory results
  - Imaging reports – MRI, CT
  - Electrocardiograms

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Additional tips

Subject documents should be labeled	Never obliterate entries on source documents	Closely Evaluate and Have Mechanisms in Place to document stopping rules
• Subject ID • Date • Signature or initials of study team member/rater	• Single line through incorrect entry • Initial & date correction (LID – line, initials, date) • Add narrative note as needed.	• Make sure all research team members are aware of them • Make sure they are addressed and documented in real time

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Concomitant Meds

IRB#:		Study Title:					
Investigator:		Subject ID:					
Has the subject used a Concomitant Medication during the study? No Yes, complete below							
Medication Name	Indication or Reason for Use	Dose (units)	Frequency	Route	Start Date	Stop Date	Check if ongoing at end of study

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Adverse Events

Unanticipated Problems

Non-compliance

Evaluate	Evaluate and take action for participant safety
Assess	Assess if reporting is necessary • Which agencies • Reporting timelines
Maintain	Maintain records

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IRB Reporting Requirements

- The IRB Requires the reporting of:
  - Adverse Events and unanticipated events which meet the definition of an unanticipated problem involving risks to human subjects or others
  - Non-compliance which:
    - Significantly adversely effects the rights or welfare of participants
    - Significantly compromises the quality of the research data

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Adverse Events

- An unfavorable medical occurrence, which may include abnormal signs (for example, abnormal physical exam or laboratory finding), symptoms, or disease, temporally associated with, but not necessarily considered related to, the subject's participation in the research study.
- Not all adverse events meet IRB reporting guidelines.

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Unanticipated Problem Involving Risks to Human Subjects or Others

- Unexpected in terms of nature, severity, or frequency
- Related, or possibly related, to a subject's participation in the research
- Places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized

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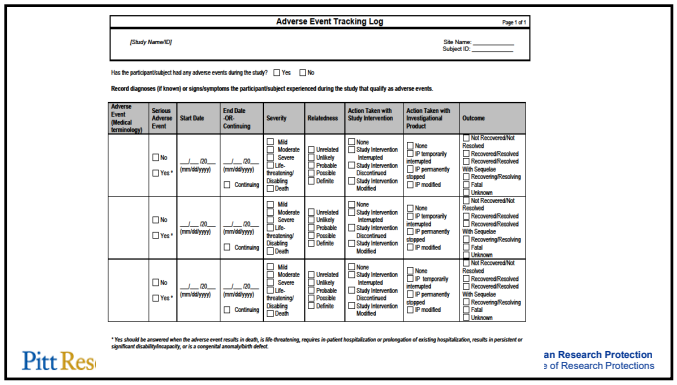

Adverse Event Tracking Log Page 1 of 1

[Study Name/ID] Site Name: _____ Subject ID: _____

Has the participant/subject had any adverse events during the study? ☐ Yes ☐ No

Record diagnoses (if known) or signs/symptoms the participant/subject experienced during the study that qualify as adverse events.

Adverse Event (Medical terminology)	Serious Adverse Event	Start Date	End Date -OR- Continuing	Severity	Relatedness	Action Taken with Study Intervention	Action Taken with Investigational Product	Outcome
	☐ No ☐ Yes *	__/__/__ (mm/dd/yyyy)	__/__/__ (mm/dd/yyyy) ☐ Continuing	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study intervention interrupted ☐ Study intervention Discontinued ☐ Study intervention Modified	☐ None ☐ IP temporarily interrupted ☐ IP permanently stopped ☐ IP modified	☐ Not Recovered/Not Resolved ☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Fatal ☐ Unknown
	☐ No ☐ Yes *	__/__/__ (mm/dd/yyyy)	__/__/__ (mm/dd/yyyy) ☐ Continuing	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study intervention Interrupted ☐ Study intervention Discontinued ☐ Study intervention Modified	☐ None ☐ IP temporarily interrupted ☐ IP permanently stopped ☐ IP modified	☐ Not Recovered/Not Resolved ☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Fatal ☐ Unknown
	☐ No ☐ Yes *	__/__/__ (mm/dd/yyyy)	__/__/__ (mm/dd/yyyy) ☐ Continuing	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study intervention Interrupted ☐ Study intervention Discontinued ☐ Study intervention Modified	☐ None ☐ IP temporarily interrupted ☐ IP permanently stopped ☐ IP modified	☐ Not Recovered/Not Resolved ☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Fatal ☐ Unknown

* *Yes should be answered when the adverse event results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.*

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IRB Reporting Requirements

- The IRB Requires the reporting of:
  - Non-compliance which:
    - Significantly adversely effects the rights or welfare of participants
    - Significantly compromises the quality of the research data

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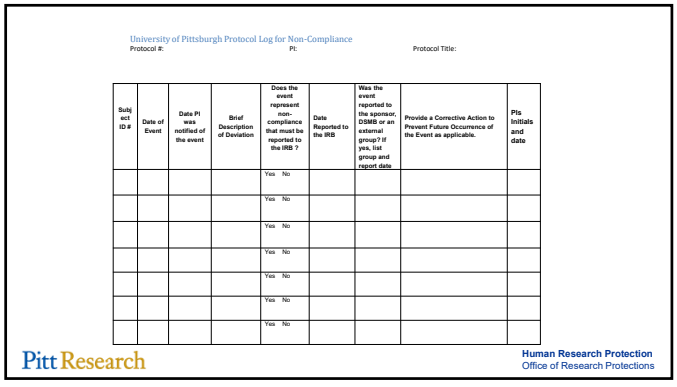

University of Pittsburgh Protocol Log for Non-Compliance

Protocol #: PI: Protocol Title:

Subject ID #	Date of Event	Date PI was notified of the event	Brief Description of Deviation	Does the event represent non-compliance that must be reported to the IRB ?	Date Reported to the IRB	Was the event reported to the sponsor, DSMB or an external group? If yes, list group and report date	Provide a Corrective Action to Prevent Future Occurrence of the Event as applicable.	PIs Initials and date
				Yes No				
				Yes No				
				Yes No				
				Yes No				
				Yes No				
				Yes No				
				Yes No				

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A-Z Guidance

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

A

- Acknowledgement of Unregulated Research Activities
- Activities Not Under the Pitt IRB Jurisdiction
- Advertisements
- Adverse Events Log
- Audit by Federal Agency

B

- Belmont Report
- Blood Drawings for Human Subject Research

C

N

- Non-English Speaking Participants
- Noncompliance/Deviation Log

Contact
Allison Gerger
Regulatory Affairs Specialist

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Additional tips

Create a Study Disposition Form

This would be used to document the subjects final date of study participation

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The Data Should Follow the ALCOA-C Principle

Attributable	• It should be clear who has documented the data.
Legible	• The documentation should be readable and the signatures identifiable.
Contemporaneous	• The notation, signature and date need to be completed at the same time.
Original	• The first recording of the information.
Accurate	• The content should be a real representation of the facts.
Complete	• Are there any missing data points?

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- Document
- Document
- Document

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Regulatory Files

Regulatory files contain all supportive study documentation for the study.

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Regulatory File Contents

Protocol – sequential versions
Informed consent document – sequential versions
IRB / HRPO correspondence and approvals
Serious and unexpected adverse events and unanticipated problems
Sponsor correspondence
Delegation of authority log / signature list
CVs, licenses, certifications
Documentation of protocol and ethics training
Data and safety monitoring

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Regulatory File Contents (cont'd)

- Investigator's Brochure, package insert, Investigational product information
- Monitoring visit log
- Site initiation visit and interim monitoring visit reports
- Drug and Device Accountability records
- Financial disclosure forms
- Laboratory certifications and range of normal values https://path.upmc.edu/links.htm

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Regulatory File Contents (cont'd)

- Include Documentation / Correspondence with Oversight Entities
- Food and Drug Administration
- Investigational Drug Service
- Radioactive Drug Research Committee / Human Use Subcommittee
- Biosafety (rDNA) Office
- Scientific review committee
- NIH

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Central Files

Central department filing – studies conducted within one division or department.

Include a note indicating the location of these files / responsible party.

May encompass:

- CV's
- Professional licenses
- Training certificates
- Laboratory certifications and range of normal values
- Staff training records

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Central Files

Document conversations – phone or email - with sponsor and regulatory agencies

Who initiated the contact	Topic of discussion	Resolution

Maintain electronically or in regulatory files

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Other Regulatory File Items

FWAs

IRB Member Lists

IRB Membership Lists

2019	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2018	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2017	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2016	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2015	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2014	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec
2013	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec

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Notes to File

- Identify a problem
- Are not a substitute for good, prospective, and complete source documents
- Should not be a common practice

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Note to file

- Describe:
  - A summary of the issue
  - The action that was taken to address the issue
  - The root cause
  - Actions to prevent recurrence
  - Date and signature

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Organization Tips

- File information
  - In chronological order
  - Immediately upon receipt
  - Separate into sections or folders or binders with labels

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Record Retention

Retain	Retain all essential study documents – regulatory and study subject records
Keep	Keep all documents in a secure location
Do not destroy	Do not destroy documents without written authorization from the sponsor

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Record Retention Times

University of Pittsburgh	FDA	ICH
7 years	2 years after FDA approval of drug or device or study is abandoned and 5 years after biologic is manufactured	2 years after approval from last ICH region or 2 years after study abandoned

Pediatric subjects – must maintain until the subject age 25

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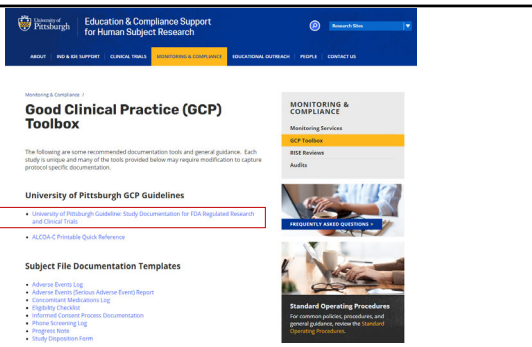

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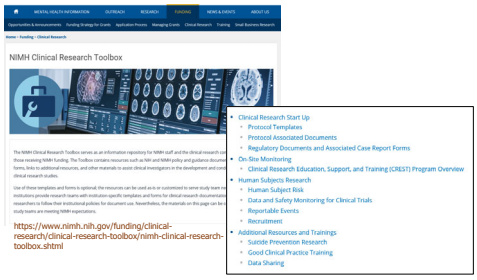
NIMH Clinical Research Education, Support, and Training (CREST) Program



https://www.nimh.nih.gov/funding/clinical-research/clinical-research-toolbox/nimh-clinical-research-toolbox.shtml

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Good Research Practices

Pittsburgh, PA

How to receive your continuing education credit?

http://cce.upmc.com

The UPMC Center for Continuing Education in the Health Sciences (CCEHS) is implementing a new continuing education management system, http://cce.upmc.com. To receive credit, you will be required to login, complete the course evaluation and claim credit within 30 days.

- As a new user, click "Register" to create a new account. Please note, you must use the same email address you used to register for this activity.
- The activity will be in your Pending Activities to complete the course evaluation and claim credit.
- Certificates will be available to download and stored for future reference in your Completed Activities.

To answer common questions or for step by step instructions please visit the FAQs available on the CCEHS Learning Portal.

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Questions????

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