FLORIDA STATE UNIVERSITY

Protocol Development Workshop

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Outline

- Key Definitions
- Human Research Protection Program (HRPP) Toolkit Overview
- Overview of Protocol Template
- Protocol Writing & Development
- Timeline for Implementation
- Questions & Answers

Key Definitions

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge

Activities that meet this definition constitute research, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Source: 45 CFR § 46.102

Key Definitions

Generally, the following activities would not be research:

- Scholarly and journalistic activities (e.g. oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information that focus directly on the specific individuals about whom the information is collected
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes

Source: 45 CFR § 46.102

Key Definitions

Generally, the following activities would not be research:

- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority
  - Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products)
  - Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters)
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions

Source: 45 CFR § 46.102

Key Definitions

Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

- Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes

Interaction includes communication or interpersonal contact between investigator and subject

Source: 45 CFR § 46.102

Key Definitions

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record)

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information

An ***identifiable biospecimen*** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen

Source: 45 CFR § 46.102

Key Definitions

- Minimal Risk:
- 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.
- The phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” should not be interpreted to include the inherent risks certain categories of subjects face in their everyday life.
- For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

"Minimal Risk" Research

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  - For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

Minimal Risk (cont'd)

- What risks are "ordinarily encountered in daily life"?
  - Absolute standard
    - Risks encountered during daily lives of normal, healthy individuals
  - Relative standard
    - Risks encountered during daily lives of individuals in the class of subjects involved in the research

HRPP Toolkit Overview

- Provides standard operating procedures, checklists, and worksheets
- Provides protocol and consent templates for creating compliant documents
- Includes an Investigator Manual designed to guide you through policies and procedures related to the conduct of human research

Overview of Protocol Template

- ***Protocol*** – a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organization of a research project
- It is a living document and can be changed over the course of the research project*
- The protocol template from the HRPP toolkit will be required for human research studies at FSU

*NOTE: all changes to the research protocol must be reviewed and approved by the IRB

Overview of Protocol Template

- "Revision History"
  - Updating your protocol in RAMP will show the history of the changes over time to streamline the review process, facilitate recordkeeping, and ensure historical accuracy
  - Protocols must be uploaded in Word document format in order to activate the revision history function

2.0 Objectives

- The primary objective serves as the basis of the sample size
- Secondary objectives may be exploratory or hypothesis-generating and the study may not be powered to achieve these objectives

*NOTE: for clinical trials, a study typically has one Primary Objective/Outcome measure. It can have more than one Secondary Outcome. Exploratory measures do not require reporting on ClinicalTrials.gov

3.0 Background

- The “knowledge gap” is that which needs to be explored by new research, either because we know little or nothing
- Provide any previous study results and applicable historical information that supports your current study
  - Cite literature and include a list of references within the protocol

4.0 Study Endpoints

- ***Endpoint*** – event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial or complete
- Each objective has (1) a corresponding endpoint and (2) a plan for analysis
  - When applicable, objectives should have a safety contingency plan

5.0 Study Intervention/Investigational Agent

- Does the intervention include a drug, behavioral test, etc.?
- For studies that are providing medication(s), give the name(s), dosage, and route of administration. For studies that have more than one arm/part, provide the above information for each.

*NOTE: the Social Behavioral (SBS) protocol template does not ask for “Investigational Agent” or related questions

6.0 Procedures Involved

- Provide a chronological description of all study procedures
  - If applicable, divide procedures into pilot, screening, and procedures performed at each visit.
  - Indicate how many total visits and approximately how long visits will last.
- Adequate detail is required to ensure that the research plan will produce valid results
- You may include tables, figures, and/or flow diagrams to show the time-order of the procedures involved

7.0 Data and Specimen Banking

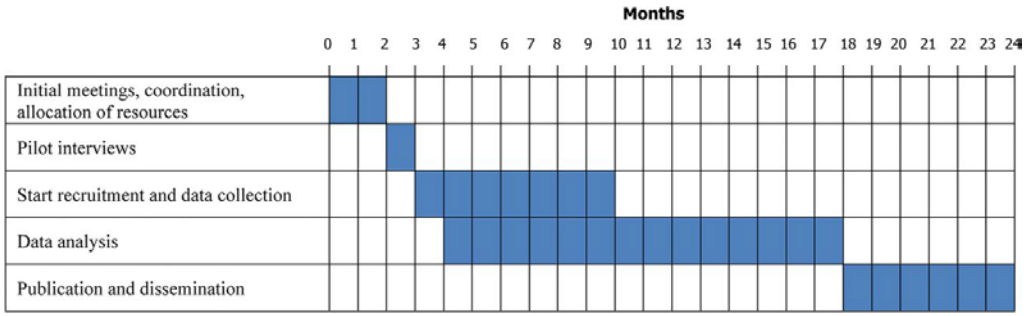
- This plan should include tracking of data/specimen use over time
- The banking/tracking of data should also be clearly explained in the consent form
- Include information about whether the data will be identifiable, coded, or de-identified
  - **Coded** – data is de-identified *and* a key to decipher the code exists, even if you cannot access it
  - **De-identified** – *all* possible links to the participant's identity have been permanently destroyed

8.0 Sharing of Results with Subjects

- If you will return individual results and/or incidental findings to subjects, you must have the proper training/licensure to return the information
  - For example, irregular heartbeat on an EKG can only be identified, evaluated, and conveyed to a participant by a clinically licensed medical professional (see local laws)

9.0 Study Timelines

- Tables are helpful show the overall study timeline
- Clinical Trials Reminder – you have 1 year from the study primary completion date to enter results on clinicaltrials.gov



Study Timetable

Project activity	7/04–12/04	1/05–6/05	7/05–12/05	1/06–6/06	7/06–12/06	1/07–6/07	7/07–12/07	1/08–6/08	7/08–12/08	1/09–6/09
Study activity										
Interrater reliability/training	X	X	X	X	X					
Database setup	XX									
Patient enrollment	XX	XXX	XXX	XXX	XXX					
Data management	XX	XXX	XXX	XXX	XXX					
Data analysis, specific aim 1					XXX	XXX				
Manuscript preparation, aim 1						X	XX			
Data analysis, specific aim 2						XX	XXX	X		
Manuscript preparation, aim 2								XXX		
Data analysis, specific aim 3								XX	XXX	X
Manuscript preparation, aim 3									X	XXX

10.0 Inclusion & Exclusion Criteria

- **Inclusion criteria** – defines who will be eligible to participate in the research; **Exclusion criteria** – defines who will *not* be eligible to participate *and why*
  - You cannot include members of vulnerable populations as subjects in your research *unless* this is indicated in your inclusion criteria. This includes incidental prisoners*.
  - Be specific: do not say "if subjects do not meet inclusion criteria, they will be excluded"
  - If you define a criterion under your inclusion criteria, do not repeat that criterion in its negative under the exclusion criteria
- Risks and benefits of the study depend on who the participants are, and the enrollment criteria also must be constructed to ensure equitable selection of subjects

*Incidental prisoner – subject who becomes incarcerated while participating in research

11.0 Vulnerable Populations

- Vulnerable populations include:
  - Cognitively Impaired Adults
  - Minors (infants, children, teenagers)
  - Pregnant women
  - Prisoners
- Refer to the appropriate HRPP toolkit Checklist for each population to ensure you have provided sufficient information
- Checklists are available on our website: https://www.research.fsu.edu/research-offices/human-subjects/templates-and-required-forms/

12.0 Local Number of Subjects

- "Local" means any site(s) the investigator is recruiting from
  - Example: 35 subjects at Gilchrest Elementary school and 25 subjects at FSU Communication Disorders Clinic, but the entire project will recruit 300 subjects by multiple investigators across Florida. The total number would be 60 for the local site.
- This number is an estimate and can be changed over time

13.0 Recruitment Methods

- Describe how potential participants will be identified and recruited for the study
- Be specific—provide location names such as FSU Student Union, Bond Health Clinic lobby, etc.
- Upload all recruitment materials that support recruitment efforts
  - All documents/images/advertisements that subjects will see must be reviewed and approved by the IRB

14.0 Withdrawal of Subjects

- Subject withdrawals should be tracked and reported to the IRB, either as reportable new information (RNI) or with the continuing review, depending on the reason(s) for withdrawal
- Provide the method that will be used to notify subjects of their withdrawal from the study
  - I.e. letter, e-mail, in person (upload materials)
- If a subject is withdrawn, will their data be used? This information needs to be clearly explained in the consent form and in the protocol.
- “Investigator discretion” may be listed as a criterion for withdrawal

15.0 Risks to Subjects

- Each risk description should include the probability, magnitude, duration, and reversibility of the risks. This information should also be included in the consent form in laymen's terms.
- Risk(s) should be described for each population (children, adults, etc.), and per study arm (intervention group, control group)
- **All research has risks that may be unforeseeable or unknown**
- Do not use the verbiage *no risk* or *minimal risk* in the consent form. Clearly list the risks so the potential participant can freely assess whether they wish to participate given the stated risks. It is up to the potential subject to decide whether they consider the risks acceptable to proceed with participation. If you can't identify tangible risks, simply state "As this is a research study, there may be risks that are unknown."

16.0 Potential Benefits to Subjects

- Should be described for each population (children, adult, etc.) and each study arm (intervention group, control group)
- Do not list payment or contribution to research as benefits. If there are no direct benefits to the participant, make this clear.

17.0 Data Management and Confidentiality

- Care in data management is a requirement to ensure valid study results. Sloppy data handling will add variability to the study assessments, and will affect the outcome of the study.
- The more sensitive the study data, the more sophisticated the methods should be to maintain confidentiality
- If you are transporting data, include a plan for how data will be kept secure during transport
- Maintain your study records, including signed and dated consent documents for at least three years after completion of the research. Maintain signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six years after completion of the research.
  - Ensure your records are organized and audit-ready
- If your project is sponsored, contact the sponsor for potential additional data retention requirements

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

- A data safety monitoring plan should address how those in charge of the monitoring will assess the evolving study progress, including data quality and possible adverse events
- This section is required when research involves more than minimal risk to subjects
- A data safety monitoring plan is not required for exempt and expedited studies

19.0 Provisions to Protect the Privacy Interests of Subjects

- ***Privacy interest*** refers to a person's desire to place limits on who they interact with, or to whom they provide personal information

20.0 Compensation for Research-Related Injury

- This section is required when research involves more than minimal risk to subjects
- Information must be included in the consent form to clearly notify participants who is/is not responsible for costs of possible injury
  - No exculpatory language is permissible (subjects cannot be told they are giving up any legal rights)
- This section is not required for exempt and expedited studies

21.0 Economic Burden to Subjects

- Economic burden to subjects could be:
  - Travel time and/or expense related to transportation to research site(s)
  - Time away from work and/or family

22.0 Consent Process

- Provide specific information regarding:
  - Who will obtain consent
  - What format will information be provided (consent form requiring signatures, electronic consent, verbal script, video presentation, booklet, etc.)
  - When the consent process will occur (at what point during study timeline)
  - Where and how consent will occur (in person, by telephone, etc.)
- Consent is an ongoing process, not just a form
- The subject should be given ample time to make a decision on whether to participate in the research

22.0 Consent Process Non-English Speaking Subjects

- A subject *cannot* be excluded due to inability to speak English if there is a potential for benefit from the study (see Belmont Report)
- The short form consent process may be used
- Plan ahead and have translation services available for written and verbal communication if required

22.0 Consent Process
Subjects who are not yet adults

- Parental permission is required to approach minors to gain assent
- Subjects over age 10 should be provided with written assent forms
- If parents are asked to participate in research, they need to be consented for their participation, and separately give permission for the child to participate

22.0 Consent Process Cognitively Impaired Adults

- The determination of a subject's capacity to consent is an ongoing assessment
- Provide a plan to address the process for what would occur if subjects lose their capacity to consent while enrolled in the study

23.0 Process to Document Consent in Writing

Refer to the HRPP toolkit “Written Documentation of Consent” procedure on our website (link on next slide)

Short form consent process:

- The short form consent document must contain the following:
  - a description of the required elements of informed consent
  - an explanation that the purpose of the research, the study procedures and the other required elements in the consent form will be presented to the subject, or legally authorized representative in their preferred language.
- Short Form Consent in Subject's Preferred Language
- Individual(s) who speaks English and the subject's preferred language to serve as
  - Interpreter
  - Witness

23.3 Waiver or Alteration of Consent Process

- Review the “Waiver or Alteration of Consent Process” checklist to ensure you have provided sufficient information for the IRB to make these determinations
- https://www.research.fsu.edu/research-offices/human-subjects/templates-and-required-forms/

24.0 Setting

- Identify research locations where research activities will be conducted. List name(s), address(es), and contact person(s).
  - For example: FSU main campus, Deerlake Middle School
- Provide an official site approval letter for each site that is outside of FSU
- Community advisory board, if applicable

25.0 Resources Available

- Describe resources the PI will have access to in order to complete the research, such as lab space, a mentor or advisor, etc.
- Describe resources that will be given to subjects, such as first aid, referrals to services, etc.

26.0 Multi-Site Research

- Research involving external collaborators
  - For example, FSU and UF are both collecting data and there is an investigator at each site
- A reliance agreement may be required for multi-site collaborative studies

Timeline for Implementation

- All new applications submitted on/after April 20th, 2019 will be ***required*** to use the HRPP toolkit protocol template
- The Human Subjects Research Office will send out notifications via the FSU IRB listserv with more information about the submission process
  - Email humansubjects@fsu.edu to be added to the listserv if you aren't currently enrolled

Questions?

Program Contacts

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