

**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &  
IMPLEMENTATION**

**OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS**

**SOP Number: 10**

**SOP Title: Amendments to IRB-approved Research**

**Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB  
Chairs, IRB Administrators, Protocol Navigators**

**Revision Approval:**

  
Deputy Director for Intramural Research      10/1/13  
Date

**Revision Implementation date:** \_\_\_\_\_

**Materials Superseded: SOP 10 rev. 1 dated 9/27/2013**

**SOP 10 AMENDMENTS TO IRB-APPROVED RESEARCH**

**TABLE OF CONTENTS**

**10.1 PURPOSE..... 1**

**10.2 POLICY..... 1**

**10.3 RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI) ..... 1**

**10.4 PROCEDURES FOR IRB REVIEW OF PROTOCOL AMENDMENTS ..... 1**

**10.5 NOTIFICATION OF THE IRB’S DECISION TO INVESTIGATORS..... 3**

**10.6 CHANGES IMPLEMENTED IN A RESEARCH STUDY WITHOUT PRIOR IRB APPROVAL ..... 3**

**REFERENCES..... 4**

**LIST OF APPENDICES ..... 4**

## **SOP 10 AMENDMENTS TO IRB-APPROVED RESEARCH**

### **10.1 PURPOSE**

This SOP outlines the responsibilities of PIs and IRBs regarding amendments to protocols already approved by the IRB.

### **10.2 POLICY**

Principal Investigators (PIs) are responsible for obtaining IRB approval of proposed amendments to an IRB-approved protocol before implementing them. The only exception to this requirement is when a change is necessary to eliminate apparent immediate hazards to subjects (see 45.CFR 46(b)(4) and SOP 19, "Investigator Responsibilities") or when the amendments are only administrative in nature and not changes to the research.

### **10.3 RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)**

The PI is responsible for submitting the following materials for IRB review of amendment requests:

- A. An NIH Intramural Clinical Protocol Amendment Application (Appendix 1).
- B. Updated drafts of any documents that would be changed by the amendment, such as the current approved protocol and consent/assent document with the proposed changes highlighted showing deletions, additions and version dates.
- C. Any new consent/assent document(s).
- D. Documentation of other required amendment reviews or approvals, if applicable, e.g., DEC, FDA, Radiation Safety Committee, or IRB approval from another site.
- E. Any additional requirements of the IRB.

### **10.4 PROCEDURES FOR IRB REVIEW OF PROTOCOL AMENDMENTS**

- A. Administrative Pre-review of Protocol Amendments: The IRB administrative staff may pre-review amendment requests to assist the IRB chair to determine if the investigator submitted all necessary information. Pre-review may also be used to determine whether the amendment would be a minor change to the research and may be eligible for expedited review (See SOP 7A “Requirements for Expedited Review of Research by NIH IRBs”).
  
- B. Expedited Review of Amendments: If the Chair or designee decides that the amendment is eligible for expedited review, it is reviewed according SOP 7A.8 (Procedures and Criteria for Expedited Review of Amendments that Constitute a Minor Change).
  
- C. Review of Amendments by the Convened IRB:
  - 1. All IRB members receive all the submitted amendment materials and will have access to the complete IRB protocol.
  - 2. IRB members must review the provided materials in order discuss them and vote at the meeting.
  - 3. The IRB Chair may assign an IRB member to perform a primary review of the amendment and lead the discussion at the IRB meeting.
  - 4. In reviewing the proposed amendment, the IRB should consider how it will affect the conduct of the study; whether it meets the regulatory criteria for approval (45 CFR 46.111); and whether or not it can be approved as written based on the IRB’s risk/benefit assessment.
  - 5. The IRB can take the following actions on amendments: unconditional approval, approval with stipulations, deferred approval, tabled or disapproved, as described in SOP 7B (“Requirements for the Conduct of Research Review at a Convened NIH IRB Meeting”).
  - 6. The IRB will document in the minutes its discussion about and vote on the amendment and its determination whether current or past subjects must be informed of the amendment, and, if so, how they will be informed (verbally and/or in writing). Current and past subjects must be notified if the study amendment affects their safety and welfare and current subjects re-consented if the amendment changes future clinical study procedures.

Correspondence or other communications with subjects shall be submitted to and approved by the IRB.

7. The IRB votes separately on new amendments that accompany continuing reviews.

#### **10.5 NOTIFICATION OF THE IRB'S DECISION TO INVESTIGATORS**

- A. Investigators are notified in writing of the decision of the IRB and of any stipulations required. Amendments are not approved by the IRB until all stipulations have been satisfied.
- B. The written amendment approval notification must state that further changes in research activity may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects.
- C. The PI may implement the changes provided in the amendment after IRB approval. If changes are required in the consent document, they are implemented after IRB approval and posting of the consent document by the Office of Protocol Services (OPS).
- D. The continuing review date is not affected by the approval of amendments.

#### **10.6 CHANGES IMPLEMENTED IN A RESEARCH STUDY WITHOUT PRIOR IRB APPROVAL**

- A. Changes to research without prospective review and approval may only occur when they are necessary to eliminate immediate hazards to subjects and must be reported to the IRB as soon as possible. Changes to research without prospective IRB review and approval are protocol deviations and must be reported according to the requirements of SOP 16, "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations."
- B. Such changes to research may or may not lead to an amendment to the protocol but, if they do, the procedures of this SOP apply.

## **REFERENCES**

- A. 45 CFR 46.103
- B. 45 CFR 46.110
- C. 45 CFR 46.111
- D. 21 CFR 50.25
- E. 21 CFR 56.111

## **LIST OF APPENDICES**

APPENDIX A: NIH Intramural Clinical Protocol Application

APPENDIX B: NIH Application Supplements

National Institutes of Health

Intramural Clinical Protocol Amendment Application

This application is for amendments to human subject research that requires IRB review and approval.

I. Protocol Information

- 1. Protocol Number *populated by the system*
- 2. Principal Investigator's (PI) Name, address and contact information *populated by the system*
- 3. Protocol Title *populated by the system*
- 4. Précis *populated by the system (update as necessary)*
- 5. Type of Review Requested: (select one)  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.110>
  - Full Board
  - Expedited

II. Changes in key research personnel:  Yes  No

*Default is set to no; select yes if you have changes to any of the key research personnel.*

- Change of Principal Investigator (PI)  
[\(http://oma.od.nih.gov/manualchapters/intramural/3014/\)](http://oma.od.nih.gov/manualchapters/intramural/3014/)

*If you select change in PI the box below will appear – complete the information for the new PI*

Name:	Degree:
Institute/Branch:	Address:
Phone:	Email:
NED Classification: <input type="checkbox"/> Employee <input type="checkbox"/> Fellow	
NED ID:	
Dates Training Completed: (A dropdown menu will appear that shows the required training for this role, select the one(s) completed and enter completion date from the certificate or from CITI)	
In Addition to the PI, Send Correspondence to:	
E-mail Address:	

SOP 10 Appendix A

- Addition of Lead Associate Investigator

<http://oma.od.nih.gov/manualchapters/intramural/3014/>

If you select the above choice, the box below will appear.

Name:	Degree:
Institute/Branch/Organization:	Address:
Phone:	Email:
NED Classification: <input type="checkbox"/> Employee <input type="checkbox"/> Contractor <input type="checkbox"/> Fellow <input type="checkbox"/> Volunteer <input type="checkbox"/> N/A	
NED ID:	
Only complete if you are adding a new LAI. Dates Training Completed: (A dropdown menu will appear that shows the required training for this role, select the one(s) completed and enter completion date from the certificate or from CITI)	
<input type="checkbox"/> BTRIS access	

- Deletion of Lead Associate Investigator

If you select the above choice, the box below will appear.

Name and Degree:	Institute/Branch/Organization:
Email:	Phone:

- Addition of Associate Investigator(s)

<http://oma.od.nih.gov/manualchapters/intramural/3014/>

If you select the above choice, the box below will appear.

Name:	Degree:
Institute/Branch/Organization:	Address:
Phone:	Email:
NED Classification: <input type="checkbox"/> Employee <input type="checkbox"/> Contractor <input type="checkbox"/> Fellow <input type="checkbox"/> Volunteer <input type="checkbox"/> N/A	
NED ID:	
Only complete if you are adding a new AI. Dates Training Completed: (A dropdown menu will appear that shows the required training for this role, select the one(s) completed and enter completion date)	
<input type="checkbox"/> BTRIS access	

- Deletion of Associate Investigators(s)

If you select the above choice, the box below will appear.

Name and Degree:	Institute/Branch/Organization:
Email:	Phone:

SOP 10 Appendix A

Addition of Referral Contact

If you select the above choice, the box below will appear.

Name:	Degree:
Institute/Branch:	Address:
Phone:	Email:
NED Classification: <input type="checkbox"/> Employee <input type="checkbox"/> Contractor <input type="checkbox"/> Fellow <input type="checkbox"/> Volunteer <input type="checkbox"/> N/A	
NED ID:	
Only complete if you are adding a new Referral Contact: Dates Training Completed: (A dropdown menu will appear that shows the required training for this role, select the one(s) completed and enter completion date from the certificate or from CITI)	

Deletion of Referral Contact

If you select the above choice, the box below will appear.

Name and Degree:	Institute/Branch/Organization:
Email:	Phone:

Addition of persons who may obtain informed consent (who are not Investigators)

If you select the above choice, the box below will appear.

Name:	Degree:
Institute/Branch/Organization:	Address:
Phone:	Email:
NED Classification: <input type="checkbox"/> Employee <input type="checkbox"/> Contractor <input type="checkbox"/> Fellow <input type="checkbox"/> Volunteer <input type="checkbox"/> N/A	
NED ID:	
Only complete if you are adding new individuals: Dates Training Completed: (A dropdown menu will appear that shows the required training for this role, select the one(s) completed and enter completion date from the certificate or from CITI)	

Deletion of persons who may obtain informed consent (who are not Investigators)

If you select the above choice, the box below will appear.

Name and Degree:	Institute/Branch/Organization:
Email:	Phone:

SOP 10 Appendix A

III. Changes in non-NIH Collaborator(s)  Yes  No

Default is set to no; select yes if you have changes

Addition

If you select the above choice, the box below will appear.

Name.	Degree.
Organization.	Address.
Phone.	Email.

*If adding a non-NIH Collaborator specify the nature of the collaboration in the protocol*

Deletion

If you select the above choice, the box below will appear.

Name.	Organization.
-------	---------------

SOP 10 Appendix A

IV. Changes in Research Enrollment Sites  Yes  No

Default is set to no; select yes if you have changes

Addition

If adding a new enrollment site the following will appear:

Search for FWA and IORG at <http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc>

Please list the name of the site, the FWA#, IORG #, site PI, address, phone # and email address in this space. (You may cut and paste from an existing document.) List the type of site from the drop-down list below.

Type of site [drop-down list values:  
Clinical Research Facility  
Mobile unit  
Home  
School  
Treatment Facility  
Other, describe:

Deletion

If deleting an enrollment site the following box will appear:

Provide the information on the enrollment site *being deleted*

Name:	
Phone:	Email:
Address:	City:
State:	Zip:

V. Conflict of Interest (if applicable)

1. Has the NIH IRP COI Guide been distributed to new NIH Investigators and non-NIH investigators? (<http://ethics.od.nih.gov/forms.htm>)

Yes  No **If no, distribute IRB Supplement D**  N/A

**SOP 10 Appendix A**

2. Has the Personal Financial Holdings Form (PFH) form been completed and submitted to the Deputy Ethics Counselor?

Yes  No **If no, complete the PFH Supplement E**

Date submitted to DEC: \_\_\_\_\_ Date cleared by DEC: \_\_\_\_\_

3. Has the Conflict of Interest Certification document been distributed to non-NIH Investigators?

Yes (If yes, the PI must maintain the Certification documentation in the regulatory files.)

No **If no, complete IRB Supplement F for each non-NIH investigator**

N/A

V. Does this amendment impact or require a Tech Transfer Agreement?

<http://www.ott.nih.gov/index.aspx>  Yes  No

**Default is set to no, select yes if you have changes**

The choices below will only appear if you select yes above  
If yes, select all that apply:

- CDA - Confidential Disclosure Agreement
- CTA - Clinical Trial Agreement
- CRADA - Cooperative Research and Development Agreement
- MTA - Material Transfer Agreement/Human Material Transfer Agreement
- MOU - Memorandum of Understanding
- Other, specify \_\_\_\_\_

VI. Changes to accrual Ceiling:  Yes  No

**Default is set to no, select yes if you have changes**

The selections below will only appear if you select yes above  
Current ceiling: \_\_\_\_\_ New ceiling: \_\_\_\_\_  
Rationale for change: \_\_\_\_\_

VII. Changes in Study Population:  Yes  No

**Default is set to no, select yes if you have changes**

The following choices only appears if you select yes above  
If yes,

Addition

SOP 10 Appendix A

Deletion

(select all that apply)

Patients

Healthy Volunteers

Other Volunteers (i.e. environmental studies, households, schools)

NIH Employees

Non-English Speaking

Vulnerable or other special populations (select all that apply)

---

Children

Children who are wards of the state

Prisoners

Pregnant Women, Fetuses, or Neonates

Adult who are or may be unable to consent

N/A

VIII. Change in Investigational New Drug/Biologic/Device or Tobacco Product?  Yes  No

Default is set to no; select yes if you have changes

The following will appear only if you select yes above

If yes,

Addition

Deletion

Product Name	Manufacturer	Type select	IND BB-IND IDE ITP Number	Sponsor Name	Monitoring Entity

Does the protocol involve a new drug/device/product that may lead you or the NIH to receive payment or royalties?

Yes  No  N/A

(If yes, add the "Statement of Disclosure" to the consent(s).)

IX. Change in Commercial Product?  Yes  No

Default is set to no; select yes if you have changes

The following only appears if you select yes above

If yes,

SOP 10 Appendix A

<input type="checkbox"/> Addition <input type="checkbox"/> Deletion			
<b>Commercially approved products used to test the research hypothesis (if applicable)</b>			
Product Name	Manufacturer(s)*	Used as indicated	Off Label
<i>*If a generic product with multiple manufacturers, enter "generic" in this column.</i>			

**X. Amendment Information**

1. Provide a description of protocol, consent and/or other document changes with section numbers where the changes occur.
2. Provide a justification for all changes.
3. Will these changes alter the risk/benefit assessment as defined by [45 CFR Part 46.111](#)?  Yes  No

If yes, explain:

4. Are there changes to the informed consent document (s)?  
 Yes  
 No

If yes, provide a description of consent changes and sections where the changes occur:

5. Are subjects currently enrolled on the study?  Yes  No

If yes, how will subjects be informed of the changes? (*provide explanation*):

Or

- This change will not affect currently enrolled subjects
- Addition of new consent(s)/assent(s)
- Use of Oral short-form consent

## SOP 10 Appendix A

### XI. Addition or changes to Recruitment Materials/Participant Letter/Information Sheets

- Yes (*If yes, please attached new or revised materials*)  
 No

**Authority** - Section 3501 of Title 44 of the U.S. Code authorizes collection of this information. The collection, maintenance & use of personally identifiable information at the NIH are governed under provisions of the Privacy Act of 1974. The information you have been asked to provide on this form is necessary for employees of the NIH to perform their assigned duties as related to the administration and reporting of intramural clinical research protocols and will be used solely for those purposes.

## SOP 10 Appendix B

### Supplement A

#### RESEARCH CHARACTERISTICS – SUPPLEMENT OBSERVATIONAL STUDY

##### 1. Research Type: (*select one*)

**Screening-** Designed to determine if individuals may be suitable candidates for inclusion in one or another study being carried out by an Institute. The NIH does not define a rigid quota of patients to be admitted for screening purposes, since this may vary widely among ICs and within an IC over time. Furthermore, specific screening protocols may be written for long-term accrual of cohorts of patients with interesting, unexplained disease presentation for the purpose of identifying new syndromes. However, the projected number of patients to be accrued to such screening protocols must be estimated in advance and subsequently monitored.

**Training-** Provides the opportunity for staff physicians and other health workers to follow particular types of patients in order to maintain or increase their professional skills. The projected number of subjects to be accrued to such training protocols must be indicated in advance and subsequently monitored.

**Natural History (NH) – Disease Progression/Physiology Protocols** designed to study normal human biology and disease pathogenesis. Such protocols may have multiple components including provision for screening, standard therapy, physiological investigations, natural history, and long-term effects of therapy.

**Sample/Data Collection or Analysis-** Protocols designed to analyze or collect samples/specimens or data. May include imaging studies, tissue collection, retrospective data review, etc.

##### 2. Study Design for the Observational Study: *Select the most appropriate term describing the protocol from each of the following elements*

a. **Observational Study Model:** The primary strategy for subject identification and follow-up:

**Cohort-** a group of individuals, initially defined and composed, with common characteristics (e.g., condition, birth year), who are examined or followed over a given time period.

**Case-control-** a group of individuals with specific characteristics (e.g., conditions or exposures) compared to groups(s) with different characteristics, but otherwise similar

**Case-only-** a single group of individuals with specific characteristics

**Case-crossover-** a single group of individuals in whom characteristics immediately prior to disease onset (sometimes called the hazard

## SOP 10 Appendix B

period) are compared to characteristics of the same individual (case) at some earlier time (i.e., control period)

- Ecologic or community studies-** geographically defined populations, such as countries or regions within a country, compared on a variety of environmental measures (e.g., air pollution intensity, hours of sunlight) and/or global measures not reducible to individual level characteristics (e.g., health care system, laws or policies median income, average fat intake, disease rate)
- Family-based- studies**—conducted among family members, such as genetic studies within families or twin studies and studies of family environment
- Other** – explain in detailed description.

**b. Number of Groups/Cohorts** - Number of study groups/cohorts (*enter 1 for a single-group study*) \_\_\_\_\_

**c. Time Perspective:** – Select the temporal relationship of the observation period to the time of subject enrollment.

- Prospective-** look forward using periodic observations collected predominantly following subject enrollment.
- Retrospective** - look back using observations collected predominantly prior to subject selection and enrollment.
- Cross-sectional-** observations or measurements made at a single point in time, usually at subject enrollment.
- Other-** explain

**d. Biospecimen Retention for future use** (*select one*)

- None Retained** – no samples retained
- Samples with DNA** – samples retained, with potential for extraction of DNA from at least one of the types of samples retained (e.g., frozen tissue, whole blood)
- Samples Without DNA** – samples retained, with no potential for DNA extraction from any retained samples (e.g., fixed tissue, plasma)

**Biospecimen Description-** Specify all types of biospecimens to be retained (e.g., whole blood, serum, white cells, urine, and tissue).

\_\_\_\_\_ (*1000 character limit including spaces*)

**3. Primary Outcome:** (*all fields are required*)

Primary Outcome Measure- measure that will be used to determine the effect of the intervention(s)	Time-Frame - Time point(s) at which outcome measure is assessed.	Is this measure assessing a safety issue?
		<input type="checkbox"/> Yes <input type="checkbox"/> No
		<input type="checkbox"/> Yes <input type="checkbox"/> No

## SOP 10 Appendix B

a. **Primary Completion Date:** The date that the final subject will be examined or an intervention received for the purposes of final collection of data for the primary outcome. \_\_\_/\_\_\_/\_\_\_\_

4. **Secondary Outcome: Currently this table is optional for Observational Studies.** (*if applicable*) – other key measures that will be used to evaluate the intervention(s).

Secondary Outcome Measure- measure that will be used to determine the effect of the intervention(s)	Time-Frame- Time point(s) at which outcome measure is assessed	Is this assessing a safety issue?
		<input type="checkbox"/> Yes <input type="checkbox"/> No
		<input type="checkbox"/> Yes <input type="checkbox"/> No

5. **Will NIH be the “responsible party” for registering the protocol with CT.gov?**  Yes  No

**If yes, select the type:**

- Sponsor (Specify Institute) \_\_\_\_\_  
Provide point of contact \_\_\_\_\_
- Sponsor-Investigator (Specify investigator) \_\_\_\_\_
- Investigator (Specify investigator) \_\_\_\_\_

**If no, provide the name of the organization who will register the protocol:** \_\_\_\_\_

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement B

#### RESEARCH CHARACTERISTICS – SUPPLEMENT FOR INTERVENTIONAL STUDY

##### 1. Research Type: *(select one)*

- Pharmacokinetics/Dynamics** (*Complete Supplement P*) - Protocol designed to study the biochemical and physiological effects of drugs.
- Clinical Trial Phase 0** (*Complete Supplement P*) - is an initial first in human study conducted under an exploratory IND involving very limited agent exposure with no therapeutic or diagnostic intent (e.g., screening studies, microdose studies). The purpose of these studies is to identify the biologic and molecular markers earlier in the development of new clinical agents for improved targeted therapies before proceeding to Phase I trials. Participants in Phase 0 studies are patients or healthy volunteers who are closely monitored. The total number of study participants varies with the drug and the clinical condition but usually includes no more than 20 – 30.
- Clinical Trial Phase I** (*Complete Supplement P*) - includes the initial introduction of an investigational new drug into humans. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase I, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase II studies. Participants in Phase I studies are patients or healthy volunteers who are closely monitored. The total number of patients and volunteers included in Phase I studies varies with the drug, but is generally in the range of 20-80.
- Clinical Trial Phase I/II** (*Complete Supplement P*) - includes both Phase I and Phase II procedures into a single trial. These studies are initiated when there is an expectation of less than usual short-term side effects and risks associated with the drug or biologic, such as vaccine trials. Once the metabolic and pharmacologic actions of the drug and the side effects are determined, the trial moves directly into determining the effectiveness of the agent. As with Phase I and II studies, the participants are closely monitored. Phase II trials involve several hundred participants.
- Clinical Trial Phase II** (*Complete Supplement P*) - includes the controlled and uncontrolled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Participants in Phase II studies are typically closely monitored. Phase II studies include a relatively small number of patients, usually no more than several hundred subjects.

## SOP 10 Appendix B

- Clinical Trial Phase III** (*Complete Supplement P*) - studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. Phase III studies usually include from several hundred to several thousand subjects under both sponsor and FDA safety monitoring.
  
- Clinical Trial Phase IV** (*Complete Supplement P*) - (From CFR 312.85) Concurrent with marketing approval, the FDA may seek agreement from the sponsor to conduct certain postmarketing (Phase IV) studies to delineate additional information about the drug's risks, benefits, and optional use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase II studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time.

**2. Study Design for this interventional study:** *Select the most appropriate term describing the protocol from each of the following elements*

**a. Primary Purpose:** *(select one)*

- Treatment** - protocol designed to evaluate one or more interventions for treating a disease, syndrome or condition.
- Prevention** - protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition.
- Diagnostic** - protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition.
- Supportive Care** - protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects or mitigate against a decline in the subject's health or function. In general, supportive care interventions are not intended to cure a disease.
- Screening** - protocol designed to assess or examine methods of identifying a condition (or risk factors for a condition) in people who are not yet known to have the condition (or risk factor).
- Health Services Research** - protocol designed to evaluate the delivery, processes, management, organization or financing of health care.
- Basic Science** - protocol designed to examine the basic mechanism of action (e.g., physiology, biomechanics) of an intervention.
- Other** - describe:  

---

## SOP 10 Appendix B

**b. Intervention Model:** intervention assignments (*select one*)

- Single Group** - single arm study
- Parallel** - participants are assigned to one of two or more groups in parallel for the duration of the study.
- Cross-over**- participants receive one of two alternative interventions during the initial phase of the study and receive the other intervention during the second phase of the study.
- Factorial** - two or more interventions, each alone and in combination, are evaluated in parallel against a control group.

**c. Masking:** knowledge of intervention assignments

- Open** - no masking is used. All involved know the identify of the intervention assignment
- Single blind** - one party, either the investigator or participant, is unaware of the intervention assignment; also called single-masked study

**Check the role that is to be masked:**(*select one*)

- Subject    Caregiver    Investigator    Outcomes Assessor

- Double blind - two or more parties are unaware of the intervention assignment.**

**Check the role that is to be masked:**(*select two or more*)

- Subject    Caregiver    Investigator    Outcomes Assessor

**d. Allocation:** participant assignment to intervention group.

- N/A** - single arm study.
- Randomized Controlled Trial** - participants are assigned to intervention groups by chance.
- Nonrandomized Trial** - participants are expressly assigned to intervention groups through a non-random method, such as physician choice.

**e. Study Classification:** (formerly endpoint) – type of primary outcome or endpoint that the protocol is designed to evaluate. (*select one*)

- N/A**- not applicable
- Safety**- show if the drug is safe under conditions of proposed use
- Efficacy**- measure of an intervention's influence on a disease or health condition
- Safety/Efficacy**
- Bio-equivalence** - scientific basis for comparing generic and brand name

## SOP 10 Appendix B

- drugs
- Bio-availability** - rate and extent to which a drug is absorbed or otherwise available to the treatment site in the body
  - Pharmacokinetics** - the action of a drug in the body over a period of time including the process of absorption, distribution and localization in tissue, biotransformation, and excretion of the compound
  - Pharmacodynamics** - action of drugs in living systems
  - Pharmacokinetics/dynamics**

**f. Primary Outcome:** *(all fields are required)*

Primary Outcome Measure- measure that will be used to determine the effect of the intervention(s)	Time-Frame - Time point(s) at which outcome measure is assessed.	Is this measure assessing a safety issue?
		<input type="checkbox"/> Yes <input type="checkbox"/> No
		<input type="checkbox"/> Yes <input type="checkbox"/> No

**g. Primary Completion Date:** The date that the final subject will be examined or an intervention received for the purposes of final collection of data for the primary outcome. \_\_/\_\_/\_\_\_\_

**h. Secondary Outcome:** *(if applicable)* –other key measures that will be used to evaluate the intervention(s).

Secondary Outcome Measure- measure that will be used to determine the effect of the intervention(s)	Time-Frame- Time point(s) at which outcome measure is assessed	Is this measure assessing a safety issue?
		<input type="checkbox"/> Yes <input type="checkbox"/> No
		<input type="checkbox"/> Yes <input type="checkbox"/> No

**i. Will NIH be the “responsible party” for registering the protocol with CT.gov?**  Yes  No

**If yes, select they type:**

- Sponsor (Specify Institute) \_\_\_\_\_  
Provide point of contact \_\_\_\_\_
- Sponsor-Investigator (Specify investigator) \_\_\_\_\_
- Investigator (Specify investigator) \_\_\_\_\_

**If no, provide the name of the organization who will register the protocol:**

\_\_\_\_\_

## SOP 10 Appendix B

### j. Study Interventions:

Interventions			
	Type (select from choices below*)	Name	Description (cover key details of the intervention) limit 1000 characters
1			
2			
3			
4			

\*Type selections include: Drug, Genetic, Biological/Vaccine, Behavioral, Device, Radiation, Procedure/Surgery, Dietary Supplement or Other.

### k. Study Arms:

Arms				
	Arm Number/Label	Arm Type (select choices from below*)	Arm Description: Brief description of the arm. (limit 1000 characters)	Intervention (identified above)
1				
2				
3				
4				

\*Arm Type selections include: Experimental, Active Comparator, Placebo Comparator, Sham Comparator, No intervention, or Other

**I. Indicate whether this trial includes an intervention subject to US Food and Drug Administration regulations?**  Yes  No

**If yes, Indicate whether this is an “Applicable Clinical Trial\*” as defined by US Public Law 110-85, Title VIII, Section 801?**  Yes  No

\*Applicable clinical trial (ACT) Interventional studies are non-Phase 0 or I (include drug, biologic, device) and at least 1 site in U.S. or IND/IDE.

[RETURN TO APPLICATION](#)

# SOP 10 Appendix B

## Supplement C

### EXPANDED ACCESS STATUS

1. Expanded Access Status: Status indicating availability of an experimental drug or device outside any clinical trial protocol. This data element is only applicable for Expanded Access records (see Expanded Access under Study Type). Select one.

- Available: expanded access is currently available for this treatment.
- No longer available: expanded access was available for this treatment previously but is not currently available and will not be available in the future.
- Temporarily not available: expanded access is not currently available for this treatment, but is expected to be available in the future.
- Approved for marketing: this treatment has been approved for sale to the public.

2. Will NIH be the “responsible party” for registering the protocol with CT.gov?

- Yes  No

If yes, select they type:

- Sponsor (Specify Institute) \_\_\_\_\_  
Provide point of contact \_\_\_\_\_
- Sponsor-Investigator (Specify investigator) \_\_\_\_\_
- Investigator (Specify investigator) \_\_\_\_\_

If no, provide the name of the organization who will register the protocol:

\_\_\_\_\_

3. Study Interventions:

Interventions			
	Type (select from choices below*)	Name	Description (cover key details of the intervention) limit 1000 characters
1			
2			
3			
4			

\*Type selections include: Drug, Genetic, Biological/Vaccine, Behavioral, Device, Radiation, Procedure/Surgery, Dietary Supplement or Other.

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement D

#### **A GUIDE TO AVOIDING FINANCIAL AND NON-FINANCIAL CONFLICTS OR PERCEIVED CONFLICTS OF INTEREST IN CLINICAL RESEARCH AT NIH December 2012 (Approved 12/09/12)**

Avoiding financial and other conflicts of interests is important for NIH, where the trust and protection of research participants is vital to our mission to improve the public health. The number and complexity of laws and regulations in this area makes it difficult to know when there is a conflict or perceived conflict and what to do. This guide is intended to assist those engaged in clinical research and NIH IRB members in avoiding real or perceived financial and non-financial conflicts of interest.

#### **I. What are potential conflicts of interest for those engaged in clinical research?**

All clinical researchers have primary obligations. These include obtaining knowledge that will promote health and health care and helping ensure the safety and health of research participants. Clinical researchers may also have other, personal or secondary interests, which could include teaching trainees, supporting a family, and earning income. These secondary interests are not, themselves, unethical, but in some circumstances they have the potential to compromise, or appear to compromise, the judgment of clinical researchers regarding their primary obligations. When these secondary interests have the potential to compromise judgment, or appear to do so, there is a conflict between the secondary and primary interests.

This guide provides information to identify and prevent or mitigate financial and other conflicts, thereby helping to ensure both the integrity of our research and the safety of participants.

#### **II. To whom does the guide apply?**

The restrictions discussed in this guide are based on the laws that apply to NIH employees.<sup>1</sup> All NIH employees should be listed as investigators<sup>2</sup> or key research personnel<sup>3</sup> in the protocol when they substantively participate in the development, conduct, or analysis of clinical research protocols (both diagnostic and therapeutic) and must adhere to the rules described below. These rules also apply to NIH employees who serve on NIH Institutional Review Boards (IRBs) and Data Safety and Monitoring Boards (DSMBs). It is expected that non-employees<sup>4</sup> who serve as investigators in key research personnel roles or as IRB or DSMB members will review this guide and adhere to the rules set out. All investigators and key research personnel (employees and non-employees) listed on a protocol shall, by initialing the NIH Intramural Clinical Protocol Submission Form, acknowledge receipt of this guide. Non-NIH Investigators should be mindful of real and potential conflicts, discuss such conflicts with the protocol's PI and sign a Certification that this has occurred. Please note that the National Institutes of Health

---

<sup>1</sup> NIH employees are those NIH staff with an appointment to the federal government pursuant to, for example, Title 5, 38 or 42, or the Commissioned Corps, and may include some fellows. Personnel appointed through an Intergovernmental Personnel Act (IPA) agreement may have federal government appointments as well.

<sup>2</sup> Investigators are those NIH employees who occupy the following positions: Principal Investigator, Associate Investigator; Accountable Investigator; Medical Advisory Investigator; Research Contacts and Lead AIs.

<sup>3</sup> Key research personnel include those NIH employees who: 1) obtain consent from human subjects; 2) recruit human subjects; 3) evaluate the response of human subjects, including adverse or unanticipated events and 4) analyze or interpret data collected, and may include research coordinators.

<sup>4</sup> Non-NIH employees include Adjunct Principal Investigators, Guest Researchers, Special Volunteers, contractors, Intramural Research and Cancer Research Training Awardees, and collaborators from academia and industry. Note: clinical investigators who are not NIH employees, but are Special Government Employees or IPA appointees, may serve as PIs on NIH clinical protocols.

## SOP 10 Appendix B

1/14/2013

expects that all non-NIH investigators will comply with the ethics and conflict of interest policies and procedures set forth by their institution or employer.

### **III. Examples of investigator, key research personnel, and IRB and DSMB member financial conflicts of interest**

As noted when applicable, some of these examples of financial conflicts of interest are prohibited by regulation for NIH employees. We list them, however, as guidance for non-employee investigators, key research personnel, and IRB and DSMB members who are reviewing this guide. It should be noted that in addition to his or her own financial interests and outside interests, an NIH employee's financial interests also include the financial interests of others, such as his or her spouse, dependent children, or household members. Examples of such interests are:

- Serving as a director, officer or other decision-maker for a commercial sponsor of clinical research (prohibited activity for NIH employees);
- Holding stock or stock options in a commercial sponsor of clinical research (unless below the applicable de minimis amount or held within a diversified, independently managed mutual fund);
- Receiving compensation for service as consultant or advisor to a commercial sponsor of clinical research (excluding expenses) (prohibited activity for NIH employees);
- Receiving honoraria from a commercial sponsor of clinical research (prohibited activity for NIH employees);
- Personally accepting payment from the clinical research sponsor for non-research travel or other gifts (for NIH employees, government receipt of in-kind, research-related travel is not included and other exceptions may apply);
- Obtaining royalties or being personally named as an inventor on patents (or invention reports) for the product(s) being evaluated in the clinical research or products that could benefit from the clinical research (special rules apply in this case when NIH holds the patent – see Section VII below);
- Receiving payments based on the research recruitment or outcomes (prohibited activity for NIH employees);
- Having other personal or outside relationships with the commercial sponsor of the clinical research (prohibited activity for NIH employees);
- Having financial interest above the applicable de minimis in companies with similar products known to the investigator to be competing with the product under study (prohibited activity for NIH employees); or
- Participating in an IRB or DSMB decision that has the potential to affect your spouse's employer (prohibited activity for NIH employees).

1/14/2013

## SOP 10 Appendix B

### IV. Examples of non-financial real or apparent conflicts of interest for IRB and DSMB members

- Voting on a protocol when the member of the IRB is the protocol's Principal Investigator, Associate Investigator or study coordinator;
- Voting on a protocol when the member of the IRB or DSMB is or has a spouse, child, household member or any other individual with whom the protocol's Principal Investigator, Associate Investigator or study coordinator has the appearance of a conflict of interest<sup>5</sup>; or
- Voting on a protocol when the protocol's Principal Investigator is the IRB member's supervisor (up the chain of command to the Clinical Director).

**As noted in Section II - The National Institutes of Health expects that all non-NIH investigators are in compliance with their institutional/employer's conflict of interest policies.**

---

### CLEARANCE OF NIH EMPLOYEES ONLY – PERSONAL FINANCIAL HOLDINGS

### V. NIH's system to assist in identifying and preventing personal financial conflicts for investigators in clinical research

The Principal Investigator is responsible for assuring that each investigator and all key research personnel listed on the protocol receive a copy of this guide. The guide should be distributed to any new investigator/ key research personnel added to a protocol while the protocol is active.

#### a. New Protocols

At the earliest point possible, the PI is responsible for providing his or her IC Deputy Ethics Counselor (DEC) with a completed copy of the **"Clearance of NIH Investigator Personal Financial Holdings" (PFH Clearance)** (see Appendix 1) which lists all investigators. Alternatively, an electronic equivalent could be used to provide this information.

Upon receipt of the Protocol PFH Clearance, the IC DEC will read the précis to determine if: 1) any commercial drugs/devices are being studied or 2) if any standard of care treatments will be used in the protocol. If there are no commercial interests associated with this protocol, the DEC may approve the research via an expedited process. This eliminates the need for review of the investigator's holdings in any organization that are significantly affected by NIH research (SAOs). The DEC always has the discretion to complete a full conflict of interest analysis if s/he feels it necessary.

<sup>5</sup> The IRB or DSMB member determines, in his/her own opinion, whether a personal relationship with the protocol's Principal Investigator or another member of the research team exists. If such a determination is made, the IRB or DSMB member shall disqualify him or herself from the protocol to avoid any appearance of a conflict of interest.

## SOP 10 Appendix B

For each protocol:

1) If the protocol involves the use of a commercial drug/device, or has the potential to affect the value of other commercial products, the DEC will verify that all investigators who are employees have a form 716/717 on file and that the personal investment information on the form 716/717 is current (within 6 months) as of the date on the PFH Clearance. The IC DEC will then review file copies of the PI's and each AI's 716 or 717 forms that enumerate stock holdings in SAOs.

2) If SAO holdings are above the de minimus values, the DEC will provide the PI with an anonymous list of AI's holdings in SAOs as reported on these forms so the PI can determine if any pose a conflict of interest for the protocol in question. Any investigator who has a potential conflict will be contacted by his or her DEC to determine how to resolve any actual or apparent conflict. The employee's supervisor and/or the Clinical Director will be consulted as necessary if a conflict exists. The conflicts review will occur in parallel to the IRB submission process.

At the completion of the personal financial holdings review, the IC DEC will return a signed copy of the Protocol PFH Clearance to the PI. The PI will then note the date of DEC clearance on the *Protocol Application* and ensure that the Protocol PFH Clearance is included in the protocol packet.

The DEC clearance form will become part of the protocol packet forwarded to the IRB Chair for final approval. The IRB chair may not provide final approval by signing a protocol until the completed Protocol PFH Clearance is included in the protocol packet.

### **b. Continuing Review**

A COI analysis will take place at the time of continuing review using the same process as described above. The Protocol PFH Clearance will be used for this process. For the conflicts analysis, the addition of new investigators, any changes related to the use of commercial products or any change to an IND/IDE will be evaluated by the IC DEC.

### **c. Amendment**

A COI analysis will take place for amendments involving the addition of NIH employee investigators to a protocol, any changes related to the use of commercial products, or any change to an IND/IDE. The Protocol PFH Clearance will be used for this process following the procedure above. If just adding a new investigator, only that investigator needs to be cleared.

Although government-wide regulations allow NIH employees to hold de minimis amounts of publicly- traded stock without triggering conflict of interest restrictions, there may be other factors to consider with respect to stock ownership. If a publication should result from the protocol, most journals require the authors to disclose individual financial holdings within the text of the published paper. Such disclosures could raise at least the appearance of the conflict of interest. Thus, all investigators should consider these outside factors when making personal financial investments.

## **VI. IRB and DSMB Clearance for COI**

- Before beginning protocol review activities, the Chair asks whether any member is aware of any real or apparent conflict of interest. The minutes will reflect which individual(s) has a real or apparent conflict of interest. No IRB or DSMB may have

1/14/2013

a member participate in the initial or continuing review of any project in which the

## SOP 10 Appendix B

member has a conflicting interest, except to provide information requested by the IRB or DSMB.

- When the Principal Investigator or Associate Investigator is the Institute Director, or Scientific Director, the protocol will be reviewed by an IRB not affiliated with that institute.
- When the Principal Investigator is the Clinical Director (CD) it shall be the prerogative of an IRB either to review such protocols or refer them to another Institute's IRB. IRBs reviewing protocols in which their CD is the PI must have a majority of voting members present at the meeting who are not employed by the CD's Institute, otherwise any alternative plan must have prior approval by the Clinical Center Director and the Deputy Director for Intramural Research.

### **VII. NIH Intellectual Property and Royalties**

In some instances, NIH clinical research protocols will evaluate or potentially advance product(s) in which NIH (i.e., the government) owns patents or has received invention reports. In such cases:

- An NIH investigator may participate in the clinical trial, even if the investigator is listed on the patent or invention report and/or may receive royalty payments from the NIH for the product(s) being tested.
- When such an investigator participates in a trial, there will be full disclosure of the relationship to the IRB and to the research subjects (i.e., information should appear in the consent form) with review and approval by the IRB. This is to ensure the quality and integrity of the data collected.
- In the case of continuing review of current protocols where NIH has a new or amended intellectual property interest in the invention, investigators should provide a new human subjects consent form or correspondence outlining the relationship, for review and approval by the IRB.
- An independent entity or individual must review the integrity/accuracy of the results/quality of data to assure the safety of human subjects and to assess whether there is a change in the risk benefit ratio or introduction of possible bias.

[RETURN TO APPLICATION](#)

# SOP 10 Appendix B

## Supplement E

### CLEARANCE OF NIH INVESTIGATOR PERSONAL FINANCIAL HOLDINGS BY IC ETHICS OFFICE (PFH)

**Instructions:** Email the completed document to the IC DEC for your Institute and include the protocol précis for ALL protocols. To facilitate this process, ensure that the list of investigators is current and complete by comparing this with the protocol face sheet and PQS (<http://pqs.cc.nih.gov/>).

<sup>1</sup>**Date Received by Ethics Office:** \_\_\_\_\_

<sup>2</sup>**Date of Memo** \_\_\_\_\_

<sup>3</sup>**Date of IRB Meeting:** \_\_\_\_\_

<sup>4</sup>**Date Protocol Expires:** \_\_\_\_\_

<sup>5</sup>New Protocol

<sup>6</sup>Continuing Review

<sup>7</sup>Amendment: check all that apply

Investigator Added

Product Added or Changed

<sup>8</sup>**To:** \_\_\_\_\_  
I.C. Deputy Ethics Counselor

<sup>9</sup>**From:** \_\_\_\_\_  
Principal Investigator  
cc:

<sup>10</sup>**Protocol #:**

<sup>11</sup>**Research Type:**

Screening

Training

Nat. History – Dx Progression/Physiology

Nat. History–Sample/Data Collection/Analysis:  Recruiting  Not Recruiting

Pharmacokinetics/Dynamics

Clinical Trial: Phase:  0  1  1-2  2  3  4

<sup>12</sup>**Title:**

<sup>13</sup>**Principal Investigator's I.C.:**

<sup>14</sup>**Responsible IRB:**

<sup>15</sup>**Does this study include any commercial interests?**  Yes  No

**Does this study involve any technology transfer?**  Yes  No

**Does this study involve any products made by a commercial interest?**  Yes  No

<sup>16</sup>**Manufacturer of study product(s) (drug, biologic or device):**

<sup>17</sup>**IND/IDE# (if applicable):**

<sup>18</sup>**IND/IDE Sponsor (if applicable):**

<sup>19</sup>**Do you know of competitors for study drug, biologic or device manufacturer(s) for purposes related to this protocol?**

**If yes, please list:**

<sup>20</sup>**Objective of the study (one sentence summary):**

<sup>21</sup>**List individuals serving on the protocol as an:** Adjunct PI, Accountable Investigator, Medical Advisory Investigator, Lead Associate Investigator, Associate Investigator and/or Research Contact, identifying for each their affiliation (i.e., outside entity) and if an NIH Employee or Non-NIH Employee.

Name, Affiliation, Employment Status (NIH Employee/Non-NIH Employee)

## SOP 10 Appendix B

The information below is for IRB information only and shall not be included on the protocol consent form.

- <sup>22</sup>  No conflicts identified for NIH employees, or conflicts have been resolved through divestiture or waiver.
- <sup>23</sup>  No conflicts exist however one or more NIH employees have a de minimis holding in the manufacturer of the product(s) used in the study. Name of manufacturer(s):
- <sup>24</sup>  No conflicts exist however one or more NIH employees have an over the de minimis holding in the manufacturer of the product(s) used in the study and has been cleared to participate by waiver. Name of manufacturer(s):

\_\_\_\_\_  
Deputy Ethics Counselor for IC of P.I.

\_\_\_\_\_  
Date Signed

\_\_\_\_\_  
Date Returned to P.I.

Ethics Office Use Only: DER

7/8/13

[RETURN TO APPLICATION](#)

# SOP 10 Appendix B

## Supplement F

### CONFLICT OF INTEREST (COI) CERTIFICATION FOR NIH EMPLOYEES, SGEs, AND IPAS SERVING AS KEY RESEARCH PERSONNEL (NOT LISTED AS INVESTIGATORS)

This form should be completed by NIH employees, SGEs, and IPAs who are Key Research Personnel but are not listed as Investigators. This form is not for NIH Employees, SGEs, or IPAs serving as investigators.

Key Research Personnel are individuals who engage in any or all of the following activities:

1. Recruiting human subjects (screening for inclusion/exclusion criteria)
2. Obtaining consent from human subjects
3. Evaluating or analyzing the data accrued by the study
4. Review and reporting of unanticipated events (problems)

Name:	
Role on Study:	
NIH Institute:	
Name of PI:	
Title of Protocol:	

I certify that I have received and read the NIH **Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Human Subjects Research at NIH** and that I will comply with the Policy. I certify I have no conflict of interest with this protocol, and if I am a financial disclosure filer, I have consulted my ethics office to confirm. In the event I become aware of any potential conflict of interest, I will contact my ethics office.

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

# SOP 10 Appendix B

## Supplement G

### CONFLICT OF INTEREST (COI) CERTIFICATION FOR NON-NIH EMPLOYEES

This form should be completed by non-NIH employees who are listed as Investigators or serve as Key Research Personnel (but who are **not** at NIH as a Special Government Employee or under an Intergovernmental Personnel Act (IPA) agreement).

Key Research Personnel are individuals who engage in any or all of the following activities:

1. Recruiting human subjects (screening for inclusion/exclusion criteria)
2. Obtaining consent from human subjects
3. Evaluating or analyzing the data accrued by the study
4. Review and reporting of unanticipated events (problems)

Name of Non-NIH Employee:	
Role on Study:	
NIH Institute:	
Home Institute:	
Name of PI:	
Title of Protocol:	

I certify that I have received and read the NIH **Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Human Subjects Research at NIH** and that I will comply with the Policy.

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

I certify that my home institution has a Conflict of Interest Policy and that I am in compliance with the Conflict of Interest policy of my home institution. I understand and agree that I must promptly inform the PI of this protocol if I am no longer in compliance with the Conflict of Interest policy of my home institution.

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

# SOP 10 Appendix B

## Supplement H

### RESEARCH INVOLVING CHILDREN AS SUBJECTS

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.

#### 1. Children as Subjects

##### a. Where will the children participate?

- NIH Clinical Center
- Other NIH Site Specify: \_\_\_\_\_
- Home
- School

(1) If yes, have you obtained the necessary permission from the school district?  
 Yes  No (Attach documentation of permission)

- Outside Clinical Site
- Other, specify: \_\_\_\_\_

##### b. Are any of the children wards of a State or any other agency, institution, or entity? (see e.g., 45 Part 46. 409)

- Yes  No.

#### 2. Risk/Benefit Assessment and parental permission for participation

Check the boxes below that best represents the degree of risk and benefit to which the children in this study will be exposed based on 45 CFR 46 Subpart D and, if applicable, 21 CFR 50 Subpart D.

Note: more than one category may be indicated such as when a protocol involves both a study group and a control group; in these cases, please specify the cohort.

For each risk category, please select the appropriate permission level.

In general, permission from both parents is required for research involving children 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. For Categories 1& 2, the IRB may find that the permission of one parent is sufficient for compliance with 45 CFR 46 but NIH may require permission of both parents.

Waiver of parental permission for research not regulated by the FDA: The IRB may waive the requirement for obtaining consent from a parent or legal guardian, except when research is regulated by the FDA (21 CFR 50.55), if:

- (1) The research meets the provisions for waiver in SOP 12 (Informed Consent) or
- (2) The IRB determines that the research study is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), provided an appropriate mechanism for protecting the children participants is substituted, and that the waiver is not inconsistent with

## SOP 10 Appendix B

applicable Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

- The proposed research poses risk no greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., minimal risk) (45 CFR 46.404).**
  - Permission will be obtained from both parents unless:
    - (1) One parent is deceased, unknown, incompetent, or not reasonably available; or
    - (2) When only one parent has legal responsibility for the care and custody of the child.
  - Permission from only one parent is being requested
  - A waiver of parental permission is being requested *(Complete Supplement K and provide justification for a waiver in the protocol.)*
- The proposed research poses a greater than minimal risk with the potential for direct benefit to subjects (45 CFR 46.405).**

Address in the protocol, how the benefit to risk assessment is at least as favorable as that presented by alternative approaches.

- Permission will be obtained from both parents unless:
  - (1) One parent is deceased, unknown, incompetent, or not reasonably available; or
  - (2) When only one parent has legal responsibility for the care and custody of the child.
- A waiver of parental permission is being requested *(Complete Supplement L and provide justification for a waiver in the protocol.)*
- The proposed research poses a greater than minimal risk with no potential for direct benefit to the individual subjects, but is likely to yield generalizable knowledge about the subjects' conditions (45 CFR 46.406).**

## SOP 10 Appendix B

Please address the following in the protocol,

1. How the risk of the protocol presents a minor increase over minimal risk.
2. How the procedure(s) present experiences to subjects that are reasonably commensurate with those inherent in their actual or expected situations.
3. How the knowledge to be gained is of vital importance for the understanding or amelioration of the condition.

Permission will be obtained from both parents unless:

- (1) One parent is deceased, unknown, incompetent, or not reasonably available; or
- (2) When only one parent has legal responsibility for the care and custody of the child.

**The proposed research does not meet the criteria in the above categories but presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children (45 CFR 46.407). ~~Requires approval by Deputy Director for Intramural Research and the Secretary of Health and Human Services and/or the Commissioner of Food and Drugs, as applicable.~~**

Address the benefit to risk ratio in the protocol and discuss the ways in which the study presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.

Permission will be obtained from both parents unless:

- (1) One parent is deceased, unknown, incompetent, or not reasonably available; or
- (2) When only one parent has legal responsibility for the care and custody of the child.

### 3. Parental Permission in a Group Setting

- a. **What permission will be obtained from the parents if the research is being conducted in a group setting (e.g., a classroom)?** (Explain in the protocol what provisions have been made for children whose parents have not given permission for them to participate.)

### 4. Assent from Children

Adequate provisions must be made for soliciting the assent of children when in the judgment of the IRB the children are capable of providing assent and for soliciting the permission of their parents or guardians.

## SOP 10 Appendix B

- a. **Please indicate below whether the children you will study are generally capable of providing assent; evaluate age, maturity and psychological state of the children involved.**
- All are capable
  - None are capable (Explain in the protocol)
  - Some are capable (Explain in the protocol)
- b. **Describe in the protocol how assent will be obtained, including what information will be provided to the subjects.**

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement I

#### RESEARCH INVOLVING PRISONERS AS SUBJECTS

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.

##### 1. Prisoners as Subjects

45 CFR 46.303 Definitions (c) *Prisoner* means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

**a. The subjects in this study include:**

- Individuals involuntarily confined or detained in a penal institution.
- Individuals detained in other facilities by virtue of statutes or commitment procedures, which provide alternatives to criminal prosecution or incarceration in a penal institution.
- Individuals detained pending arraignment, trial, or sentencing.
- Other individuals involuntarily detained under a criminal or civil statute.

**b. Specify in the protocol where the prisoners are located.**

**c. Do you have permission from the facility and the appropriate authorities?**  
(Attach all documentation to the application)  Yes  No

**d. Are any of the subjects in this research minors in the jurisdiction where the research is taking place?**  Yes  No (If yes, complete IRB Supplement G)

##### 2. Allowable Risk/Benefit Categories

Check the category below that best represents the nature of the research and the degree of risk and benefit to which the prisoners in this study will be exposed.

**Note:** The definition of minimal risk for prisoners is slightly different from the definition for other subjects. The definition of minimal risk for research involving prisoners given in 46.303(d), is as follows:

Minimal risk is the **probability** and **magnitude** of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Select the appropriate risk/benefit assessment below and provide a rationale for the assessment in the protocol to support your selection.

## SOP 10 Appendix B

- Category 1- 45 CFR 46.306 (a) (2) (i):** The study of the possible causes, effects, and processes of incarceration, and of criminal behavior, where the study presents no more than minimal risk and no more than inconvenience to the subjects
- Category 2- 45 CFR 46.306 (a) (2) (ii):** The study of prisons as institutional structures or of prisoners as incarcerated persons, where the study presents no more than minimal risk and no more than inconvenience to the subjects.
- Category 3- 45 CFR 46.306 (a) (2) (iii):** The study of conditions particularly affecting prisoners as a class (for example, research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults). (Additional procedures are required for approval. Contact the OHSRP for more information.)
- Category 4- 45 CFR 46.306 (a) (2) (iv):** The study of practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. (Additional procedures are required for approval. Contact the OHSRP for more information.)
  - a. **Does the study in Category 4 involve a control group, which will not receive a benefit from being in the study?**  Yes  No (If yes, additional procedures are required for approval. Contact the OHSRP for more information.)

### 3. Additional Criteria

- a. **Are there any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired?**  Yes  No
- b. **Are the risks involved in the research commensurate with risks that would be accepted by non-prisoner volunteers?**  Yes  No
- c. **Are the procedures for the selection of subjects within the prison fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners?**  Yes  No
- d. **Is the information presented in language that is understandable to the subject population?**  Yes  No
- e. **Does adequate assurance exist that a parole Board will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole?**

## SOP 10 Appendix B

Yes  No (Explain the rationale for this in the protocol and the consent)

- f. **If there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoner's sentences, and for informing subjects of this fact?**  Yes  No

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement J

#### RESEARCH INVOLVING PREGNANT WOMEN, FETUSES OR NEONATES

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.

##### 1. Research involving Pregnant Women and Human Fetuses (SOP 14.B)

In order to be approved, the level of risk must be the least possible for achieving the objectives of the research. If research is greater than minimal risk, it must provide prospect of direct benefit for the pregnant mother or fetus (45 CFR 46.204.)

**a. Does this research pose a greater than minimal risk to the:**

Woman  Yes  No  
Fetus  Yes  No

**b. Does the research hold out the prospect of direct benefit for the:**

Woman  Yes  No  
Fetus  Yes  No

For research that does not hold out the prospect of direct benefit to the fetus or woman, explain in the protocol how the purpose of the research is the development of important biomedical knowledge, which cannot be obtained by any other means.

**c. Where scientifically appropriate, have preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, been conducted to provide data for assessing potential risks to pregnant women and fetuses?  Yes  No**

##### Informed Consent

Describe how you will ensure that individuals providing consent\* are fully informed regarding the reasonably foreseeable impact of the research on the fetus.

If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father must be obtained, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest. Otherwise, the consent of the mother is sufficient.

The legally effective informed consent of either parent, when required as above, may be waived because of unavailability, incompetence, or temporary incapacity, in which case the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of CFR 45 part 46.

## SOP 10 Appendix B

**Check off that the Principal Investigator assures that:**

- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

### 2. Research involving Neonates (SOP 14.B.3) (45 CFR 46.202(d))

Newborns are only considered neonates until they are determined to be viable. Once they are determined to be viable, they are considered children. (Supplement A should be completed for viable newborns).

When neonates of uncertain viability and nonviable neonates are to be involved in research please answer the following questions, provide information in the protocol to support your responses:

**a. Will there be any added risk to the neonate resulting from the research?**

Yes  No

**b. The Principal Investigator assures that individuals engaged in the research will have no part in determining the viability of the neonate:**

Yes  No

**c. Where scientifically appropriate, have preclinical and clinical studies been conducted to provide data for assessing potential risks to neonates?**

Yes  No

**d. Does the research hold out the prospect of enhancing the probability of survival of the neonate to the point of viability, and is any risk the least possible for achieving that objective?**  Yes  No

**e. Is the purpose of the research the development of important biomedical knowledge that cannot be obtained by other means and will there be no added risk to the neonate as a result of the research?**  Yes  No

**f. Will legally effective informed consent from either parent<sup>1</sup> be obtained in the case of a neonate of uncertain viability?**  Yes  No

<sup>1</sup>45 CFR 46.205(b)(2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. Nonviable neonate means a neonate after delivery that, although living, is not viable.

## SOP 10 Appendix B

- g. Will legally effective informed consent from both parents<sup>2</sup> be obtained in the case of nonviable neonates?**  Yes  No
- i. In the case of nonviable neonates, will vital functions of the neonate be artificially maintained?**  Yes  No
- ii. In the case on nonviable neonates, will the research terminate the heartbeat or respiration of the neonate?**  Yes  No

<sup>2</sup>46 CFR 46.205(c)(5) The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement K

#### RESEARCH INVOLVING ADULTS WHO ARE OR MAY BE UNABLE TO CONSENT

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.

**1. For research involving adults who are or may be unable to consent, provide the following information in the protocol (SOP 14.E):**

- a. Provide the justification for the inclusion of this population.
- b. Explain why these subjects need to be included in this research.
- c. Are any of these subjects institutionalized? (if applicable, complete Supplement H).
  - i. If yes, describe the setting. (Provide documentation of permission from the institution.)

**2. Risk/Benefit Assessment**

Are the risks to subjects in this research no more than minimal?  Yes  No

If no, and the research involves greater than minimal risk to subjects, are there direct benefits to the individual subjects?  Yes  No

**3. Consent and Assent**

The decision-making capacity of individual subjects should not be assumed because of a condition or diagnosis. The decision-making capacity of individual subjects should be determined through the use of a standardized measure or by consultation with a qualified professional.

- a. Describe in the protocol the procedures to be used to determine the individual subject's capacity to provide consent.
- b. For subjects where it has been determined that they lack the capacity to give consent, describe the provisions for obtaining consent from the subjects' legally authorized representative.
- c. Describe how the assent, if any, of the subjects will be obtained and documented.

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement L

#### REQUEST FOR WAIVER OF CONSENT AND/OR DOCUMENTATION OF CONSENT (INCLUDING RESEARCH INVOLVING DECEPTION)

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.<sup>1</sup>

#### 1. Request for waiver of documentation of consent (45 CFR.46.117(c))

**a. Please select one of the following:**

- The research involves no more than minimal risk; and involves only procedures that do not require written consent outside of research.
- The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.

- b.** Please explain, in the absence of written informed consent, how consent will be documented, e.g. tape recordings, videos, chart notes, etc.

#### 2. Request for waiver of informed consent

**a. In order to waive the requirement for informed consent, ALL of the following criteria must be met:**

- The research involves no more than minimal risk.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects.
- The research could not be carried out without the waiver or alteration.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

#### 3. Deception

APA Code of Ethics 6.15 (Hotlink)

**a. Will deception, including withholding of information, be used in this research?**

Yes  No

- i. If yes, provide the following information in the protocol:
- ii. Describe the deception being used in this study
- iii. Explain why deception is necessary in this research.

---

<sup>1</sup> See SOP 15 for FDA-regulated research.

## SOP 10 Appendix B

- iv. Are the risks to subjects in this research greater than minimal?
  - Yes (If yes, then deception cannot be used in this research.)
  - No
- v. Describe what information is being provided to subjects when they decide to participate.
- vi. Describe the how the subjects will be provided with additional pertinent information after participation (debriefing).

[RETURN TO APPLICATION](#)

## SOP 10 Appendix B

### Supplement M

#### RESEARCH INVOLVING STORED DATA/SPECIMENS FOR FUTURE USE

Indicate your responses below and explain your selections in the protocol. Do not provide details in this document.

#### 1. Access

**a. Who is expected to use the data/specimens? Check all that apply:**

- Study investigators associated with this protocol for this protocol
- Study investigators associated with this protocol for another protocol/purpose
- Other researchers at other NIH ICs
- Researchers at other institutions
- Future use is unknown at this time

Note: New uses of these data/specimens by the Principal Investigator or Study investigators will require an amendment submission or new protocol submission to the IRB for approval.

**b. If the data/specimens are to be released to other researchers, outside the NIH, please provide the FWA# for the other institution(s). Contact the Office of Technology Transfer/Development for your IC before sharing any data/specimens.**

#### 2. Storage

**a. Describe how the data/specimens are to be stored, including location.**

**b. Describe protections in place, if any, to restrict access to authorized persons.**

**c. Will the stored data be identifiable [i.e. retains Personally Identifiable Information (PII)]?**

- Yes If yes, explain why this is necessary, provide justification
- No If no, explain how the data will be de-identified.

**d. Will the data/specimens be coded?  Yes  No**

**If yes, explain how the data will be coded and how the key will be secured.**

#### 3. Consent

**a. The consent must include permission to have the data/specimens stored for future use.**

**b. Will results of future use data/specimens be shared with participants?**

- Yes  No If yes, explain in the protocol/consent.

[RETURN TO APPLICATION](#)

**SOP 10 Appendix B**

**IRB Supplement N  
CHANGE IN STATUS**

Protocol Title: \_\_\_\_\_

Protocol #: \_\_\_\_\_

Principal Investigator: \_\_\_\_\_

STUDY OPEN (select all that apply)                      Date: \_\_\_\_\_

NO RECRUITMENT PLANNED

*Definition: study is data or specimen analysis only; no participants will be recruited or enrolled.*

NOT YET RECRUITING

*Definition: participants are not yet being recruited.*

RECRUITING

*Definition: participants are currently being recruited.*

ENROLLING BY INVITATION

*Definition: protocol requires previous enrollment in another study in order to participate, excludes screening protocols.*

HOLD

*Definition: recruiting or enrolling participants has been stopped prematurely but potentially may resume.*

NO LONGER RECRUITING, SUBJECT FOLLOW-UP ONLY

*Definition: study is ongoing, but participants are not currently being recruited or enrolled.*

OPEN FOR DATA ANALYSIS

*Definition: Subjects have completed follow-up and the data is being analyzed.*

\_\_\_\_\_  
PRINTED NAME OF PRINCIPAL INVESTIGATOR

\_\_\_\_\_  
PI SIGNATURE

Date: \_\_\_\_\_

## **SOP 10 Appendix B**

### **SUPPLEMENT O**

#### **TRAINING REQUIREMENTS**

**Log on to OHSRP Website for Training Requirements**

**<https://federation.nih.gov:443/ohsr/nih/>**

**[RETURN TO APPLICATION](#)**

# SOP 10 Appendix B

## Supplement P

### PLANNED ENROLLMENT REPORT

Is the NIH site responsible for conducting and coordinating the overall clinical study across multiple study sites (i.e. coordinating site)?  Yes  No

If yes, provide the numeric distribution (not percentages) for the total number of participants planned for the study. Provide separate tables for the following: 1) NIH CC Site, 2) All Other Domestic Sites Combined, and 3) Foreign Sites Combined. For additional guidance, see: [http://nih-extramural-intranet.od.nih.gov/nih/topics/inclusionwo\\_main.htm](http://nih-extramural-intranet.od.nih.gov/nih/topics/inclusionwo_main.htm)

If no, complete the table only for the NIH CC site.

This report format should NOT be used for data collection from study participants

**Name of Site:** [NIH Site, Domestic, or Country (by name)] \_\_\_\_\_

**Study Title:** \_\_\_\_\_

**Principal Investigator:** \_\_\_\_\_

**Total Enrollment:** \_\_\_\_\_ **Protocol Number:** \_\_\_\_\_

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More Than One Race	0	0	0	0	0
<b>Total</b>	0	0	0	0	0

[RETURN TO APPLICATION](#)

# SOP 10 Appendix B

## Supplement Q

### CUMULATIVE INCLUSION ENROLLMENT REPORT

**This report format should NOT be used for collecting data from study participants.**

Is the NIH site responsible for conducting and coordinating the overall clinical study across multiple study sites (i.e. coordinating site)?

Yes  No

If yes, complete a separate Inclusion Enrollment Report Form (IER) for the following: 1) NIH CC Site, 2) All Other Domestic Sites Combined, and 3) Foreign Sites Combined.

If no, complete the IER only for the NIH CC site.

Select Site: [NIH CC Site, Domestic, or Foreign] \_\_\_\_\_

Principal Investigator (Last, first, middle) \_\_\_\_\_

Study Title: \_\_\_\_\_

Total Enrollment: \_\_\_\_\_ Protocol Number: \_\_\_\_\_

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/Not Reported	Female	Male	Unknown/Not Reported	Female	Male	Unknown/Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More Than One Race	0	0	0	0	0	0	0	0	0	0

[RETURN TO APPLICATION](#)