The Review and Approval Process for NIEHS Clinical Studies

NIEHS Non-Epidemiology Branch Reference Guide

Version 1.0

Date Published: November 1, 2008

Other Guides:

NIEHS Epidemiology Branch Reference Guide

NIEHS IRB Reference Guide

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INTRODUCTION

Purpose of This Document

The purpose of this document is to explain the pre-Institutional Review Board (IRB) review and approval process for all clinical research within the NIEHS Clinical Research Program (CRP). This document provides an explanation of the individual reviews that comprise the pre-IRB review process, followed by the policies and procedures used to ensure a consistent, standardized process.

Scope

While the overall review and approval process is the same for all studies conducted at NIEHS by the Division of Intramural Research (DIR), operational differences exist within the process depending upon whether an investigator is affiliated with the Epidemiology Branch (EB) or not. This document refers only to the policies and procedures/processes that non-EB investigators must follow. Refer to the *NIEHS Epidemiology Branch Reference Guide* for the policies and procedures/processes that EB investigators must follow. Information that is identical between the two guides is listed in both guides.

This document describes the policies and procedures for all of the pre-IRB reviews required for conducting clinical research at NIEHS from review of initial research concept through submission of materials to the NIEHS IRB to assure ethical conduct of research and human subjects' protections. This document does not cover the policies and procedures that govern the NIEHS IRB, as this information is covered in the *NIEHS IRB Reference Guide*.

Additionally, this document describes policies and procedures that involve interaction with third parties to obtain some approvals (e.g., OMB for clinical exemption, OHSR for IRB exemption); however, this document does not cover the processes performed by these outside organizations. Where appropriate, references are made to applicable public information sources or contacts for more information about an external organization's particular policies, processes, or procedures.

How This Document Is Organized

This document is divided into the following parts:

1. Understanding the Pre-IRB Review Process:
   Explains the individual reviews that comprise the overall pre-IRB review process for reviewing, approving and monitoring clinical research at NIEHS.
2. Pre-IRB Review Policies:
   Describes all policies affecting the pre-IRB review process of reviewing, approving and monitoring clinical research at NIEHS.

3. Standard Operating Procedures:
   Gives an explanation of procedures/steps developed to support the policies governing the pre-IRB review process of reviewing, approving and monitoring clinical research.

Electronic versions of this document and all supporting documents (forms, templates, etc.) can be found at both the OHRC and CRP websites at http://www.niehs.nih.gov/about/orgstructure/boards/irb/index.cfm and http://www.niehs.nih.gov/research/clinical/program/index.cfm, respectively.

Acronyms Used in This Document

The following acronyms are frequently used in this document:

Acronym	Meaning
BC	Branch Chief
CAC	NIEHS Clinical Advisory Committee
CC	NIH Clinical Center (NIH Campus in Bethesda)
CD	NIEHS Clinical Director
CERC	Clinical Exemption Review Committee
COI	Conflict of Interest
CRP	NIEHS DIR Clinical Research Program
CRU	Clinical Research Unit (NIEHS' on-site facility)
EB	Epidemiology Branch
IR	Initial Review (first review by the IRB)
IRB	Institutional Review Board
OHRC	NIEHS Office of Human Research Compliance
OHRP	DHHS Office for Human Research Protections
OHSR	NIH Office of Human Subjects Research
OMB	Office of Management and Budget
OPS	Office of Protocol Services
PCB	Project Clearance Branch
PO	Project Officer
SD	Scientific Director NIEHS Division of Intramural Research

Acronym	Meaning
SME	Subject Matter Expert
SRC	Scientific Review Committee
WA	Work Assignment

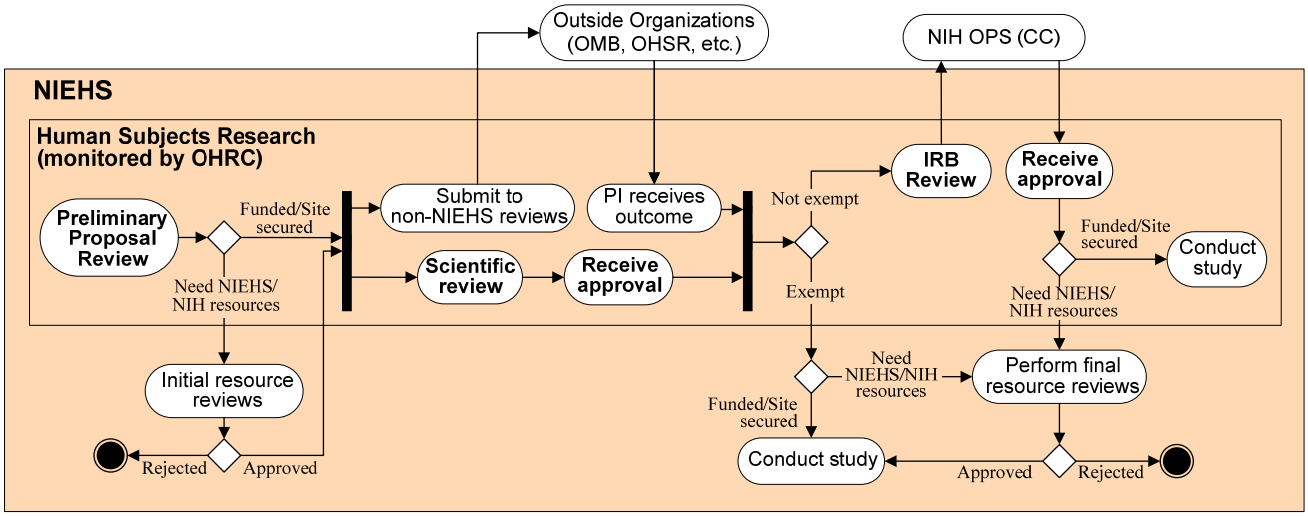
Questions or Comments?

For questions or comments regarding information contained within this document or to suggest the addition of content that may be missing from this document, please contact the Director, Office of Human Research Compliance (OHRC) Joan P. Packenham, Ph.D. by telephone at 919-541-0766 or by email at packenhm@niehs.nih.gov. Alternatively, you may provide feedback at the following websites:
OHRC: http://www.niehs.nih.gov/about/orgstructure/boards/irb/index.cfm
CRP: http://www.niehs.nih.gov/research/clinical/program/index.cfm

UNDERSTANDING THE PRE-IRB REVIEW PROCESS

Process Overview

Developing a clinical protocol that is scientifically sound, meritorious, ethical, protects human subjects, and complies with applicable federal regulations and DHHS/NIH policies is a complex process that involves submitting the protocol to a number of review committees. The graphic below depicts the typical review process, including the individual reviews involved in obtaining approval before subjects can be enrolled in clinical research at NIEHS.



In order to comply with federal regulations and to obtain/maintain an accredited human subjects protections program, the Office of Human Research Compliance (OHRC) facilitates and monitors preliminary proposal review, scientific review, and Institutional Review Board (IRB) review to 1) ensure adherence to DHHS/NIH/federal policies and procedures, 2) correct any deviations in ways that prevent recurrence, and 3) improve the quality of the program.

Below is an explanation of each of the reviews shown in the graphic above:

- Preliminary Proposal Review: Before submitting to other review committees, the PI must first present their proposal/protocol to the Clinical Advisory Committee (CAC). This committee is comprised of personnel from across DIR and may also include outside experts at the discretion of the CAC Chair. This committee is designed to provide feedback to the PI concerning his/her protocol at an early stage. By receiving feedback early, the PI can minimize the number of revision cycles that typically take place when feedback is received piecemeal through sequential reviews. PIs may take advantage of this committee by presenting their concept early in the development process and subsequently presenting it again to the committee as the proposal/protocol matures. Refer to Appendix A for a high-level flow diagram of the preliminary proposal review process. This committee review is optional for members of the NIEHS Epidemiology Branch but mandatory for other NIEHS DIR investigators. The primary contact

person for this committee is Bill Schrader, Ph.D., Deputy Scientific Director. Members of the Epidemiology Branch should consult with Dale Sandler, Ph.D. to be sure that they are in compliance with Branch requirements for preliminary review of research.

- Initial/Final Resource Reviews: Resource reviews are necessary when the PI requires funds or the use of NIH facilities in order to conduct the research. The PI must submit information to the respective committee(s) that controls the desired resources (initial resource review). Because requirements and costs can change as the proposal/protocol moves through the overall review process, resources are not committed until all review committees have reviewed and approved the final protocol (final resource review). As there are no federal regulations governing resource reviews, these reviews are not monitored by the OHRC. The PI may apply for resources from one or more of the following resource review committees on a study by study basis:
    - NIEHS Clinical Research Unit (CRU) Utilization Review: If a PI desires to use the NIEHS CRU, the PI must submit information explaining what services, staff, equipment and other resources are needed prior to, during, and after a subject's visit, as well as the anticipated budget. The CRU committee will determine if the CRU can handle the proposed research, if the resources can be allocated at the proposed time for the proposed duration, and how the cost burden will be distributed between the CRU and the PI. Refer to Appendix A for a high-level flow diagram of the review process. The primary contact for this committee is Stavros Garantziotis, M.D.
    - NIH Clinical Center (CC) Utilization Review: A PI has the option of using the facilities at the NIH CC in Bethesda, Maryland. The first step in the process is to use this committee to develop a protocol that covers what is necessary to run a study at the NIH CC. Upon approval by all applicable NIEHS committees, the proposal will be reviewed by the NIH Clinical Center Director as the final step of the review process. Upon approval by the NIH CC Director, the PI must work with the respective departments at the NIH CC to appropriately credential and train any personnel that will interact with subjects. Additionally, the PI bears the burden of coordinating support/logistics with the necessary primary and secondary support staff within the NIH CC (e.g., recruiting, MRI, x-ray, blood draw) as there is no centralized function that provides this coordination. Refer to Appendix A for a high-level diagram of the process to conduct studies at the NIH CC. The primary contact for developing a protocol to be run at the NIH CC is Fred Miller, M.D., Ph.D.
    - Clinical Support Contract Resource Review: If a PI desires to use the Clinical Support Contract with Constella/SRA to conduct research, the PI must submit an application explaining what services are requested from the contractor. If the request is within the scope of the contract and funds are available, the PI and the Contractor work together to develop the detailed plans (e.g., statement of work, budget) that will be reviewed by the committee. Refer to Appendix A for a high-level flow diagram of the review process. The primary contact for this committee is Mr. Michael Spencer.
- Scientific Review: All research must undergo biostatistical and scientific review, the extent of which is determined by the complexity of the study and the risk to human subjects. Refer to

Appendix A for a high-level flow diagram of the review process. The primary contact for this review is Bill Schrader, Ph.D., Deputy Scientific Director.

- Other Regulatory Reviews: In some situations, an organization outside of NIEHS may be responsible for providing a review. In these situations, the OHRC will work with the PI to facilitate the process and act as a central point of contact. Due to the lengthy time required to perform some of these reviews, it is recommended that the PI prepare and submit required materials as soon as possible and in parallel with internal reviews, wherever possible. The following reviews are conducted by organizations outside of NIEHS:
    - OMB Clearance Review: The Paperwork Reduction Act requires that collection of information from the public (e.g., surveys, questionnaires) be approved through the Office of Management and Budget (OMB) to reduce the burden on the public. NIH has developed the Project Clearance Branch (PCB) as the central point of contact for all information collection requests from NIH to the OMB. The OHRC shall act as a liaison between the PI and the PCB. Refer to the respective policies and procedures to determine if this review is applicable.
    - OMB Clinical Exemption Review: Collection of information from individuals undergoing treatment or examination for a clinical condition is designed in the interest of the public, and therefore, does not require OMB review and approval. However, NIH closely monitors these special cases and requires review by the NIH Clinical Exemption Review Committee (CERC) to approve such an exemption. The OHRC shall act as a liaison between the PI and the NIH CERC. Refer to the respective policies and procedures to determine if this review is applicable.
    - IRB Exemption Review: The NIH Office of Human Subjects Research (OHSR) determines if proposed research fits within one or more of the categories defined by the Code of Federal Regulations that are exempt from the requirements of the NIH Federal Wide Assurance (FWA), and therefore, from IRB review. Categories of exemption have been devised for research involving human subjects that involves little or no physical, social, or ethical risk. Only the OHSR is authorized to determine if a PIs research can receive this exemption. The OHRC shall act as a liaison between the PI and the OHSR. Refer to page 51 for steps to submit a request to obtain exemption from IRB review.
- IRB Review: All intramural research programs that conduct research involving human subjects or human specimens must undergo IRB review to ensure that the research protects the rights and safeguards the welfare of human research subjects. Refer to the *NIEHS IRB Reference Guide* for the policies and procedures that govern the IRB. The primary contacts for this review are the IRB Chair (David Resnick, J.D., Ph.D.) and the OHRC staff.

What Reviews Are Required for My Research?

While most studies require an investigator to go through all reviews, certain scenarios exist where a particular review is not required. The unique requirements of a study determine whether a review can be omitted. The table below shows some common scenarios and the corresponding reviews required. To

determine if a study not fitting one of the scenarios listed can skip a particular review, contact Joan Packenham, Ph.D. (OHRC Director) or the Clinical Director.

KEY
✓ = required
? = depends on the research being conducted
Blank cell = review not required

Standard Scenario[1]	**Preliminary Review**	**Resource Review**	**Scientific Review**	**NIEHS IRB Review**	**Outside IRB Review**
▪ Research involves human subjects ▪ Investigators are engaged at NIEHS and/or at other site(s) ▪ Additional funding and resources required	✓	✓	✓	✓	?
Common Alternate Scenarios[2]	**Preliminary Review**	**Resource Review**	**Scientific Review**	**NIEHS IRB Review**	**Outside IRB Review**
Alternate Scenario 1: ▪ Research involves human subjects ▪ Investigators are not engaged at NIEHS; only Investigators at other site(s) are engaged ▪ Additional funding and resources required	✓	✓	✓	?†	?
Alternate Scenario 2: ▪ Research is exempt from IRB Review* ▪ Research is above cost threshold (e.g., costs more than $100,000)‡ ▪ Additional funding and resources required	✓	✓	✓		
Alternate Scenario 3: ▪ Research is exempt from IRB Review* ▪ Research is below cost threshold (e.g., costs less than $20,000) ‡ ▪ Using own funds; no additional funding or resources required	? ‡				
Alternate Scenario 4: ▪ Research involves human subjects ▪ Investigators are engaged at NIEHS and/or at other site(s) ▪ Using own funds; no additional funding or resources required	✓		✓	✓	?

† Contact Office of Human Research Compliance (OHRC) or IRB Chair for guidance
‡ Contact the Clinical Director for guidance
* IRB exemption requires approval by the NIH Office of Human Subjects Research (OHSR)

[1] This list is intended to represent only the most common standard research scenarios. Other scenarios may exist.
[2] This list is intended to represent only the most common alternate research scenarios. Other scenarios may exist.

PRE-IRB POLICIES

POLICY NAME

Administering Preliminary Proposal Review

POLICY NUMBER

OHRC – 2008 – 0001

PURPOSE

This policy sets forth the requirements to prepare, conduct, and complete a preliminary proposal review by the Clinical Advisory Committee (CAC) for clinical research proposals involving human subjects. The goal of this policy is to 1) improve the quality of research proposals, and 2) provide investigators with the opportunity to receive feedback early in the review process from physician-scientists, epidemiologists, biostatisticians and IRB members.

SCOPE

This policy applies to all non-Epidemiology Branch (EB) investigators within the NIEHS Clinical Research Program. Refer to the *NIEHS Epidemiology Branch Reference Guide* for the preliminary proposal review policy followed by EB investigators.

ROLES INVOLVED

The following roles are involved with this policy:

- Principal Investigator
- CAC Facilitator
- Clinical Director
- OHRC Director
- IRB Representative
- Biostatistics Representative
- Subject Matter Expert(s)

POLICY

1. All non-EB investigators affiliated with the Clinical Research Program must present their studies to the Clinical Advisory Committee (CAC) before submitting to other review committees (e.g., scientific review, resource reviews, IRB review).

    1.1. A summary of the key discussion points, as well as the written feedback by reviewers shall be provided to the Investigator.

    1.2. Investigators are not required to respond to feedback/comments but are asked to consider the feedback/comments as they develop their study proposal.

    1.3. Investigators may present the same study at more than one meeting.

2. The CAC shall meet the 4th Tuesday of every month.

    2.1. Timing and frequency of review meetings shall be reviewed periodically to ensure the needs of the Program are met.

    2.2. The Chair has the discretion to schedule additional, out-of-cycle meetings to meet the needs of the Program.

    2.3. The meeting is scheduled to occur as planned, unless notification has been sent that states the meeting has been modified (e.g., location change, day/time change) or has been canceled.

    2.4. The CAC shall publish a meeting schedule that shows the date, time and location of the meeting. The schedule shall clearly indicate meetings that have been canceled.

3. Attendance

    3.1. The following CAC members are required to be in attendance when a study is presented for that study to be considered ratified: CAC Chair; CAC Facilitator; OHRC Director or designee representing human subjects protections; Biostatistical Representative; at least three (3) additional CAC members; at a minimum, one Subject Matter Expert (SME); and, the primary reviewers of the study. (Note: the SME and primary reviewers can be included in the three additional Committee members required to be in attendance)

        3.1.1. Excused absence: Required attendees are responsible for finding suitable replacements for their particular role in the event that a scheduling conflict arises and for notifying the Facilitator of the change. In the event a suitable replacement cannot be found, the Facilitator has the option of rescheduling the meeting or postponing the meeting to the next regularly scheduled date.

        3.1.2. Leaving early or coming late: Required attendees are responsible for notifying the CAC Chair at least 24 hours prior to the meeting if they cannot attend for the entire meeting and a replacement cannot be found.

        3.1.3. Emergency leave: In the event that a required CAC member must leave the meeting during the presentation, the CAC Chair will determine whether the presentation may continue or if the meeting needs to be adjourned and the proposal brought back to the Committee. The CAC Chair will determine whether remaining presentations scheduled for that meeting will continue or not.

    3.2. It is expected that all CAC Committee members will attend the scheduled meetings.

4. Conflict of Interest

    4.1. CAC members will not be assigned as reviewers for studies in which they are involved; however, they may participate in the meeting.

4.2. An Acting CAC Chair will be appointed by the Facilitator for a preliminary review of a protocol that the CAC Chair is involved in as a Principal Investigator

5. Documentation

5.1. The Facilitator will document the meeting date that a proposal was presented and store for validation purposes.

5.2. The Facilitator or designee will document for each presentation the key discussion points, which shall be retained, along with a copy of the feedback from the reviewers, for a minimum of three (3) years.

5.3. The Facilitator will provide copy of key discussion points and primary reviewer feedback document to the presenting investigator

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- CAC-CRP-1: Preparing for Preliminary Proposal Review (Investigator)
- CAC-CRP-2: Preparing for Preliminary Proposal Review (Clinical Advisory Committee)
- CAC-CRP-3: Conducting the Preliminary Proposal Review
- CAC-CRP-4: Completing the Preliminary Proposal Review

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0001		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

POLICY NAME

Administering NIEHS Clinical Research Unit (CRU) Utilization Review

POLICY NUMBER

OHRC–08–0401

PURPOSE

This policy defines how NIEHS shall review requests to utilize the CRU facility, resources, and/or staff.

SCOPE

This policy applies to anyone who wishes to utilize the NIEHS CRU facility, resources and/or staff.

POLICY

1. All requests to utilize the NIEHS CRU facility, resources, and/or staff shall be reviewed by a committee.

    1.1. Members of the NIEHS CRU Utilization Committee include the CRU Medical Director (Committee Chair), Senior Research Coordinator, and CRU Administrator.

    1.2. Conflict of Interest - If the Chair of the NIEHS CRU Utilization Committee is the Principal Investigator on a study that has submitted a request to utilize the CRU, the Chair must find a suitable replacement to perform the Chair's role.

    1.3. Submitted documents that are changed subsequent to review by the CRU Utilization Committee, especially as the result of review by other committees in the overall review process, must be submitted to the CRU Chair and will be re-reviewed by the CRU Utilization Committee.

2. The Chair will forward Committee recommendations to the Clinical Director for final approval.

    2.1. Conflict of Interest – The Clinical Director must find a suitable replacement to make the final decision on approval/disapproval if he/she is the Principal Investigator on a request to utilize the CRU.

    2.2. Approvals for studies that have not passed scientific review are considered provisional and are not final. Obligation of resources shall not occur until *final* approved study documents are presented to the CRU Utilization Committee.

3. The committee will meet *ad hoc* to review requests.

    3.1. Timing and frequency of review meetings shall be reviewed periodically to ensure the needs of the Program are met.

    3.2. Review meetings must be attended by a quorum of Committee members either in person or remotely by teleconference or videoconference.

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- RR-CRU-1: NIEHS CRU Utilization Review (Investigator)
- RR-CRU-2: NIEHS CRU Utilization Review (Committee)

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0401		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

POLICY NAME

Administering NIH Clinical Center (CC) Utilization Review

POLICY NUMBER

OHRC–08–0450

PURPOSE

Protocols to be conducted at the NIH CC require a sufficient level of maturation and detail to pass the NIH Clinical Center Director's review and to run smoothly at the NIH CC. To facilitate the protocol development process and reduce overall delays in the protocol approval process, this Committee has been established to work with investigators early in the process to assist them with proposal-specific issues pertinent to the NIH CC environment. This policy defines how NIEHS shall review requests to conduct a clinical study at the NIH CC.

SCOPE

This policy applies to investigators in the NIEHS Clinical Research Program who wish to conduct a study at the NIH CC.

GUIDANCE

This policy establishes a committee to review the purpose and design of protocols that are intended to be conducted at the NIH CC. Approval by this committee does not grant approval to begin performing the study at the NIH CC; however, review by this committee ensures the best chance of the protocol being approved by the NIH CC Director. Review by the NIH CC Director occurs when documents are submitted to the Office of Protocol Services.

POLICY

1. Any investigator planning to conduct a study at the NIH CC must have their protocol approved by the NIH CC Utilization Review Committee Chair.
2. Outcomes from the reviews performed by the Chair shall be forwarded to the Clinical Director for final approval.
3. Approvals for studies that have not passed scientific review are considered provisional and are not final. Documents changed as the result of review by other committees in the overall review process must be submitted to the Committee Chair for re-review.

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- RR-NIHCC-1: Conducting NIH CC Utilization Review

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0450		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

POLICY NAME

Administering Clinical Support Contract Resource Review

POLICY NUMBER

OHRC–08–0501

PURPOSE

This policy defines how NIEHS shall review requests to utilize resources through the Clinical Support Contract with Constella/SRA.

SCOPE

This policy applies to anyone who wishes to utilize resources through the Clinical Support Contract with Constella/SRA.

ROLES INVOLVED

The following roles are involved with this policy:

- Principal Investigator
- Clinical Support Contract Review Committee
- Clinical Director

POLICY

1. All requests to utilize resources through the Clinical Support Contract with Constella/SRA shall be reviewed by a committee led by the Clinical Support Contract Review Committee Chair.

    1.1. Members of the Clinical Support Contract Review Committee include the Project Officer for the contract (Committee Chair), the Alternate Project Officer, and the Medical Director of the NIEHS CRU,

    1.2. The Chair determines at time of submission whether to appoint members *ad hoc* to contribute to the review of a request, and determines the members' voting status (i.e., voting or non-voting).

2. The committee will meet on an *ad hoc* basis to review requests.

    2.1. Timing and frequency of review meetings shall be reviewed periodically to ensure the needs of the Program are met.

    2.2. Review meetings must be attended by all Committee members, including *ad hoc* members, either in person or remotely by teleconference, videoconference or electronic mail correspondence.

    2.3. Committee approval is by unanimous decision only.

3. Outcomes from the reviews performed by the Clinical Support Contract Review Committee shall be forwarded to the Clinical Director for final approval.

    3.1. The Clinical Director must find a suitable replacement to make the final decision on approval/disapproval if he/she is the Principal Investigator on the proposal to use the Clinical Support Contract.

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- RR-CSC-1: Conducting a Clinical Contract Resource Review

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0501		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

POLICY NAME

Conducting Scientific Review

POLICY NUMBER

OHRC–08–0101

PURPOSE

This policy defines how the Scientific Review Committee (SRC) shall conduct a scientific review of research involving human subjects. The goal of this policy is to ensure all research receives a rigorous scientific evaluation and only the highest quality research goes forward. The Scientific Review must precede IRB Review, but can be concurrent with resource reviews including CRU Utilization Review, NIH CC Utilization Review, and Clinical Support Contract Resource Review. For non-EB investigators, Scientific Review must be preceded by Preliminary Proposal Review.

This policy has been developed to be consistent with the guidelines and regulations defined in *The Standards for Clinical Research within the NIH Intramural Research Program, The Guidelines for the Conduct of Research in the Intramural Research Program at NIH,* and the Code of Federal Regulations, as well as with the best practices being used in other NIH ICs.

SCOPE

This policy applies to all non-EB investigators affiliated with the NIEHS Clinical Research Program who wish to conduct clinical research. Refer to the *NIEHS Epidemiology Branch Reference Guide* for the scientific review policy followed by EB investigators.

ROLES INVOLVED

The following roles are involved with this policy:

- Principal Investigator
- SRC Chair
- Scientific Reviewers
- Biostatistics Reviewer(s)

POLICY

1. All non-EB investigators must submit their research for scientific review.

    1.1. Scientific review is required for all new studies (i.e., submission of an initial review application for IRB review),

    1.2. Scientific review is required for all amendments to continuing studies that substantively change the level of risk and/or the complexity of the study. The requirement for scientific review for amendments to continuing studies will be determined by the OHRC Director in consultation with the Clinical Director and IRB Chair.

    1.3. All studies must be reviewed by a biostatistician in addition to being reviewed by experts in the field of study.

2. Investigators will abide by NIH policies to resolve any real or perceived potential conflicts of interest that may arise during the review process.

    2.1. Investigators affiliated in any way with a study cannot be involved with the review or approval of that study.

    2.2. The Clinical Director, Scientific Director, and Institute Director must find suitable replacements to fulfill their respective roles when studies with which they are associated are presented for review and approval.

3. The SRC Chair shall determine the review path/method of review based upon the complexity of the research and the risk to human subjects as defined by OHSR Information Sheet 3 (derived from 45CFR46.102(i)).

    3.1. SRC Chair will involve the Clinical Director, the OHRC Director, and/or the IRB Chair, as necessary, to make the appropriate determination of the review path.

    3.2. Low complexity/minimal risk to human subjects:

        3.2.1. All research documents shall be sent for review and comment to at least one (1) biostatistician and one (1) or two (2) subject matter experts not affiliated with the study.

        3.2.2. In the event that feedback is mixed, the SRC Chair has the option of setting up a teleconference to reach consensus and/or to send the research proposal to additional reviewers.

    3.3. Low complexity/more than minimal risk to human subjects

        3.3.1. All research documents shall be sent for review and comment to at least one (1) biostatistician and two (2) or three (3) subject matter experts not affiliated with the study.

        3.3.2. In the event that feedback is mixed, the SRC Chair has the option of setting up a teleconference to reach consensus and/or to send the research proposal to additional reviewers.

    3.4. High complexity/more than minimal risk to human subjects

        3.4.1. All research documents shall be sent for review and comment to at least one (1) or two (2) biostatisticians and four (4) to six (6) subject matter experts not affiliated with the study.

        3.4.2. In the event that feedback is mixed, the SRC Chair has the option of setting up a teleconference to reach consensus and/or to send the research proposal to additional reviewers.

        3.4.3. For studies using this classification, the SRC Chair, in lieu of waiting for individual feedback, has the discretion to set up a teleconference or convene a review panel to discuss the research proposals. In such circumstances, reviewers shall have a minimum of five (5) business days to review the documentation before the call/meeting.

4. Possible outcomes of the scientific review

    4.1. Approved - Proposals receiving this outcome have passed scientific review and are able to move to the next phase in the overall clinical research approval process.

    4.2. Provisionally Approved - Proposals receiving this outcome have a scientifically sound proposal; however, some issues/details need to be resolved before the committee can determine if the proposal should be approved. Remediation of the issues is required before the proposal can be approved to move to the next phase in the overall clinical research approval process.

    4.3. Tabled – Proposals receiving this outcome have been deemed not scientifically sound and require considerable rework, after which the proposal may be resubmitted for consideration as a *de novo* proposal.

    4.4. Rejected – Proposals receiving this outcome have been refused and may not be resubmitted.

5. Approval

    5.1. Only the Clinical Director, or designee by the Clinical Director, may approve the scientific review.

    5.2. Acceptance of investigators' responses to stipulations, if any, must occur before approval can be granted.

    5.3. A proposal may be submitted up to a total of three (3) times to receive approval; if the proposal cannot be approved after the third submission, it is automatically rejected.

6. Documentation

    6.1. Records of scientific review shall be retained for 3 years after the research has terminated.

    6.2. Documentation will be maintained by the SRC Chair.

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- SR-CRP-1: Conducting a Scientific Review
- SR-CRP-3: Conducting a Scientific Review Due to Amendment

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0101		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

POLICY NAME

Collecting Information from the Public

POLICY NUMBER

OHRC–08–0201

PURPOSE

This policy establishes the rules governing the process of collecting information from the public.

SCOPE

This policy applies to all investigators affiliated with the NIEHS Clinical Research Program (CRP)

ROLES INVOLVED

The following roles are involved with this policy:

- Principal Investigator
- OHRC Staff
- NIH Project Clearance Officer

POLICY

1. The CRP shall follow the policies and procedures established in NIH Policy Manual Chapter 1825 to govern collection of information from the public, and which states the following:

    1.1. Federal law "provides that a Federal agency shall not collect or sponsor a collection of information on identical items from 10 or more public respondents without: (1) obtaining approval from the Office of Management and Budget (OMB) for the data collection plans and instruments and for the information requirements in regulations; and (2) displaying a currently valid OMB control number and expiration date."

    1.2. All requests for OMB approval of data collection plans must be submitted to the NIH Project Clearance Officer, now part of the Project Clearance Branch (PCB), the National Institutes of Health's (NIH) control point for the Office of Management and Budget (OMB) clearance functions concerning public information collection activities. Information collection activities include forms such as the PHS 398, regulations, survey interviews, customer satisfaction surveys, web site questionnaires and epidemiology research.

    1.3. A special case exists for a clinical exemption from OMB review and approval; specifically, "The OMB definition of 'information' at 5 CFR 1320.7(j) (5) generally excludes facts and opinions obtained from individuals under treatment or clinical examination. Therefore, collections of information from such individuals do not require OMB review and approval. However, they do require approval from the NIH Clinical Exemption Review Committee" (CERC).

2. All requests for OMB clearance (1.2) or clinical exemption (1.3) shall be processed through the OHRC, which in turn shall work with the NIH PCB and the CERC to obtain the appropriate approval.

    2.1. For answers to common questions pertaining to the topic of clinical exemption, refer to the frequently asked questions section of the PCB website:

    http://odoerdb2-1.od.nih.gov/oer/policies/project_clearance/pcb.htm

    http://odoerdb2-1.od.nih.gov/oer/policies/project_clearance/faq_clinical_exemption.htm

SUPPORTING PROCEDURES

The following SOPs have been created to provide guidance and ensure adherence to this policy:

- OMB-CRP-1: Obtaining OMB Approval
- OMB-CRP-2: Obtaining Clinical Exemption from OMB Review

EFFECTIVE DATE

November 1, 2008

Policy Number	OHRC – 2008 – 0201		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

STANDARD OPERATING PROCEDURES

Preparing for Preliminary Proposal Review (Investigator)

Standard Operating Procedure

POLICY SUPPORTED

This SOP supports the following policy:

- OHRC–08–0001: Administering preliminary proposal review

For more information about this policy, refer to page 8.

DESCRIPTION

This SOP describes the materials that a Principal Investigator (PI) must prepare to present to the Clinical Advisory Committee (CAC), as well as the steps a PI must take to present at a scheduled meeting.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- OHRC Staff
- CAC Facilitator

PROCEDURAL STEPS

Guidance

It is strongly recommended that PIs plan for their presentation well in advance of the scheduled review day. PIs who have submitted ***completed*** materials by the submission deadline will be scheduled for the next available meeting; PIs who provide submission materials after the submission deadline, but before the meeting day, will have their presentations assigned to a future scheduled meeting. PIs who submit incomplete materials will not be scheduled.

The PI may make a presentation on the same concept/protocol at more than one CAC meeting, if needed. PIs are encouraged to present at multiple meetings as a concept matures into the final proposal.

Steps

1. PI notifies the OHRC of intent to present by the notification deadline. A list of scheduled meetings with notification and submission deadlines is posted on the OHRC website http://www.niehs.nih.gov/about/orgstructure/boards/irb/index.cfm. To present at a scheduled meeting, the PI must notify the OHRC of the intent to present *at least four (4) weeks in advance* of a meeting date (i.e., the notification deadline) by sending an e-mail message to NIEHS-OfficeofHRC@niehs.nih.gov. The OHRC shall record the PIs request as tentative. When the

OHRC confirms that a PI has submitted all required materials, the PI will be notified of the presentation schedule.

NOTE: The CAC Facilitator has the discretion to cancel any meetings for which no requests have been received by the notification deadline.

2. PI prepares materials for review. The PI must submit the following for review by the CAC:

   - CAC Review Checklist: Located on the OHRC website, this form indicates what the PI is submitting for review. The checklist also contains a section where the PI can recommend specific reviewers to be a part of the CAC review (PI must provide contact information if suggested reviewer is not at NIEHS).
   - Scientific Review Form, Part I – Study Overview: Located on the OHRC website, this form describes attributes of the study, including study description, study design, planned study sites and key study personnel.
   - Study Summary PowerPoint presentation: All presentations must contain the following mandatory sections: history/background; study rationale; study hypothesis; study aims; study design; primary and secondary outcomes; PI assessment of participant risk. PIs should plan presentations that are 15-20 minutes in length.
   - Study abstract or protocol (optional, only if developed)
   - Anticipated budget and resource requirements

3. PI submits all review materials to the OHRC by the submission deadline. The PI must send all items listed in Step 2 to OHRC *at least 3 weeks prior* to a scheduled meeting. Materials should be emailed to NIEHS-OfficeofHRC@niehs.nih.gov. Materials will be reviewed for completeness by OHRC staff.

4. PI receives notification of presentation date. As soon as the OHRC confirms receipt of a completed submission package, the OHRC shall provide the PI with the date that the presentation has been scheduled and the approximate time to present. The PI is encouraged to attend for the entire meeting, but is expected to arrive 15 minutes before his/her estimated start time.

5. Contact OHRC regarding modifications to presentation. – The PI should not present materials that are substantially different than what was submitted by the submission deadline. Minor modifications to presentation materials will be accepted up to two (2) business days prior to the meeting date. If the PI makes substantive changes to submission materials, the presentation may be rescheduled to the next scheduled meeting date at the discretion of the Facilitator. The PI should contact the OHRC if substantive changes are required to determine the impact of the changes.

CONCLUSION

Once the completed materials have been submitted and the OHRC has scheduled the date of the presentation, the PI is not required to do anything until the day of the meeting. See 'Conducting the Preliminary Proposal Review' for the next steps.

EFFECTIVE DATE

November 1, 2008

SOP Number	CAC_CRP_1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Preparing for Preliminary Proposal Review (Clinical Advisory Committee)

Standard Operating Procedure

POLICY SUPPORTED

This SOP supports the following policy:

- OHRC–08–0001: Administering preliminary proposal review

For more information about this policy, refer to page 8.

DESCRIPTION

This SOP describes how members of the Committee process a PI's request to present at a meeting.

ROLES INVOLVED

The following are involved with this SOP:

- OHRC Staff
- CAC Facilitator
- CAC Members
- CAC Guest Members

PROCEDURAL STEPS

1. The OHRC reviews the PI's request to present at a meeting. Upon receipt of a request, the OHRC shall:

    A. Tentatively schedule the PI to the next scheduled meeting for which the notification deadline has not passed.

    B. Determine if the PI has asked for specific reviewers to be present at the CAC meeting. If the PI has requested specific reviewers, the OHRC shall notify the CAC Facilitator who will make a decision regarding their involvement. If approved, the OHRC shall determine if the reviewers can attend at the scheduled day/time. The OHRC shall update the PI about their request. In the event that a requested reviewer cannot attend the desired meeting, the OHRC shall determine how the PI wants to proceed.

    C. Four (4) weeks prior to a meeting day for which no requests to present have been received, the OHRC shall notify the CAC Facilitator, who shall determine whether to exercise the option to cancel a meeting; the CAC Facilitator shall notify the CAC members and the OHRC shall update the schedule accordingly.

2. The OHRC verifies all required items have been submitted. The OHRC shall check the submission to verify that all required items have been submitted. If all items are submitted, the OHRC shall forward

to the CAC Facilitator for review; otherwise, the PI is notified of the incomplete submission and items that are missing.

3. Facilitator reviews all materials submitted. Upon receipt of submission materials from OHRC, the Facilitator shall review materials for completeness and understanding.

    A. If materials are complete and understood, the Facilitator notifies OHRC to schedule the PI for the next planned meeting for which the submission deadline has not passed; then, continue to step 4.

    B. If materials are not complete or are not understandable, the Facilitator shall work with the PI until they are complete and understood. If, by the submission deadline, the materials are still not complete or understandable, the Facilitator shall determine if the presentation must be postponed to the next scheduled meeting.

        i. In the event that the Facilitator hasn't received completed materials for *any* scheduled presentations by the submission deadline, the Facilitator has the discretion to cancel the meeting and postpone all scheduled presentations to the next scheduled meeting. The Facilitator shall notify the PI and all CAC members, and update the meeting schedule accordingly.

4. Facilitator identifies two CAC members to be primary reviewers for each presentation. At least one of the primary reviewers should be a subject matter expert.

5. Facilitator forwards submitted materials to all CAC members and guest reviewers (if applicable) for review. The following shall occur when the CAC Facilitator forwards the submitted materials:

    A. All CAC members and guest reviewers review the materials to familiarize themselves with the content.

    B. CAC members who have been identified as primary reviewers shall review the materials and complete the CAC Reviewer Feedback form.

6. OHRC notifies PI and guest reviewers. The OHRC performs the following:

    A. Develops the meeting agenda and distributes to the Committee members

    B. Sends PIs confirmation of the day and time they are scheduled to present.

    C. Sends guest reviewers confirmation of the day and time of the presentation associated with the PI who requested their attendance.

7. OHRC finalizes meeting preparation. The OHRC performs the following prior to the meeting:

    A. Ensures the files for the scheduled presentation are loaded on to the computer.

B. Ensures the following is disseminated to any members who have to participate remotely:

i. Adobe Connect link or PowerPoint file is sent via e-mail

ii. Dial-in number is sent via e-mail, if applicable

CONCLUSION

Once the presentations have been scheduled and all CAC members have pre-reviewed the submission materials, no further steps are required until the day of the meeting. See 'Conducting the Preliminary Proposal Review' for the next steps.

EFFECTIVE DATE

November 1, 2008

SOP Number	CAC_CRP_2		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Conducting the Preliminary Proposal Review

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0001: Administering preliminary proposal review

For more information about this policy, refer to page 8.

DESCRIPTION

This SOP describes how to conduct a preliminary review from start to finish.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- CAC Members/Primary Reviewers
- Guest Reviewers
- CAC Facilitator
- CAC Chair

PROCEDURE

1. OHRC ensures remote users are connected. If nobody has to attend remotely, skip to step 2; otherwise, the OHRC ensures the following:

    A. The phone line is connected to the conference line and the phone is set to speakerphone.

    B. Remote users are on the line and told to mute their phones when not participating in the discussion.

    C. The Adobe Connect session is started so that presentations can be viewed remotely. Alternatively, PowerPoint presentations can be sent to remote participants in advance of the meeting so that they can follow along with the presentation.

2. Chair calls the meeting to order and calls a scheduled presenter.

3. PI presents. During the interactive presentation:

    A. The PI opens the pre-loaded presentation and runs through the presentation so that the majority of the meeting time can be spent on content/issues. The expectation is that PIs will spend no more than 15-20 minutes on their presentation. The presentation must include information on the following: history/background, study rationale, study hypothesis, study aims, study design, primary and secondary outcomes, and PI assessment of participant risk

B. Committee members ask questions and/or provide feedback.

C. Primary reviewers update pre-written feedback to reflect discussion.

D. The Facilitator (or a designee identified prior to the meeting), captures key points.

E. The Facilitator monitors presentation time and flow to keep the meeting on schedule

4. Chair calls presentation to a close. The Chair shall determine when it is appropriate to wrap up questions/feedback and end the presentation. Ending the presentation involves the following:

   A. Presenter closes any files and leaves the presentation area.

   B. Primary Reviewers determine if their pre-written feedback is sufficient to give to the PI. If not, the Primary Reviewers update the feedback and give to the PI within two business days.

   C. Facilitator captures which Primary Reviewers need additional time to update the feedback.

5. Chair calls next presenter. If other presentations are scheduled, repeat steps one through three until all scheduled presentations have completed; otherwise, continue to the next step.

6. Chair calls meeting to a close. Once the meeting is closed, the following occurs:

   A. Services for remote users are ended (i.e., phone is hung up, Adobe Connect session is closed)

   B. The presentations from the completed review are deleted from the machine.

CONCLUSION

After the Preliminary Proposal Review meeting is conducted, a few post-meeting activities must be carried out. See 'Completing the Preliminary Proposal Review' for more information.

EFFECTIVE DATE

November 1, 2008

SOP Number	CAC_CRP_3		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Completing the Preliminary Proposal Review

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0001: Administering preliminary proposal review

For more information about this policy, refer to page 8.

DESCRIPTION

This SOP describes post-meeting activities that are needed to complete the Clinical Advisory Committee (CAC) review.

ROLES INVOLVED

The following are involved with this SOP:

- OHRC
- CAC Facilitator
- Primary Reviewers

PROCEDURE

The following steps should be performed:

1. Facilitator completes the CAC Review Summary form and forwards to the OHRC, highlighting any studies that need to be rescheduled because minimum requirements had not been met.

2. Facilitator sends key points from the meeting to the PI within 2 business days of the meeting.

3. Primary Reviewers who need additional time after the meeting to update their feedback send the updated CAC Reviewer Feedback form to the PI, copying the Facilitator and the OHRC, within 2 business days of the meeting.

EFFECTIVE DATE

November 1, 2008

SOP Number	CAC_CRP_4		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

NIEHS CRU Utilization Review (Investigator)

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0201: Administering NIEHS Clinical Research Unit (CRU) Utilization Review

For more information about this policy, refer to page 11.

DESCRIPTION

This SOP describes how a PI submits a request to utilize the NIEHS CRU facility, resources, and/or staff.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- CRU Utilization Committee Chair

PROCEDURE

1. PI submits required materials. The PI submits the following forms to the CRU Utilization Committee Chair Dr. Stavros Garantziotis at the following email address: garantziotis@niehs.nih.gov
   - Scientific Review Form , Part 1 – Study Overview
   - CRU Review Form, Part 2 – Utilization Details

2. PI responds to questions from CRU Chair. After reviewing the utilization form, the CRU Chair may require additional information to appropriately review the proposal. The CRU Chair communicates directly with the PI to obtain this information.

3. CRU Committee Chair communicates form to other Committee members and arranges for *ad hoc* meeting.

4. PI receives decision. The PI shall receive one of the following outcomes:

   A. Approved: The request has been approved as submitted. If there are any changes in the request, the PI must resubmit for approval. Refer to the policy for information regarding the obligation of resources and/or changes to documents after the request has been reviewed.

   B. Conditionally Approved: Typically used when the cost burden must be shared between the PI and the CRU, this outcome shall state the conditions that need to be accepted by the PI for the request to be approved. The PI may propose alternatives to the Clinical Director to satisfy the

conditions. Refer to the policy for information regarding the obligation of resources and/or changes to documents after the request has been reviewed.

C. Rejected: The request has not been approved as submitted.

CONCLUSION

Upon receiving the outcome of the request, the PI determines how to continue through the overall clinical review process. The PI is encouraged to contact the Committee Chair to determine the impact of changes that occur to the study from other review committees. The PI must submit all final study documents to the Committee Chair at the conclusion of the overall review process (i.e., IRB review for most studies or scientific review for IRB-exempt studies). The committee will perform a final resource review if any documents have changed since the initial review and will notify the PI of the impact to the resources requested.

Upon receiving all necessary approvals, the PI should ensure that all staff are appropriately trained and credentialed. For more information about training and credentialing at the CRU, contact: Mr. Michael Spencer; 919-541-1168; spencermi@niehs.nih.gov.

EFFECTIVE DATE

November 1, 2008

SOP Number	RR_CRU_1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

NIEHS CRU Utilization Review (Committee)

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0201: Administering NIEHS Clinical Research Unit (CRU) Utilization Review

For more information about this policy, refer to page 11.

DESCRIPTION

This SOP describes how to process a request to utilize the NIEHS CRU facility, resources, and/or staff.

ROLES INVOLVED

The following are involved with this SOP:

- CRU Chair
- CRU Committee
- Clinical Director

PROCEDURE

1. CRU Chair reviews incoming requests. The CRU Chair reviews the submitted documents for completeness and understanding.

2. CRU Chair contacts the PI. Upon reviewing the incoming requests, the CRU Chair shall contact the PI to:

   - Get more details, if needed
   - Notify the PI that the request is undergoing review (if all necessary information is available)
   - Notify the PI that the CRU cannot handle the request as submitted. If modifications to the request cannot be made, then the request shall be disapproved.

3. CRU Chair forwards submitted documents to Committee members for review.

4. CRU Committee convenes to discuss the proposal and determine the outcome. Following the meeting, the CRU Chair completes CRU Review Form, Part 3 – Review History. If the outcome can be determined (i.e., the CRU is appropriate, the CRU is not appropriate), proceed to the next step; otherwise, repeat steps 2 through 4 until an outcome can be determined, documenting all reviews that occur.

5. CRU Chair documents the outcome. The CRU Chair completes the following forms:

    - CRU Review Form, Part 4 – Chairperson Initial Review Summary
    - CRU Review Form, Part 5 – Initial Review Outcome

6. CRU Chair forwards recommendation to Clinical Director for review. The CRU Chair submits all completed CRU Review forms (Parts 2, 3, 4, and 5) to the Clinical Director approval.

7. Clinical Director documents decision and returns it to the CRU Chair. Upon making a decision, the Clinical Director completes CRU Review form, Part 6 – NIEHS Clinical Director Initial Review Decision. The Clinical Director sends the packet to the CRU Chair.

8. CRU Chair notifies PI of decision.

CONCLUSION

Upon receiving the outcome of the request, the PI continues through the overall clinical review process. At the conclusion of the overall review process, the PI must submit final documents to the Committee Chair. If no changes have occurred since the initial review or changes do not impact the resource request, perform steps 5-8 using the final review versions of the forms explaining the status in the comments fields. If changes have occurred that have an impact on the resource request, perform steps 3 – 8, using the final review forms for steps 5 – 8.

EFFECTIVE DATE

November 1, 2008

SOP Number	RR_CRU_2		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Conducting NIH CC Utilization Review

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0450: Administering NIH Clinical Center (CC) Utilization Review

For more information about this policy, refer to page 13.

DESCRIPTION

This SOP describes the steps involved in approving a protocol to be conducted at the NIH CC.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- NIH CC Utilization Review Committee Chair
- Clinical Director

GUIDANCE

Approval by this committee is not an approval to use the NIH CC facility; rather, this committee helps the PI to develop a protocol that covers what is necessary to run a study at the NIH CC. Upon approval by all applicable NIEHS committees, the proposal will be reviewed by the NIH Clinical Center Director as the final step of the review process. Upon approval by the NIH CC Director, the PI must work with the respective departments at the CC to appropriately credential and train any personnel that will interact with research subjects. Additionally, the PI bears the burden of coordinating support/logistics with the necessary primary and secondary support staff within the NIH CC (e.g., recruiting, MRI, x-ray, blood draw) as there is no centralized function that provides this coordination. Refer to Appendix A for a high-level diagram of the process to conduct studies at the NIH CC.

PROCEDURE

1. PI submits required materials to the NIH CC Utilization Review Chair. As soon as possible after the PI incorporates feedback from the CAC review, the PI submits materials to Fred Miller, M.D., Ph.D. The following materials should be sent to MILLERF@mail.nih.gov:

   - Scientific Review Form , Part 1 – Study Overview
   - Study Abstract or Protocol

2. NIH CC Utilization Review Chair reviews incoming submissions. The Chair reviews the submission and contacts the PI to discuss details/plans for the study. The Chair provides feedback to the PI based upon what was received and works with the PI to improve the protocol, if necessary

3. PI incorporates feedback and submits revised materials, if necessary.

4. NIH CC Utilization Review Chair documents review outcome and forwards to the NIEHS Clinical Director. The Chair completes the NIH CC Review – Chair Summary form and submits to the Clinical Director.

5. Clinical Director documents decision and returns packet to the NIH CC Utilization Review Chair. The Chair completes the NIH CC Review – Clinical Director Decision form and returns it to the NIH CC Utilization Chair.

6. NIH CC Utilization Review Chair notifies PI.

   NOTE: While not part of the NIH CC Utilization Review Committee process, the PI, if using an IND/IDE as part of the study, should contact the FDA at the time of scientific review to have a pre-IND consult and/or to begin the IND approval process.

   NOTE: While not part of the NIH CC Utilization Review Committee process, the PI should begin searching for, credentialing, and scheduling training for study personnel during this step, as the credentialing process can take several months to complete. Contact the Office of Credentialing Services (301-496-5937) to begin the process. Soon after staffing has been finalized, the PI should begin contacting the applicable departments/collaborators (e.g., Patient Recruitment Public Liaison, pulmonary team, CC Pharmacy) and assessment staff (e.g., x-ray, MRI) in the CC to work through logistical issues. Upon completion of credentialing all staff members and coordination with all applicable departments, the PI can begin recruiting/enrolling subjects.

CONCLUSION

Upon receiving the outcome of the request, the PI determines how to continue through the overall clinical review process. The PI is encouraged to contact the Committee Chair to determine the impact of changes that occur to the study from other review committees. The PI must submit all final study documents to the Committee Chair at the conclusion of the overall review. The Committee Chair will perform a final resource review by performing steps 4-6, using the final review versions of the forms..

EFFECTIVE DATE

November 1, 2008

SOP Number	RR_NIHCC_1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Conducting a Clinical Support Contract Resource Review

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0501: Administering Clinical Support Contract Resource Review

For more information about this policy, refer to page 15.

DESCRIPTION

This SOP describes the steps involved to approve a request to utilize resources through the Clinical Support Contract with Constella/SRA.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- Clinical Support Contract Review Committee
- Clinical Director

PROCEDURE

1. PI/Task Leader completes the Work Assignment (WA) form. There are three types of requests that PIs can make to obtain resources through the Clinical Support Contract. The three types of requests are:

    - Type I: Submit this type of work assignment when resources are needed to help develop a protocol as it matures from a concept until it is approved by an IRB.
    - Type IIA: Submit this type of work assignment when resources are needed to implement a study that has already received approval by an IRB.
    - Type IIB: Submit this type of work assignment when resources are needed for study implementation, but the study has not yet received IRB approval, and the Clinical Support Contract will not be used to help obtain IRB approval.

    The PI completes the Clinical Support Services Contract Work Assignment form and submits it, along with proof of CAC Review to the Committee's primary contact, Mr. Michael Spencer at spencermi@niehs.nih.gov.

2. Committee records receipt of WA form. The primary contact logs details about the request, verifies that CAC review has occurred, and reviews the request for completeness/adequacy. If CAC review

has not occurred or the request lacks sufficient details, the request is returned to the PI; otherwise proceed to the next step.

3. Committee reviews the request. For requests that are complete, the primary contact forwards the request all submitted documents to the full committee and schedules an *ad hoc* meeting to assure the following:

    - The request meets the scope of the contract (by definition, Type I work assignments are within the scope).
    - Enough detail exists for the contractor to respond appropriately.
    - Funds are available in the contract based upon the government's best estimate of cost.

    If the conditions in step 3 are not met, the primary contact notifies the PI and/or works with the PI to assure that the requirements are met before proceeding to the next steps.

4. Committee Chair documents outcome of the preliminary review. Committee Chair completes the Clinical Support Contract Review – Initial Review Outcome form.

5. Contractor and PI/Task Leader submit detailed plans. If approved after preliminary review, the primary contact forwards the work assignment to the contractor and copies the PI /Task Leader. Together, they will develop a full budgetary and technical plan that is submitted to the primary contact.

6. Committee reviews detailed plans and documents outcome. The primary contact forwards the plans to the entire committee and schedules a meeting to perform a full technical and budgetary/business review. Following the meeting, the Committee Chair completes the Clinical Support Contract Review – Final Review Outcome form. If the committee votes either approved or disapproved, proceed to step 9; otherwise, proceed to step 7.

7. Contractor and PI/Task Leader respond to issues. When the committee votes that further clarifications are necessary, the primary contact will forward to the contractor and PI/Task Leader a list of issues that need to be addressed. The contractor/PI/Task Leader should address each issue in a point-by-point fashion and return to the committee for re-review.

8. Committee reviews responses. The committee will review the responses and vote. Following the review, the Committee Chair updates the Final Review Outcome form. If the committee votes either approved or disapproved, proceed to step 9; otherwise, repeat steps 7-8 until a vote of approved or disapproved can be reached.

9. Committee forwards recommendation to the Clinical Director. The Chair puts together a package of all documents (i.e., technical and budgetary plans, committee reports, responses to committee requests) including the Preliminary Review Outcome and Final Review Outcome forms, writes a cover memo documenting the committee's recommendation, and forwards to the Clinical Director.

10. Clinical Director documents outcome of the request. The Clinical Director completes the Clinical Support Contract Review – Clinical Director Decision form and returns the packet to the Committee Chair.

11. The primary contact notifies the PI of the outcome. The primary contact prepares an electronic PDF of the entire package, and sends to the contract Project Officer. If the request is approved, the contract Project Officer and the Contracting Officer sign the final version of the Contractor Response to Initial Work Assignment form. Once the Contracting Officer approves, the primary contact then notifies the contractor and PI by e-mail that the WA has been authorized.

CONCLUSION

Upon receiving the outcome of the request, the PI continues through the overall approval process.

EFFECTIVE DATE

November 1, 2008

SOP Number	RR_CSC_1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Conducting a Scientific Review

Standard Operating Procedure

POLICY SUPPORTED

This SOP supports the following policy:

- OHRC–08–0101: Conducting a scientific review

For more information about this policy, refer to page 17.

DESCRIPTION

This SOP describes the steps to perform a scientific review, as well as the conditions when the procedures change to support different methods of review.

ROLES INVOLVED

The following roles are involved with this SOP:

- PI
- OHRC Staff
- SRC Chair
- Scientific Reviewers
- Clinical Director

PROCEDURAL STEPS

1. PI submits package to OHRC. The PI submits the following items by email to NIEHS-OfficeofHRC@niehs.nih.gov:

    A. Scientific Review Form, Part I – Study Overview

    B. Proposal with any supporting documentation.

    C. List of experts the PI would like to be involved in the review.

    D. List of individuals that the PI would like to exclude as reviewers due to potential for conflict of interest.

2. OHRC works with SRC Chair to set up the selected method of review. Upon receipt of package, the following occurs:

    A. OHRC logs the submission and contacts the SRC Chair.

    B. The SRC Chair determines the method of review per policy guidelines (OHRC-08-0101, Rule 3).

    C. The SRC Chair identifies potential reviewers.

D. OHRC contacts the reviewers to confirm availability.

E. In the event a potential reviewer is unavailable, repeat steps 2C and 2D until the required number and type of reviewers are available.

F. OHRC documents the final set of reviewers.

3. Conduct the review.

A. If sending for review and comment only, the following occurs:

1. OHRC forwards the following to the individual reviewers: the submission package, Scientific Review Form, Part II – Reviewer Findings, and a cover letter stating the due date for return of the review findings to the OHRC. The OHRC will capture what was sent to whom and when.

2. Within the time allotted, each reviewer reviews the submission package, completes the Reviewer Findings form, and returns it to the OHRC.

3. Once all reviews are received, OHRC forwards the reviews to the SRC Chair.

4. Upon receiving all reviewer forms, the SRC Chair analyzes the feedback.

a) If there are issues with the biostatistics, the SRC Chair documents the issue and notifies the PI that these issues must be fixed and a revised proposal resubmitted. Repeat steps 3.A.1. through 3.A.4. when the PI submits the updated proposal.

b) If there are no issues with the biostatistics, but the feedback is mixed, the SRC Chair shall attempt to obtain consensus by discussing with the reviewers as a group. The SRC Chair may also submit the study to other reviewers or perform another review cycle with a different set of reviewers. If consensus or a majority opinion still cannot be reached, the SRC Chair has the discretion to stop the process, notify the OHRC and discuss with the PI how to proceed. The Chair completes the Scientific Review form, Part III – Review History documenting the outcome of all reviews that occurred.

c) If there are no issues with biostatistics and the feedback is consistent, continue to Step 4.

d) If there are no issues to which the PI needs to respond, continue to step 7.

B. If coordinating a call or convening a panel, the following occurs:

1. Prior to the call/meeting, OHRC performs the following:

a) Forwards to the individual reviewers the submission package, and captures what was sent to whom and when.

b) Coordinates the schedules of all parties to determine the meeting date/time.

c) Secures the appropriate meeting resources (e.g., call-in number for a call, meeting room with appropriate equipment for a panel meeting).

d) Sends out the meeting details (day, time, call-in number) to all parties.

e) Ensures someone is available on the day of the call to capture key points/issues.

2. On the call or at the panel meeting, the SRC Chair moderates the discussion amongst the reviewers and documents the key points.

3. At the conclusion of the call or panel meeting, the SRC Chair recalls for the group the issues raised and action items/next steps.

4. The SRC Chair determines how to proceed based upon the discussion.

a) If there are issues with the biostatistics, the SRC Chair documents the issue and notifies the PI that these issues must be fixed and resubmitted to continue. Repeat steps 3.A.1. through 3.A.4. when the PI submits the updated proposal.

b) If there are no issues with biostatistics, but the feedback is mixed, the SRC Chair may also submit the study to other reviewers or perform another review cycle with a different set of reviewers. If consensus or a majority opinion still cannot be reached, the SRC Chair has the discretion to stop the process, notify the OHRC, and discuss with the PI how to proceed.

c) If there are no issues with biostatistics and the feedback is consistent, continue to Step 4.

d) If there are no issues to which the PI needs to respond, continue to step 7.

4. Scientific Review Chair documents meetings and summarizes feedback to be sent to the PI. The Chair completes the Scientific Review form, Part III – Review History documenting the outcomes of all reviews, calls, meetings that have occurred. The SRC Chair compiles the feedback and forwards to the OHRC. OHRC staff log and copy the review, before sending to the PI.

5. PI responds to issues and resubmits. The PI formally responds to the issues in a point-by-point fashion, updates the protocol, and submits by email to NIEHS-OfficeofHRC@niehs.nih.gov. OHRC logs and reviews the updated submission, then forwards to the SRC Chair.

6. SRC Chair reviews PI response. The SRC Chair reviews the response to ensure the issues are resolved. The SRC Chair also forwards the response to any of the reviewers that have asked to see a response from the PI. If issues persist, repeat steps 4 – 6 until resolved; otherwise, continue to the next step.

7. SRC Chair documents final recommendation for review by the Clinical Director. The SRC Chair completes Scientific Review Form, Part IV – Chairperson Summary and Part V – Review Outcome, and sends to the OHRC. The OHRC then sends the entire packet (i.e., all research documents, Scientific Review Form Part I, Part II for each reviewer, Part III, Part IV, and Part V) to the Clinical Director for review.

8. Clinical Director documents decision. The Clinical Director reviews the entire package, then completes Scientific Review form, Part VI – Clinical Director Decision and returns the entire packet to the OHRC to notify the PI.

CONCLUSION

Once approved, the PI selects one of the following paths:

- If funding or site is already secured, and not waiting for an IRB exemption or an OMB approval/exemption, proceed with the IRB review process.

- If receiving support contract funds or using NIH facilities (i.e. NIEHS CRU, NIH CC), submit the most recent version of the protocol to the respective resource review committees for final review before proceeding.

EFFECTIVE DATE

November 1, 2008

SOP Number	SR_CRP_1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Conducting a Scientific Review for an Amendment

Standard Operating Procedure

INTRODUCTION

This SOP supports the following policy:

- OHRC–08–0101: Conducting scientific review

For more information about this policy, refer to page 17.

DESCRIPTION

This SOP describes the steps that occur when an active study requires a scientific review due to an amendment that substantively changes the level of risk and/or complexity of the study. The requirement for scientific review for amendments to active studies will be determined by the OHRC Director in consultation with the Clinical Director and IRB Chair.

ROLES INVOLVED

The following roles are involved with this SOP:

- PI
- OHRC Staff
- SRC Chair
- Scientific Reviewers
- Clinical Director

PROCEDURAL STEPS

Guidance

For an amendment to an IRB-approved study that substantively changes the level of risk and/or complexity of the study, the PI must submit the proposed amendment to the SRC Facilitator for scientific review before the amendment is submitted to the IRB. Amendment requests that meet these criteria that are submitted to the IRB without a scientific review will be forwarded automatically to the SRC Facilitator.

Steps

Follow all the steps identified in the SOP: SR_CRP_1 – Conducting a Scientific Review.

CONCLUSION

An amendment request must be approved by the IRB overseeing the study before the requested changes can be implemented.

EFFECTIVE DATE

November 1, 2008

SOP Number	SR_CRP_3		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Obtaining OMB Approval

Standard Operating Procedure

POLICY SUPPORTED

This SOP supports the following policy:

- OHRC–08–0201: Collecting Information from the Public

For more information about this policy, refer to page 21.

DESCRIPTION

This SOP describes the steps necessary to obtain clearance from OMB to collect information from the public for studies that have not received a clinical exemption.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- OHRC Staff

PROCEDURAL STEPS

Guidance

By regulation, the OMB clearance process takes a minimum of 120 days, and can take as long as 180 days. As such, the PI should begin this process as soon as possible.

Steps

1. PI submits package to OHRC. From the OHRC website, the PI should download and fill out the following:

   - Supporting statement A
   - Supporting statement B, if applicable
   - Worksheet, part I
   - Worksheet part II

   Additionally, the PI should have already prepared the following:

   - Data collection instruments
   - Introductory and follow-up letter to respondents, including consent forms
   - Other relevant documentation

The PI should send all documents as attachments by e-mail to NIEHS-OfficeofHRC@niehs.nih.gov.

2. OHRC processes request. OHRC staff shall review the documents and follow-up with the PI if there are any questions/concerns. Upon completion of the review, the OHRC staff shall submit the request to the Project Clearance Branch. The OHRC shall be the point of contact during the clearance process.

3. OHRC logs response and notifies PI. Upon receipt of decision by the OMB, through the Project Clearance Branch, the OHRC logs response details and forwards to the PI.

CONCLUSION

Once approved, the PI continues through the overall clinical research approval process. If IRB approval has already been received from all applicable sites when OMB clearance is obtained, then the PI can begin enrolling subjects.

EFFECTIVE DATE

November 1, 2008

SOP Number	OMB_CRP _1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Obtaining Clinical Exemption from OMB Review

Standard Operating Procedure

POLICY SUPPORTED

This SOP supports the following policy:

- OHRC–08–0201: Collecting Information from the Public

For more information about this policy, refer to page 21.

DESCRIPTION

This SOP describes the steps to take when a PI seeks a clinical exemption from OMB review.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- OHRC staff

PROCEDURAL STEPS

Guidance

- Clinical exemption is not required for intramural research except in the case of a contract with an extramural organization to conduct the research. If intramural research is being conducted entirely via a contract mechanism, the PI should contact Sherry Mills, M.D., M.P.H. in the Project Clearance Office for guidance on the need, if any, for OMB clearance or clinical exemption. Studies done by intramural researchers using contract staff to augment the research team do not require OMB clearance or clinical exemption. Clinical Exemption is also not needed for grants.
- Clinical exemption is limited to activities and research that involve individuals actually undergoing treatment or examination for a specific clinical condition. Projects designed to study a population (as opposed to individuals) do not qualify for a clinical exemption. For questions related to clinical exemptions, contact the OHRC or Sherry Mills, M.D., M.P.H. in the Project Clearance Office.
- If clinical exemption is a possibility, then the PI should submit, as soon as possible, a request for clinical exemption, as the process can take up to eight (8) weeks; if denied a clinical exemption, the PI must start the process for OMB clearance, which, by regulation takes 120 days, but may take up to 180 days.
- If a study is being conducted at the NIEHS CRU or at the NIH CC, the study is automatically considered to have a clinical exemption and the PI does not need to apply for one.

Steps

1. PI completes online request at PCB website. The PI access the online submission system (http://odoerdb2-1.od.nih.gov/oer/policies/project_clearance/pcb.htm) from behind the NIH firewall, clicks the Request Clinical Exemption button, and completes all required fields on the request form. A response regarding the clinical exemption is typically provided within 4-6 weeks of submission.

2. Notify OHRC of outcome.

CONCLUSION

If approved, the PI continues through the overall clinical research approval process. If denied, the PI must begin the process for OMB approval while continuing through the overall clinical research approval process.

EFFECTIVE DATE

November 1, 2008

SOP Number	OMB_CRP _2		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

Obtaining Exemption from IRB Review

Standard Operating Procedure

DESCRIPTION

This SOP describes the steps to take when a PI seeks an exemption from IRB review.

ROLES INVOLVED

The following are involved with this SOP:

- PI
- OHRC staff

PROCEDURAL STEPS

Guidance

- Only the OHSR is authorized to determine if a study is or is not exempt from IRB review. The PI must receive written approval for an exemption from OHSR before the study can be conducted.
- While the OHSR permits a PI to submit the form directly to them, the process at NIEHS is to send the form to the OHRC which will then submit the form to OHSR on the PIs behalf.
- For information regarding the types of activities that may qualify for exemption from the IRB review and approval process, contact the IRB Chair (David Resnick, J.D., Ph.D.) or the OHRC staff. A PI may contact OHSR directly by calling 301-402-3444. Additionally, the following public sites have information about IRB-exempt research:
    - Title 45, Subpart 46.101(b) of the Code of Federal Regulations
    - OHSR Information Sheet 8 – (Frequently Asked Questions), Answer 11
    - Office of Human Research Protections (OHRP) website, Decision Chart 2: Is the Human Subjects Research Eligible for Exemption?

Steps

1. PI fills out worksheet and submits to OHRC. From the CRP or OHRC websites, the PI should download and complete the Request for Review of Research Activity Involving Human Subjects form. For help filling out the form, contact the OHRC. Once completed, send the signed worksheet and any supporting material to the OHRC.

2. OHRC staff reviews the form and submits to OHSR. OHRC staff shall log receipt of submission, review the form, resolve any issues with the PI, and submit the form with supporting materials to OHSR by fax or mail, as appropriate.

3. PI receives written response from OHSR. This response usually takes less than one week.

4. PI forwards the response to the OHRC.

5. OHRC logs receipt of response and stores all correspondence.

CONCLUSION

If approved for exemption, the PI may conduct the study when scientific review and funding reviews, if applicable, are complete. If denied, the PI must submit the study to the IRB for review and continue following the overall clinical research approval process.

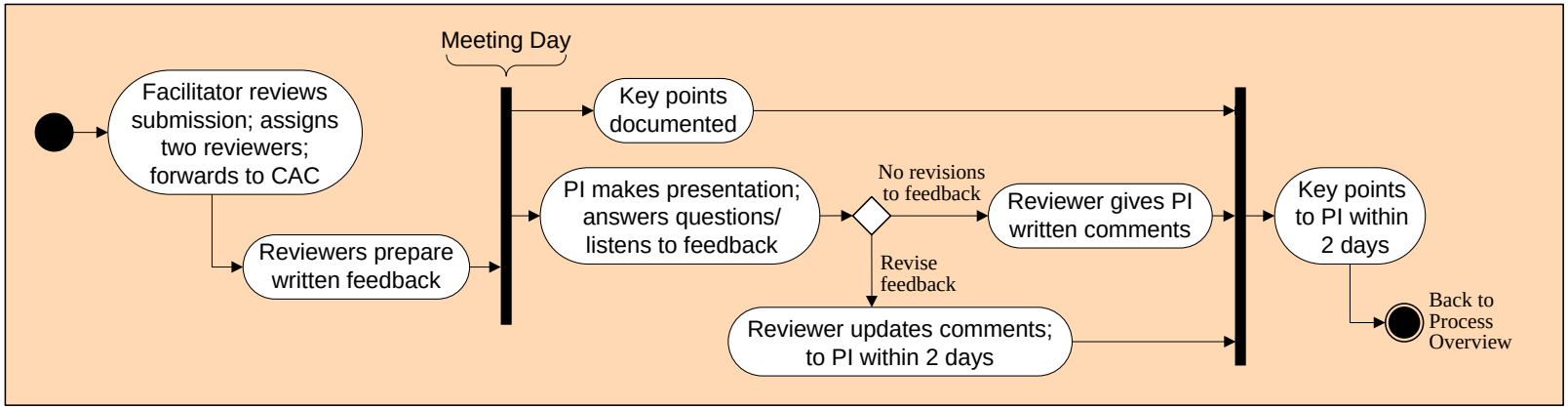
EFFECTIVE DATE

November 1, 2008

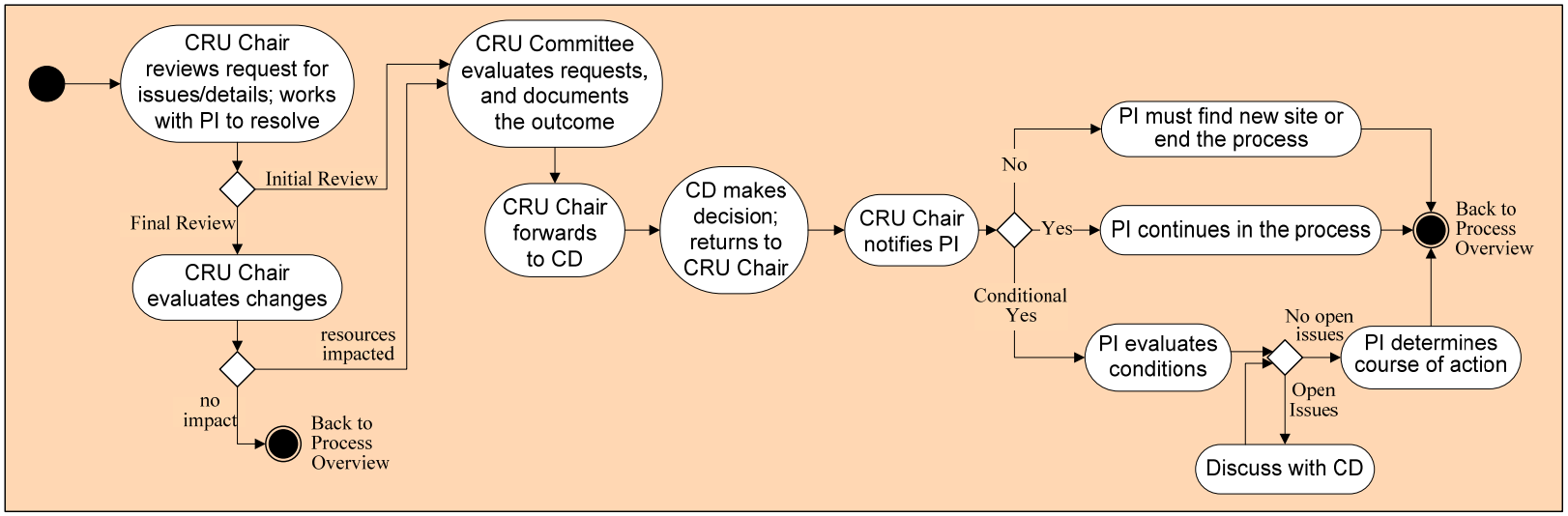
SOP Number	IRB-E_CRP _1		
Approved By: Scientific Director	Signature	Date	Date First Effective:
Approved By: Clinical Director	Signature	Date	

APPENDIX A: FLOW DIAGRAMS

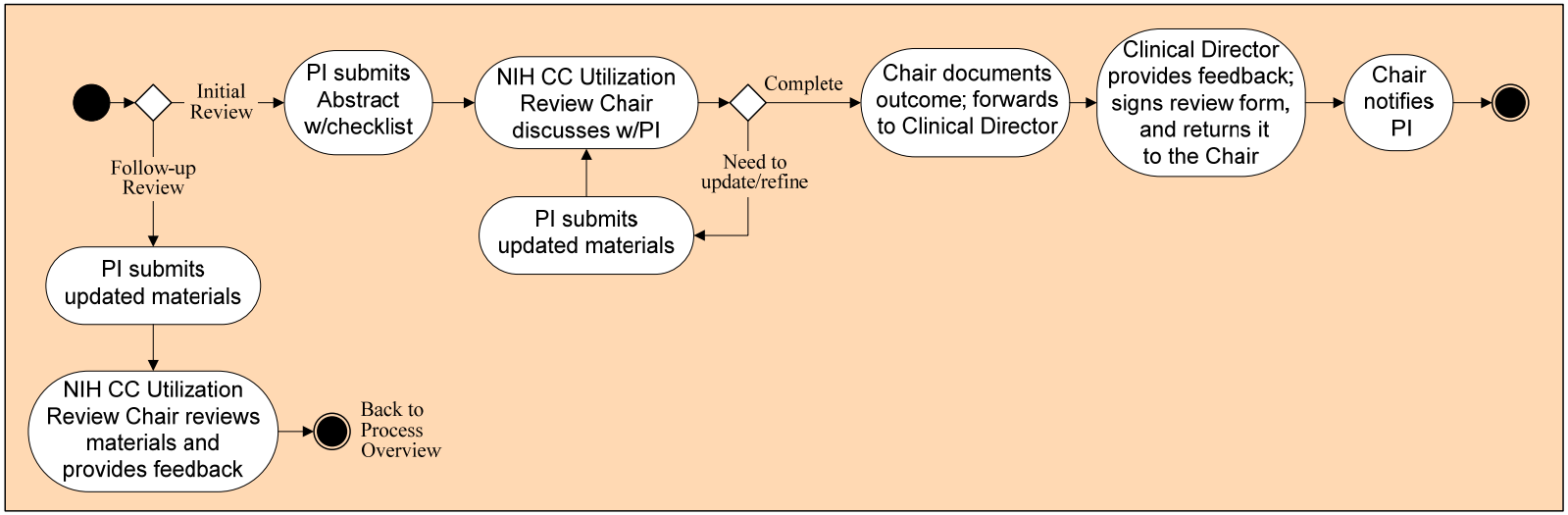
High-Level View of CAC Review Process



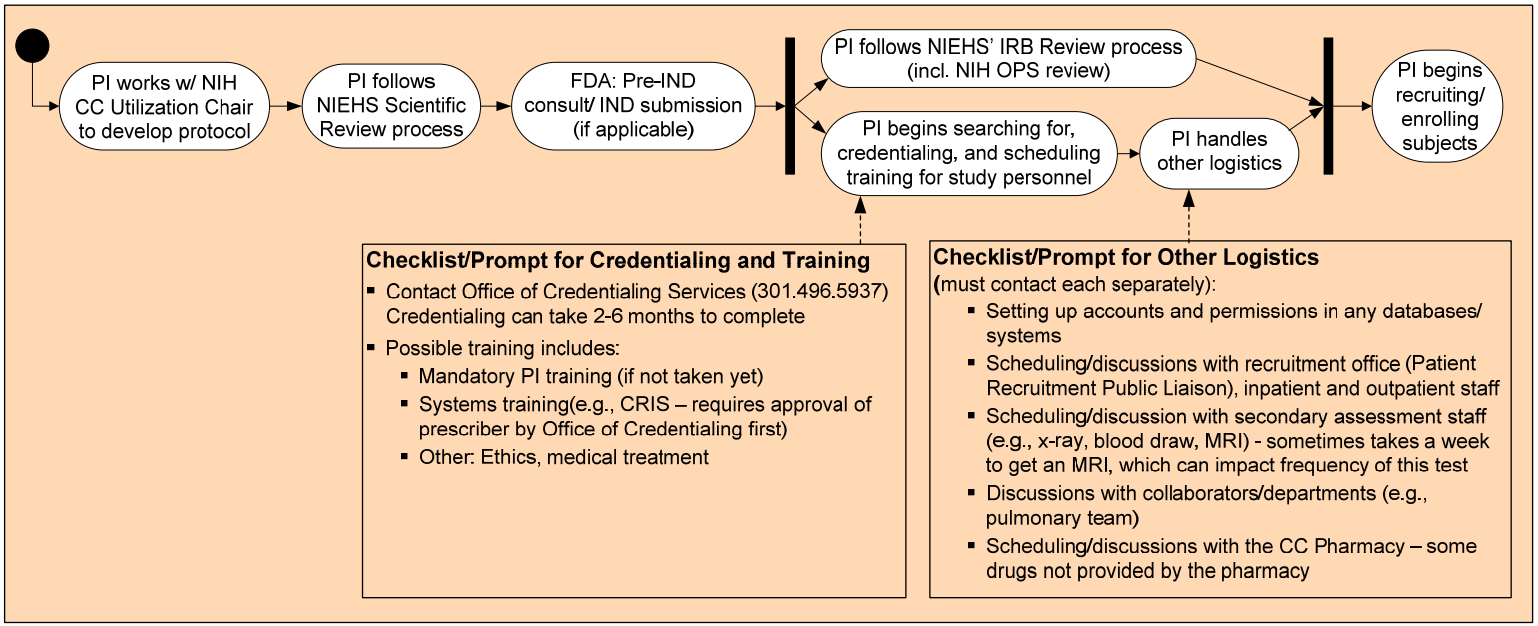
High-Level View of CRU Utilization Review Process



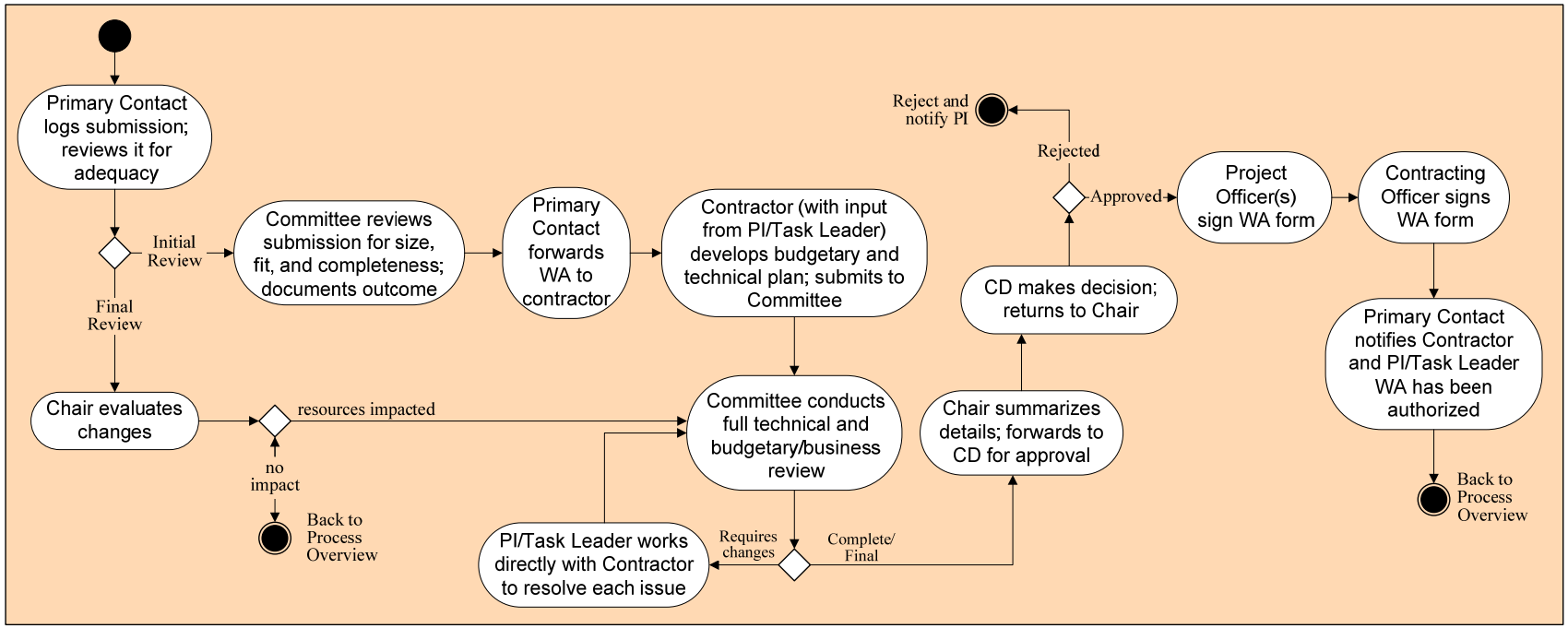
High-Level View of NIH CC Utilization Review



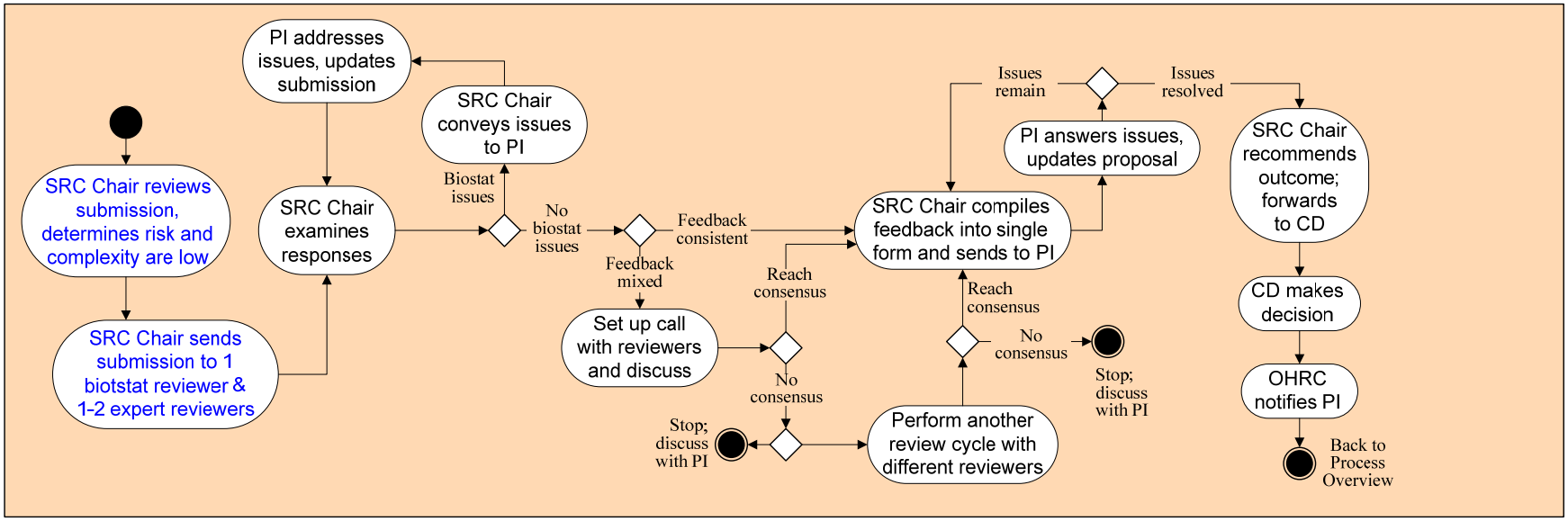
High-Level View of the Overall Process to Conduct Studies at NIH CC (assumes funding obtained)



High-Level View of Clinical Support Contract Resource Review Process



High-Level View of Scientific Review for Low Complexity/Low Risk



High-Level View of Scientific Review Process More than Minimal Risk with Low or High Complexity