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**SOP Title: TRAINING REQUIREMENTS FOR THE NIH HUMAN RESEARCH
PROTECTION PROGRAM (HRPP)**

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

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**SOP 25: TRAINING REQUIREMENTS FOR THE NIH HUMAN RESEARCH
PROTECTION PROGRAM (HRPP)**

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SOP 25: TRAINING REQUIREMENTS FOR THE NIH HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

25.1 PURPOSE

This SOP describes training requirements for researchers in the NIH Human Research Protection Program (HRPP), including key research personnel as defined below in Section 25.3.

25.2 POLICY

All Intramural Research Program (IRP) scientists are required to complete training in order to assure that they understand when research activities involve human subjects research and what is required when they conduct this type of research.

Clinical researchers and clinical research support staff are required to have additional training commensurate with their roles and responsibilities. This includes Good Clinical Practice (GCP) training when research is regulated by the Food and Drug Administration (FDA) (see SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”). IRBs may require additional training for investigators who do not demonstrate understanding of specific areas or when investigators undertake a new type of research (for example, research with prisoners).

25.3 DEFINITIONS

- A. **Behavioral Research:** Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or survey, interview, oral history or focus group research, program evaluation, human factors evaluation, or quality assurance methodologies (see 25.5.2, below).

- B. **Biomedical Research:** Basic, clinical, and translational medical research conducted to investigate the causes, treatments, and cures for both common and rare diseases.

- C. **Clinical Research:** Research that includes interactions with humans; including studies of mechanisms of disease; therapies or interventions for disease; clinical trials; or studies to develop new technologies related to disease.

- D. **Collaborative Institutional Training Initiative (CITI):** CITI is a subscription service that provides research ethics education to the members of the research community. For more information about features of the CITI courses see Appendix 1 “CITI Training Information”.

- E. **(The) Ethical and Regulatory Aspects of Clinical Research:** This seven (7) week course is offered by the Clinical Center Bioethics Department each fall and provides a comprehensive overview of the ethical issues in human subjects research in the United States. For more information see Appendix 2 “Training Resources”, item K.

- F. **Epidemiological Research:** is the study of the patterns, causes, and effects of health and disease conditions in defined populations.

- G. **FDA regulated Research:** Includes all clinical investigations regulated by the FDA under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic (FD and C) Act, as well as clinical investigations that involve test articles subject to regulation under the FD and C Act or under sections 351 or 354-360F of the Public Health Service Act, 21 CFR 56.102 (j), including any drug for human use, biological product for human use, medical device for human use, human food additive, color additive or electronic product. FDA regulated research does not include research that has been determined to be exempt from FDA regulation. (For more information see SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”) NIH Investigators who conduct FDA-regulated research at sites in the United States must follow FDA Guideline for Good Clinical Practice (GCP) guidance (see item H below).

- H. **Guideline for Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that

the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

- I. **Investigator:** For the purposes of the HHS regulations, the Office for Human Research Protections (OHRP) interprets an “investigator” (see Appendix 2, item H) to be any individual who is involved in conducting human subjects research studies. Such involvement may include:
 1. Obtaining information about living individuals by intervening or interacting with them for research purposes;
 2. Obtaining identifiable private information about living individuals for research purposes;
 3. Obtaining the voluntary informed consent of individuals to be subjects in research; or
 4. Studying, interpreting, or analyzing identifiable private information or data for research purposes

Investigators can include physicians, scientists, nurses, administrative staff, teachers, and students, among others. Some research studies are conducted by more than one investigator, and usually one investigator is designated the “Principal Investigator” (PI) with overall responsibilities for the study. In every human subjects research study, investigators have certain responsibilities regarding the ethical treatment of human subjects. (For more information see Appendix 2, item H for the link to the OHRP FAQ, “Who are “investigators”?”).

The PI may designate some investigators as a sub-type of investigator, e.g., “Associate Investigators” (AIs).

- J. **Key Research Personnel (KRP):** Key research personnel are those individuals who: 1) obtain consent from human subjects; 2) recruit human subjects; 3) evaluate the response of human subjects, including adverse or unanticipated events; or 4) analyze or interpret identifiable study data.
- K. **NIH Intramural Clinical Protocol Application:** A completed Application submitted to an NIH IRB at the time of initial or continuing review, study

closure or amendment. It includes a statement of training completed by investigators and other study staff/personnel listed on the Application.

- L. **Social Behavioral Research:** Research involving the study of the interactions of biological factors with behavioral or social variables and how they affect each other. This includes but is not limited to, individual or group characteristics or behavior (e.g., research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior). Methodologies may include basic and applied research; research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

25.4 TRAINING RESOURCES

Training curricula are specified on the OHSRP website (see below) for each type of research conducted or reviewed; categories include: Clinical Research, Epidemiological and Social Behavioral Research, or HRPP staff (IRB Chairs, Members and staff, and OHSRP professional staff).

Courses are accessed via the OHSRP website under the “Required HRPP Training” link (see Appendix 2, item J). Each user should select the link below the appropriate research category to gain access to the correct curriculum.

IRB member training is provided under the “HRPP Staff: Chairs, Members and Staff of the NIH IRBs and OHSRP professional staff” link on the OHSRP website (see Appendix 2, item J).

On-line training courses include those offered by CITI (See Appendix 1 for details about this option) and the NIH Clinical Research Training (CRT, see Appendix 2 “Training Resources” item C)).

The Ethical and Regulatory Aspects of Clinical Research course is an in-person course offered annually by the CC Bioethics Department. Credit for successful completion of this course may be applied towards clinical research/biomedical training or used as a refresher course for the clinical research or biomedical training. In order to receive credit for this course the student must attend at least 6 of 7 classes and pass the exam with a score of at least 80 percent. For more information contact the Department of Bioethics or see Appendix 2, item K for the link.

25.5 TRAINING REQUIREMENTS FOR THE NIH HRPP COMMUNITY

The NIH HRPP community includes NIH investigators, Key Research Personnel, NIH IRB members and staff and OHSRP professional staff.

For an overview of training requirements by role and type of research conducted, see Appendix 3 “NIH IRP HRPP Training Requirements”. These requirements apply to NIH staff.

25.5.1 NIH INVESTIGATORS ENGAGED IN CLINICAL RESEARCH

Courses are accessed via the HRPP Training page for “Clinical Research” (see Appendix 2, item J for the link). Additional courses may be required by the PI or IRB according to the type of research to be conducted, (see Section 25.5.5 below for more information).

A. Investigators engaged in non-FDA regulated Research

1. Required training:

- a. NIH Clinical Research Training (CRT); or
- b. CITI Biomedical course; or
- c. The Ethical and Regulatory Aspects of Clinical Research offered by CC Bioethics

- 2. Optional or Just-in-time Training: includes additional courses listed on the OHSRP training website pages or any of the just-in-time CITI Courses in Section 25.5.5 below. NIH IRBs or ICs may also require that investigators conducting non-FDA-regulated research take GCP training.

B. Investigators and engaged in FDA-regulated Research

The training below is required for investigators conducting FDA-regulated research. For more information, see SOP 15

“Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”. However, NIH IRBs or ICs may also require that investigators conducting non-FDA-regulated research take GCP training.

1. Required training:
 - a. Either the NIH Clinical Research Training (CRT);
or
 - b. CITI Biomedical course; or
 - c. The Ethical and Regulatory Aspects of Clinical Research offered by CC Bioethics.
2. The NIAID Good Clinical Practice (GCP) course or one of the CITI Good Clinical Practice for courses based on the role of the investigator on the study.
3. Optional or Just-in-time Training: includes additional courses listed on the OHSRP training website pages or any of the just-in-time CITI courses in Section 25.5.5 below.

25.5.2 NIH INVESTIGATORS ENGAGED IN EPIDEMIOLOGICAL OR SOCIAL BEHAVIORAL RESEARCH

Courses are accessed via the HRPP Training page for “Epidemiological and Behavioral Research” (see Appendix 2 for the link).

A. Investigators and engaged in epidemiological or social behavioral research

1. Required training:
 - a. NIH Clinical Research Training (CRT); and
 - b. CITI Social and Behavioral course
2. Optional or Just-in-time Training: includes additional courses listed on the OHSRP training website pages or

any of the just-in-time CITI courses in Section 25.5.5 below

25.5.3 KEY RESEARCH PERSONNEL (KRP)

A. Key Research Personnel engaged in research (e.g., biomedical, epidemiological or social behavioral):

1. Required training: NIH Clinical Research Training (CRT)
2. Optional or Just-in-time Training: includes additional courses listed on the OHSRP training website pages or any of the just-in-time CITI courses in Section 25.5.5 below

25.5.4 HRPP STAFF: CHAIRS, MEMBERS AND STAFF OF THE NIH IRBS AND OHSRP PROFESSIONAL STAFF

Courses are accessed via the HRPP Training page (see Appendix 2, item J). Non-NIH IRB members should contact OHSRP to gain access to the required training resources.

A. All HRPP Staff including IRB Chairs and Members, IRB Administrative Staff, and OHSRP professional staff

1. Required training:
 - a. NIH Clinical Research Training (CRT); or
 - b. CITI Biomedical course or CITI Social and Behavioral course; or
 - c. The Ethical and Regulatory Aspects of Clinical Research offered by CC Bioethics.
2. Either the NIAID GCP course or the CITI GCP for PI's course
3. Optional or Just-in-time Training: The IRB Chair may determine that the additional CITI modules will be required according to the type of research reviewed by

the IRB, but are otherwise optional, see Section 25.5.5 below.

B. Incoming IRB Members

In addition to the requirements listed above, incoming IRB members must also complete the following requirements prior to becoming an active member:

1. Required training:

- a. NIH IRB Member Training, (see Appendix 2 for the link)
- b. Attend the OHSRP IRB member in-person orientation; and
- c. Attend and observe one IRB meeting in-person

25.5.5 OPTIONAL OR JUST-IN-TIME TRAINING

In general, the just-in-time CITI courses listed below are optional (e.g. GCP courses are optional, for investigators who do not conduct FDA-regulated research.) However, IRBs or PIs may require investigators or KRP to complete these courses and IRB Chairs may require IRB members or staff to take these courses based on the type of research reviewed by the IRB.

- A. Biomedical- Vulnerable Subjects - Research with Children
- B. Biomedical- Vulnerable Subjects- Research with Pregnant Women, Human Fetuses or Neonates
- C. Biomedical- Vulnerable Subjects- Research with Prisoners
- D. Biomedical- Vulnerable Subjects- Workers/Employees
- E. Genetic Research in Human Populations
- F. Stem Cell Research Oversight
- G. NIAID GCP course

- H. CITI GCP modules
 - I. International Studies- ICH Overview and ICH- Comparison Between ICH GCP E6 and US FDA Regulations, available to those staff who complete the CITI GCP course
 - J. Unanticipated Problems and Reporting Requirements in Biomedical Research
 - K. Unanticipated Problems and Reporting Requirements in Social and Behavioral Research

25.6 REFRESHER TRAINING FOR THE NIH HRPP COMMUNITY

Courses are accessed via the HRPP Training page on the OHSRP website, (see Appendix 2 for the link). Refresher types are specified for each type of research conducted: Clinical Research, Epidemiological and Social Behavioral Research.

- A. Refresher Cycle: Refresher courses must be completed on a three (3) year cycle. All refreshers must be completed by December 31st in the year of expiration.
- B. The IRB, Clinical Director or PI may stipulate the type of refresher training to be taken, or may require training sooner than three-year intervals. In the absence of a prescribed refresher course, investigators may choose to take other modules relevant to the type of research conducted (see 25.6.D below).
- C. OHSRP may require additional courses when new policies or regulations go into effect. OHSRP will designate whether such courses may be considered to meet the requirement for refresher training.
- D. Other refresher courses may be chosen according to the type of research conducted.
 - 1. The following courses may be refreshed using CITI; the refresher courses will appear in CITI after the expiration date of the previous course in the series (e.g. 3 years after the user completed the basic CITI course):

- a. Clinical Research: CITI Biomedical refresher modules
 - b. Epidemiological and Social Behavioral: CITI Social and Behavioral refresher modules
2. Other CITI modules, or The “Ethical and Regulatory Aspects of Clinical Research” offered by CC Bioethics may be taken as refresher courses.

25.7 DOCUMENTATION OF NIH HRPP REQUIRED TRAINING, REFRESHER TRAINING AND OPTIONAL TRAINING FOR NIH STAFF

- A. NIH staff are responsible for downloading a Certificate of Completion for each completed course to provide proof of training. NIH staff must maintain proof of training in their research records and/or regulatory binders.
- B. OHSRP will maintain a read-only database for the verification of required HRPP training courses, refresher courses, and optional training courses by completion date.
- C. Transfer of proof of training:
 1. Newly employed NIH staff coming to the NIH can transfer CITI training courses completed in the last 12 months, through CITI to the NIH CITI account. However, the user must establish an NIH CITI account before contacting the CITI helpdesk. For assistance transferring credits, contact the CITI helpdesk at 305-243-7970. Courses completed within 12 months of transfer will provide credit towards initial training.
 2. Newly employed NIH staff coming to the NIH can transfer their NIAID GCP training completed at a non-NIH institution in the last 12 months, by providing the proof of training to OHSRP for inclusion in the HRPP training database.
- D. OHSRP will maintain the training records of IRB Chairs, Vice Chairs, Members, IRB administrative staff and OHSRP professional staff.

- E. IRB Administrative Staff Training Records will be maintained in the IRB Office.

25.8 REQUIRED TRAINING FOR NON-NIH INVESTIGATORS AND KRP

This applies to non-NIH Investigators or KRP working on NIH intramural protocols. The NIH HRPP does not provide training for these investigators.

- A. Non-NIH investigators and KRP working on NIH intramural protocols that are reviewed by a non-NIH IRB must comply with training as required by their home institution.
- B. If the home institution of a non-NIH Investigator (e.g. such as a physician in private practice), does not require human subjects protections or GCP training (as applicable) the investigator must take and provide evidence of training. Possible training sources include free, open-access courses such as “Protecting Human Research Participants” offered by the NIH Office of Extramural Research or NIAID GCP offered to non-NIH users (see Appendix 2 “Training Resources” items M and E). Alternatively, investigators could use other publically available sources for a fee (e.g. Collaborative Institutional Training Initiative (CITI)), (see Appendix 2 “Training Resources” item C).

25.9 ACTIVITIES THAT MAY NOT COMMENCE UNTIL TRAINING REQUIREMENTS ARE MET

- A. Investigators and KRP may not serve on an IRB-approved study unless they have satisfied the applicable NIH HRPP training requirements. IRBs are responsible for confirming that investigators and KRP have satisfied the NIH HRPP training requirements as a condition of approval. For more information see SOP 7 “Requirements for the Ethical and Regulatory Review of Research by NIH Institutional Review Boards (IRB)”.
- B. IRB Chairs, Vice Chairs or members or staff may not serve or continue to serve on an NIH IRB unless they have satisfied the NIH HRPP training requirements.

25.10 LIST OF APPENDICES

Appendix 1- CITI Training Information

Appendix 2- Training Resources

Appendix 3- NIH IRP HRPP Training Requirements

APPENDIX 1- CITI TRAINING INFORMATION

- A. The following CITI modules offer test-out:
 - 1. CITI Good Clinical Practice both PI and non-PI
 - 2. Biomedical Modules
 - 3. Social and Behavioral Modules
- B. Test-out is not offered for just-in-time, optional or refresher courses.
- C. To test-out of a required course, the user must score 80% in the required content area.
- D. Each module takes 20-30 minutes to complete.
- E. If the user cannot complete the entire training, the user should complete the current module and return to the course at a later time.
- F. The user must achieve a score of 80% for each module quiz in order to receive a Certificate of Completion for each module.
- G. If you have completed CITI courses at another institution in the last 12 months and would like credit for those courses, contact the CITI helpdesk at 305-243-7970 and request that your records be merged with your NIH account. However, you must first establish an NIH account prior to contacting CITI and provide an NIH CITI Member ID in order for the transfer to be completed.
- H. CITI training is transferrable to other non-NIH institutions when you leave the NIH or as may be required by other collaborating institutions, contact the CITI helpdesk at 305-243-7970 for assistance.
- I. CITI offers Continuing Medical Education credits for a fee; for more information select "CE Credits Status" on the CITI landing page.

APPENDIX 2- TRAINING RESOURCES

- A. Behavioral Research (Taken from 45 CFR 46.110(a) List of Categories item #7): <http://www.hhs.gov/ohrp/policy/expedited98.html>
- B. Clinical Research Training: <https://federation.nih.gov/ohsr/nih/biomed.php>
- C. Collaborative Institutional Training Initiative (CITI): www.citiprogram.org
- D. FDA Good Clinical Practice (GCP): Guidance for Industry E6 Good Clinical Practice Consolidated Guidance:
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf>
- E. NIAID GCP Learning Center:
<https://gcplearningcenter.niaid.nih.gov/Pages/default.aspx>
- F. NIH Clinical Research Training (CRT) Course:
<http://crt.nihtraining.com/login.php>
- G. NIH IRB Member Training: <https://federation.nih.gov/ohsr/nih/irbmenu.php>
- H. OHRP FAQ, "Who are "investigators"?:
<http://answers.hhs.gov/ohrp/questions/7214>
- I. OHSRP website: <https://federation.nih.gov/ohsr/nih/index.php>
- J. Required HRPP Training: <https://federation.nih.gov/ohsr/nih/investigator-training.php>
- K. The Ethical and Regulatory Aspects of Clinical Research:
<http://www.bioethics.nih.gov/hsrc/>
- L. "Protecting Human Research Participants" offered by the NIH Office of Extramural Research: <http://phrp.nihtraining.com/users/login.php>

APPENDIX 3- NIH IRP HRPP TRAINING REQUIREMENTS TABLE

Table 1- The table below describes the NIH Intramural Research Program (IRP) Human Research Protection Program (HRPP) Training Requirements for Clinical, Epidemiological and Social Behavioral Investigators, Key Research Personnel and HRPP Staff including IRB Chairs, Members, Staff and OHSRP Professional Staff

| ROLES: | Clinical Principal Investigators (PIs) and Associate Investigators (AIs) for non-FDA regulated Studies | Clinical PIs and AIs conducting FDA-regulated Research | Key Research Personnel | Epidemiological/ Behavioral/ Social Science/ Health Outcomes and Health Services Investigators | HRPP Staff (including IRB Members, Staff and OHSRP Professional Staff) |
|--|---|---|-------------------------------|---|---|
| COURSES | | | | | |
| Clinical Center On-line Clinical Research Training (CRT) | X | | X | X | X |
| CRT w/out Regulatory Module | | X | | | |
| | OR | OR | | | OR |
| CITI Bio-Medical Modules | X | X | | | X* |
| | OR | OR | | | OR |
| Ethical and Regulatory Aspects of Clinical Research | X | X | | | X |
| CITI Behavioral Research Training Modules | | | | X | X* |
| KEY | X = Required *HRPP staff should check w/their Chairs to determine if they should complete the CITI Biomedical or CITI Social Behavioral modules. | | | | |

| ROLES: | Clinical Principal Investigators (PIs) and Associate Investigators (AIs) for non-FDA regulated Studies | Clinical PIs and AIs conducting FDA-regulated Research | Key Research Personnel | Epidemiological/ Behavioral/ Social Science/ Health Outcomes and Health Services Investigators | HRPP Staff |
|--|--|--|------------------------|--|------------|
| NIAID GCP Modules 2-4 | | X | | | X |
| | | OR | | | OR |
| CITI GCP Training and as applicable below* | | X | | | X |
| New Member: OHSRP On-Line IRB Member Training | | | | | X |
| New Member: Attend the OHSRP IRB member in-person training | | | | | X |
| New member: Attend an IRB meeting | | | | | X |
| Additional Courses | Any course above or additional CITI courses may be required by the Institute/Center, Clinical Director or IRB, depending on the investigator role and research subjects. They are otherwise optional unless indicated under the roles above. | | | | |
| KEY | X = Required | | | | |

| CITI GCP Modules | |
|--|------------------|
| GCP Introduction | X |
| Overview of New Drug Development | X |
| ICH Overview | If International |
| ICH - Comparison Between ICH GCP E6 and U.S. FDA Regulations | If International |
| Conducting Investigator-Initiated Studies According to FDA Regulations and Good Clinical Practices | X |
| Investigator Obligations in FDA-Regulated Clinical Research | X |
| Managing Investigational Agents According to GCP Requirements | X |
| Conducting Clinical Trials of Medical Devices | ONLY if IDE |

| CITI Just-in-Time Training |
|---|
| Vulnerable Subjects - Research w/Children |
| Vulnerable Subjects - Pregnant Women, Human Fetuses, and Neonates |
| Vulnerable Subjects - Research Involving Prisoners |
| Vulnerable Subjects -Workers/Employees |
| Genetic Research in Human Populations |
| Stem Cell Research Oversight (Part I) |
| Stem Cell Research Oversight (Part II) |
| International Studies (see CITI GCP for optional modules regarding ICH in an international setting) |

| CITI GCP Modules | |
|--|--------------|
| Informed Consent-An Ongoing Process | X |
| Detection and Evaluation of Adverse Events | X |
| Reporting Serious Adverse Events | X |
| Audits and Inspections in Clinical Trials | Per role |
| Monitoring of Clinical Trials by Industry Sponsors | Per protocol |

| CITI Just-in-Time Training |
|---|
| Unanticipated Problems and Reporting Requirements in Biomedical Research |
| Unanticipated Problems and Reporting Requirements in Social and Behavioral Research |