The NIEHS Human Research Protection Program
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Human research subject protection must be at the core of any clinical research enterprise. Institutional Review Boards (IRBs) help to implement this goal, but are not sufficient to ensure the best regulatory compliance and human subject protection. The NIEHS Office of Human Research Compliance (OHRC) was established in 2007 to monitor and improve the systems that protect individuals who participate in clinical research and to ensure compliance with institutional, local, state, and federal laws and regulations. The OHRC will ensure that researchers employ the highest ethical standards in the conduct of human research, will give guidance to ensure sound research design and scientific integrity, and will provide education and monitoring for clinical research projects.

Mission and Vision of the NIEHS OHRC

The mission of the NIEHS OHRC is to provide leadership, oversight and management of a comprehensive Human Research Protection Program (HRRP) at NIEHS. Maintaining a comprehensive HRPP requires that the NIEHS OHRC consistently improves the system that protects the rights, welfare and well being of individuals who participate in clinical research. In order to fulfill this mission, it is important that the following six key elements are maintained:

- Compliance with local, state and federal laws and regulations;
- Compliance with NIEHS and NIH policies and regulations;
- Retention of the highest ethical standards for human research;
- Guidance to ensure sound research design, scientific integrity, and confirmation that the research contributes to generalizable scientific/clinical knowledge and is worth exposing subjects to risk;
- High quality education and training of individuals at all levels within the clinical research program;
- Continual quality assurance/quality improvement monitoring for all clinical research performed by NIEHS investigators.

The primary goals of NIEHS OHRC are to provide professional advice, leadership, oversight and management for the NIEHS HRPP. The NIEHS OHRC provides ethical and regulatory oversight of research that involves human subjects by:

- Constantly improving human research protections by employing the highest ethical standards for human research and by adhering to the ethical principles outlined within the Belmont report (Respect for Persons, Beneficence and Justice);
- Assuring regulatory compliance;
- Improving the quality of research by employing the highest standards of quality;
- Improving risk management;
- Improving education and training for all involved in clinical research and making sure all are informed and educated about new regulations, guidance and policy;
- Working collaboratively with the clinical PIs;
- Improving consistency;
- Increasing efficiency;
- Increasing communication to the public in an effort to build public trust.

Key Components of the NIEHS Human Research Protection Program(HRPP)

The OHRC provides professional advice leadership and oversight to NIEHS through an integrated approach. This integrated approach is the Human Research Protection program and includes the following:

- Maintaining compliance within the NIEHS Clinical Research Program and providing clarification and guidance in interpreting 45CFR46 and, when appropriate, 21CFR50 & 56 (the Federal Regulations for the protection of human subjects);
- Monitoring and analyzing new legislation, policies, program initiatives, regulations and requirements and implementing the new guidance within the NIEHS HRPP; Analyzing current NIEHS policies, standards and guidelines; and determining which policies need to be revised based upon updated policies and procedures from DHHS and NIH;
- Working with NIH Office of Human Subjects Research (OHSR) as appropriate to formulate policies and procedures consistent with the regulations as well as implementing those policies and procedures within the OHRC Program at NIEHS;
- Providing guidance to PIs during protocol development;
- Managing the administration of the pre-IRB review process.
- Managing the daily administration of the NIEHS IRB;
- Establishing educational and training programs with the goal of creating a culture of respect for and awareness of the rights and welfare of human research participants at NIEHS and its affiliated sites;
- Establishing a Quality Assurance and Improvement Program which includes monitoring the quality of human research protections;
- Implementing and maintaining electronic resources and management systems for the NIEHS OHRC;
- Giving guidance and serving as the NIEHS central point of contact during the AAHRPP accreditation process; after accreditation has been achieved, the NIEHS OHRC will develop guidelines and internal processes to maintain accreditation.

The Pre-IRB Review Process

NIEHS has developed a comprehensive pre-IRB review process for clinical research protocols. This process allows for a thorough review of all NIEHS clinical protocols and provides assurance of sound scientific design, and the highest standards of quality. The steps within the pre-IRB review process are as follows:

- Preliminary Proposal Review. The Principal Investigator (PI) must first present their proposal to the Clinical Advisory Committee (CAC). This committee is comprised of physician-scientists, basic scientists, epidemiologists, biostatisticians, and IRB representatives. This committee is designed to provide feedback to the PI concerning his/her protocol at an early.
- Resource Reviews: If NIEHS CRU resources, NIH Clinical Center resources or clinical support contract resources are needed in order to conduct the research, the PI must submit information to the respective committees that control the desired resource. .
- Biostatistical and Scientific Review: All research must undergo in depth *ad hoc* biostatistical and scientific review. The extent of the review is determined by the complexity of the study and the risk to human subjects.

- Human Research Protection Review: After the protocol has passed scientific and biostatistical review, the protocol is then forwarded to the IRB for human research protections review.

Currently, NIEHS has 61 active clinical protocols. Fifty-two protocols are NIEHS reviewed and nine protocols are reviewed outside of NIEHS (3 at NIAID, 5 at NIDDK and 1 at NHGRI). Eighteen of the 61 protocols are reviewed by the full board and 34 protocols undergo expedited review. The total number of active Epidemiology Branch protocols is 42 whereas the total number of active Non-Epidemiology Branch protocols is 19.

Currently, the NIEHS has 16 IRB Members. There are 11 affiliated members and 5 non-affiliated or community members. In addition, the IRB has 2 alternate IRB members from NCI.

NIEHS Human Research Protection Training

The NIEHS OHRC has developed a comprehensive education and training program for investigators, study staff, IRB members and OHRC staff. There is mandatory NIH required training for all individuals who are associated with clinical research. In addition, there is ongoing education and training offered by NIH and NIEHS.

NIEHS QA/QI Program

The NIEHS OHRC has implemented a Quality Assurance/Quality Improvement program to monitor the conduct of clinical research at NIEHS as part of its risk management program. The mission of the QA/QI program is to provide routine monitoring of clinical research studies, assure that the rights and welfare of human research participants are appropriately protected, improve the conduct of clinical research, and ensure that clinical studies are being monitored by an objective body.

The QA program is comprised of five components:

- Monitoring of the NIEHS IRB for compliance with NIEHS HRPP policies and procedures
- Routine Monitoring of clinical research study conduct
- For-cause auditing to investigate allegations of non-compliance with HRPP requirements
- Due-diligence (directed) auditing to assess clinical research conduct for new investigators or to investigate concerns in clinical research conduct (Good Clinical Practices) identified by the IRB or other staff involved in the conduct of the clinical research.

The Quality Improvement Program

The quality improvement program identifies issues and improves human research protections by :

- Additional and supportive education and training
- Correctly identifying the issue, taking corrective measures and developing a prevention plan
- Checking the status of improvement plans

NIEHS OHRC Sharepoint Site
The NIEHS OHRC has developed an interactive website (http://sharepoint.niehs.nih.gov/ohrc/default.aspx) that contains relevant information for PIs, IRB members and OHRC staff. Reference Guides and electronic forms have been developed for each phase of the review process.

NIEHS Customized Protocol Tracking and Management System (PTMS)
The NIEHS has implemented a Protocol Tracking and Management system that provides a paperless, electronic method for the submission, signing, tracking, review and approval of information related to all NIEHS IRB activities.

Association for the Accreditation of Human Research Protection Programs (AAHRPP).
NIH is in the process of seeking AAHRPP accreditation. The purpose of accreditation is for Institutions to improve their Human Research Protection Program. The NIH Office of Human Subjects Research Protections is the NIH office responsible for the overall leadership and oversight for accreditation. Each NIH Institute is responsible for its own Human Research Protection Program. NIH has been preparing for accreditation since 2008 and plans to submit the application package sometime in 2011.