

Standard Operating Procedure

Central DOE Institutional
Review Board (CDOEIRB)

December 2011



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Central DOE Institutional Review Board

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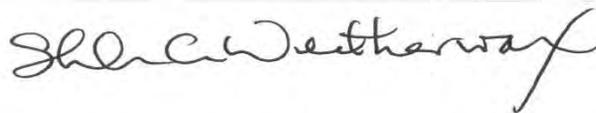
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Acronyms

Beryllium	Be
BeLPT	Beryllium Lymphocyte Proliferation Test
CBeIRB	DOE's Central Beryllium (Be) IRB
CDOEIRB	Central Department of Energy (DOE) Institutional Review Board (IRB)
CITI	Collaborative Institutional Training Initiative
CFR	Code of Federal Regulations
DHHS	U.S. Department of Health and Human Services
DOE	Department of Energy
FDA	Food and Drug Administration
FWA	Federal-wide Assurance
FWP	Former Worker Medical Screening Program
HSP	Human Subjects Program
HSS	DOE Office of Health, Safety and Security
HTM	Human Terrain Mapping
IAA	IRB Authorization agreements
IDE	Investigational Device Exemption
IN	DOE Office of Intelligence and Counterintelligence
IND	Investigational New Drug
IO	Institutional Official
IRB	Institutional Review Board
IRBNet	Electronic submission and management system
NNSA	National Nuclear Security Administration

OHRP	HHS Office for Human Research Protections
PHI	Protected Health Information
PII	Personally Identifiable Information
POC	Point of Contact
SOP	Standard Operating Procedure
SC	DOE Office of Science

CHAPTER 1: PURPOSE, BACKGROUND, AND SCOPE

Purpose

The purpose of this manual is to document the operating procedures [10 Code of Federal Regulations (CFR) Part 745.103(b) (4) & (5)] of the Central Department of Energy (DOE) Institutional Review Board (IRB) (CDOEIRB), or the Board. The functions of the CDOEIRB are to assure that the risks to human participants involved in research under its purview are minimized and reasonable in relation to the anticipated benefits and to protect the rights and welfare of study participants in accordance with applicable Federal regulations, state laws, DOE directives, and existing ethical principles. Imperative for the Board to carry out this function is its autonomy in performing reviews that maintain the protection of the rights and welfare of human subjects in an atmosphere of independence as reflected in these standard operating procedures (SOPs).

Background and Scope

The CDOEIRB was established in January 2010 by four DOE Headquarters organizations: the [Office of Science](#) (SC), the [Office of Health, Safety and Security](#) (HSS), the [National Nuclear Security Administration](#) (NNSA), and the Office of Intelligence and Counterintelligence (IN).

This IRB evolved from DOE's Central Beryllium (Be) IRB (CBeIRB), which was established in 2001 to bring vision, expertise, and consistency to the review of all DOE-funded/conducted human subjects' research and screening related to occupational exposure to beryllium. The CBeIRB ensured that all such projects (many of which are still ongoing today) had informational materials and consent forms that were clear, accurate, and consistent regarding chronic beryllium disease, beryllium sensitization, benefits and risks of screening, and the DOE Energy Employees Occupational Illness Compensation Program. This was particularly important because DOE used the beryllium lymphocyte proliferation test (BeLPT) to determine if former workers had developed beryllium sensitization as a result of their exposure to beryllium at DOE facilities. There were, and continue to be, concerns regarding the risks associated with an abnormal test result, namely, the potential loss of or the inability to obtain various types of insurance and/or employment for a program participant.

In 2010, the scope of the CBeIRB was expanded and the name was changed to the CDOEIRB, or the Board. The [CDOEIRB](#) serves as DOE's IRB of record for purposes of satisfying the human subjects' protection requirements of the DOE and U.S. Department of Health and Human Services (DHHS) for study protocols that involve employees of DOE or its contractors and/or are explicitly funded by, or conducted by, DOE or other agencies or institutions in the following areas:

- Beryllium exposure-related studies sponsored by DOE or involving the DOE workforce.

- Multi-site research involving the health and/or productivity of current workers at DOE facilities.
- A portion of the energy efficiency-related human subjects' research funded by DOE and conducted by outside organizations.
- The Former Worker Medical Screening Program (FWP), including the beryllium sensitization screening component.*
- Human terrain mapping (HTM) projects conducted by DOE laboratories that do not manage their own IRBs**

* The FWP has evolved over the years and now is operated as a service program for any interested former worker from any DOE site. The DOE Office of Health, Safety and Security (HSS) has made a policy decision to continue to require projects under this program to undergo review by the CDOEIRB, despite the fact that they no longer see these projects as traditional human subjects' research. IRB review is required because there are multiple separate screening providers involved and DOE wants to ensure that participants receive clear, accurate, and consistent information regarding:

- The purpose of the program;
- The screening tests they will be offered, such as the BeLPT and, in some workers, the CT scan for early lung cancer detection;
- The potential implications of their participation in the program; and
- How their data will be protected.

The CDOEIRB will be asked to review the protocols, informational materials, and consent forms, using a checklist available in IRBNet, to determine whether the DOE requirements have been met.

** [DOE Order 443.1B, *Protection of Human Research Subjects*](#), Section 4a(2), dated March 17, 2011, outlines DOE requirements for HTM activities. DOE limits engagement of its Laboratories in HTM projects to: 1) development of models and software for use by the Department of Defense (DoD) and other Federal agencies in their analyses of collected HTM data; and 2) analysis of de-identified as defined in the definitions section of this Standard Operating Procedure (SOP) or publicly available data. It is DOE's policy that, prior to initiation, such projects be approved by DOE Headquarters, the DOE or NNSA human subjects protection (HSP) program manager (see Chapter 3), and if intelligence-related, also IN-10). DOE Headquarters will engage the CDOEIRB, and potentially, the DOE laboratory principal investigator (PI), in confirming that the intention of the PI is to work only with de-identified or publicly available data. Once the project is initiated, the recognized DOE IRB (and in the case of DOE laboratories that do not have their own site IRB, the CDOEIRB) is the only entity authorized to determine whether the HTM data received by the PI after project initiation meets the DOE criteria for de-identification. The CDOEIRB, therefore, will be responsible for working with certain DOE laboratory

PIs to: 1) discuss the datasets received from the sponsor and/or any other data to be used to ensure they are sufficiently de-identified for the PI to begin work; and 2) complete and sign a data security agreement with the PI using the DOE-provided template ([Human Terrain Mapping Data Review Process/Standard Operating Procedure](#)). DOE also expects that the CDOEIRB will periodically (not less than once a year) follow up with the PI to check on progress and scope of the work being conducted. Any modifications in scope would require both Headquarters and CDOEIRB approval.

Several emerging issues may become challenging enough to warrant the CDOEIRB serving as the DOE IRB of record for related research. These could potentially include issues such as health impacts of exposure of nanomaterials and other topics not yet identified.

SC, NNSA, HSS, and IN will collectively determine which, if any, emerging issues warrant the CDOEIRB to be the lead IRB.

Exclusions

The scope of the CDOEIRB excludes those projects that are classified, in part or in totality, which will be overseen by the CDOEIRB-Classified.

Also, the scope for the CDOEIRB specifically excludes all health/medical services provided by DOE site occupational medical clinics to current workers.

Within DOE, SC-23 and NNSA-SH-40¹ are responsible for making final decisions as to what constitutes DOE-related human subjects' research and how human research subjects must be protected. When questions or uncertainties arise regarding the applicability of human subjects protection regulations to research, the final resolution is made by the DOE HSP program manager, SC-23, or the NNSA HSP² program manager, NNSA-SH-40.

¹ For Projects funded by NNSA, conducted at NNSA sites, or using NNSA data.

² For NNSA-related research.

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CHAPTER 2: OVERVIEW

Numerous Federal statutes set forth the requirements and expectations for IRB performance. The root of all these requirements is the fundamental desire that all human research subjects be treated with respect, dignity, and an assurance that risk will be held to the lowest achievable level consistent with the goals of the research. The principles that underlie the protection of human subjects today are found in three main documents:

- [The Nuremberg Code](#)³
- [The Declaration of Helsinki](#), 2008
- [The Belmont Report](#)⁴

Basic Ethical Principles

The CDOEIRB is guided by the ethical principles set forth in these documents, including the following three principles outlined in the Belmont Report:

Respect for Persons: requires that potential subjects be given the information they need, in language they understand, to decide whether or not to participate in a study, as well as the time and opportunity necessary to make that decision without any pressure to participate.

It further requires protection of subject privacy, confidentiality of data, and increased protection for vulnerable populations.

Beneficence: requires that researchers (and their institutional organizations) minimize the probable risks and maximize the potential benefit(s) to the subjects and/or society in which they participate.

Justice: requires that the benefits and burdens of research be distributed fairly. Subjects should be recruited on the basis of their relation to the problem under study rather than their easy availability, their compromised position, or their malleability. Investigators should base inclusion/exclusion criteria on those factors that most effectively and soundly address the research problem. For example, subjects should not be denied access to a study simply because they may not speak English.

3 Reprinted from Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182. Washington, D.C.: U.S Government Printing Office, 1949

4 The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979

IRB Role

IRB Review Requirements

All domestic and foreign institutions or sites where research involving human subjects is conducted or funded by DOE or that use information or data on DOE employees are required to perform this research in keeping with applicable Federal regulations (45 CFR Part 46, *Protection of Human Subjects*), and DOE-specific requirements (articulated in 10 CFR Part 745, *Protection of Human Subjects* and DOE Order 443.1B, *Protection of Human Research Subjects*). Subpart A of the federal regulations, 45 CFR Part 46, is replicated word for word in the DOE-specific regulations, 10 CFR 745. While 10 CFR Part 745 does not address the additional sub-parts of 45 CFR Part 46, DOE Order 443.1B requires compliance with these additional Sub-parts.

A determination made by the Federal oversight office for human research, the HHS Office for Human Research Protections (OHRP), requires prospective and continuing review and approval of human subjects' research activities by a committee, usually called an IRB. The primary mandate of IRBs is to protect the rights and welfare of humans who are the subjects of research. Regulations require that the membership of the IRB be diverse in order to provide expertise in and sensitivity to a broad range of scientific and ethical considerations.

As mentioned above, DOE requires that all IRBs under its purview comply with [10 CFR Part 745](#) (which is identical to Subpart A of 45 CFR Part 46), and also with [45 CFR Part 46](#), Subparts B, C, D, and E, as well as [DOE Order 443.1B](#).

Criteria for IRB Approval of Research Involving Human Subjects

Federal regulations allow an IRB to approve research only after it has determined that all of the following requirements are satisfied (per 10 CFR Part 745.111):

- (1) Risks to subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk. Whenever appropriate, researchers should employ procedures that are being performed on subjects for diagnostic or treatment purposes.
- (2) Risks to subjects are reasonable relative to
 - a. anticipated benefits, if any, to subjects, and
 - b. the importance of the knowledge that may reasonably be expected to result.
- (3) The selection of subjects is fair and equitable, taking into account the purposes of the research and the setting in which it will be conducted. The IRB must be particularly attentive to any special problems that may arise when research involves vulnerable populations, such as children, pregnant women, prisoners, mentally disabled persons, or economically or educationally disadvantaged persons. If any one of the subjects is likely to be susceptible to undue influence or coercion, the IRB may require additional safeguards in the study to protect such subjects.

- (4) Informed consent will be sought from each prospective subject, or the subject's legally authorized representative, generally by means of a written consent document. The IRB will carefully review these documents to assure that they contain the required elements of informed consent (see 10 CFR Part 745) and are understandable to a lay person.
- (5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 10 CFR Part 745.117.
- (6) The research plan makes adequate provisions for ensuring the safety of subjects.
- (7) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- (8) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects. These requirements are incorporated in the CDOEIRB review standards. For all initial protocol reviews, these standards must be addressed and recorded in the minutes.

IRB PROTOCOL REVIEW STANDARDS Minimal regulatory requirements for IRB review	
Regulatory review requirement	Suggested questions for IRB discussion
1. The proposed research design is scientifically sound and will not unnecessarily expose subjects to risk.	(a) Is the hypothesis clear? Is it clearly stated? (b) Is the study design appropriate to test the hypothesis? (c) Will the research contribute to generalizable knowledge and is it worth exposing subjects to risk?
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result.	(a) What does the IRB consider the level of risk to be? (b) What does the PI consider the level of risk/discomfort/inconvenience to be? (c) Is there prospect of direct benefit to subjects or to the advance of scientific knowledge?
3. Subject selection is equitable.	(a) Who is to be enrolled? Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously ill persons? Healthy volunteers? (b) Are these subjects appropriate for the protocol?

IRB PROTOCOL REVIEW STANDARDS Minimal regulatory requirements for IRB review	
Regulatory review requirement	Suggested questions for IRB discussion
<p>4. Informed consent is obtained from research subjects or their legally authorized representative(s).</p> <p>5. Informed consent will be appropriately documented in accordance with, and to the extent required by 10 CFR Part 745.116.</p>	<p>(a) Does the informed consent document include the eight required elements (see below)?</p> <p>(b) Is the consent document understandable to subjects?</p> <p>(c) Who will obtain informed consent (PI, nurse, other) and in what setting?</p> <p>(d) If appropriate, is there a children's assent?</p> <p>(e) Is the IRB requested to waive or alter any informed consent requirement?</p>
<p>6. The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</p>	<p>(a) What is the nature and scope of foreseeable risks to the subjects?</p> <p>(b) Does the research design minimize risks to subjects?</p> <p>(c) Would use of a data and safety monitoring board or other research oversight process enhance subject safety?</p>
<p>7. Subject privacy and confidentiality are maximized.</p>	<p>(a) Will personally identifiable research data be protected to the extent possible from access or use?</p> <p>(b) Are any special privacy and confidentiality issues properly addressed, e.g., use of genetic information?</p> <p>(c) Should a data management plan be required?</p>
<p>8. If vulnerable populations are involved, additional safeguards have been included.</p>	<p>(a) Are children, prisoners, pregnant women, mentally disabled persons, or other disadvantaged persons involved in the research?</p> <p>(b) DOE also considers worker and former worker participants a vulnerable population and thus asks that its reviewers consider whether appropriate safeguards have been provided.</p>
Additional considerations	
<p>1. Ionizing radiation</p>	<p>(a) If ionizing radiation is used in this protocol, is it medically indicated or for research use only?</p> <p>(b) Is there need for review by a radiation safety committee?</p>
<p>2. Cooperative research</p>	<p>(a) Is this domestic/international cooperative research?</p> <p>(b) If so, are FWAs or other assurances required for the sites involved?</p> <p>(c) Is there a Cooperative Research and Development Agreement?</p>
<p>3. FDA-regulated research</p>	<p>(a) Is an IND or IDE involved in this protocol?</p>

Eight Required Elements of Informed Consent⁵

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.
- (2) A description of any reasonably foreseeable risks or discomforts to the subject.
- (3) A description of any benefits to the subject or to others that may reasonably be expected from the research.
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- (6) For research involving more than minimal risk, an explanation as to whether any compensation and/or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
- (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Risk/Benefit Assessment

Regulatory definition of minimal risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [[10 CFR Part 745.102\(i\)](#)]. Risks considered to be minimal for most individuals may be considered greater than minimal in a vulnerable population.

The risk categories are:

- The research involves no more than minimal risk to subjects;
- The research involves more than minimal risk to subjects;

⁵ The statement that the study involves research in the first element, as well as the fourth element of informed consent, are optional for FWP projects.

- The risk(s) represents a minor increase over minimal risk; or
- The risk(s) represents more than a minor increase over minimal risk.

Benefit: A research benefit is something of health-related, psychosocial, or other value to an individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Money or other compensation for participation in research is not considered a benefit. Benefits will typically fall into one of the following categories:

- No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition;
- No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge to further society's understanding of the disorder or condition under study; or
- The research involves the prospect of direct benefit to individual subjects.

CHAPTER 3: AUTHORITIES AND RESPONSIBILITIES

Protecting the subjects of research is a shared responsibility involving institutional officials, research investigators, IRBs and research subjects.

DOE

DOE shall operate and maintain the CDOEIRB in accordance with 10 CFR Part 745 and with 45 CFR Part 46, [*Protection of Human Subjects*](#) Sub-parts B, C, D, and E, as well as DOE Order 443.1B.

Senior DOE Official (Institutional Official)

The Associate Director of Science for the Office of Biological and Environmental Research is the senior DOE official, or institutional official (IO), and is responsible for:

- Ensuring the CDOEIRB complies with applicable Federal and DOE regulations;
- Ensuring that the OHRP Federal wide Assurance (FWA) and CDOEIRB registration are properly maintained and current;
- Serving as SC's management liaison to the CDOEIRB (see below);
- Making final determinations on CDOEIRB composition and membership, taking into consideration recommendations from the CDOEIRB chair, the DOE management team, and other senior DOE management liaisons. Issuing appointment letters to Board members;
- Making final determinations on selection of the CDOEIRB manager (voting member) and the associate CDOEIRB manager (alternate to the CDOEIRB manager), who do not have term limits; and
- Terminating, with input from the chair and the management team, members for cause.

Senior DOE Management Liaisons

SC, NNSA, HSS, and IN will each name a senior management liaison to the CDOEIRB, who will be jointly responsible for:

- Ensuring appropriate allocation of funding/resources for the CDOEIRB;
- Determining scope of CDOEIRB activities;

- Attending meetings as non-voting, ex-officio representatives and/or designating an individual from their organizations to serve in that capacity. During meetings, the senior DOE management liaisons may share information on the background and context of DOE program(s) but will not contribute to the CDOEIRB's deliberations about any particular proposal;
- Approving recommendations for resolving unanticipated problems and/or adverse events;
- Approving recommendations for resolving serious noncompliance; and

Human Subjects Protection (HSP) Program Managers

The [DOE HSP program manager](#) (SC-23.2) and the [NNSA HSP program manager](#) (NA-SH-40) are responsible for:

- Coordinating efforts and corresponding on a regular basis with their respective Senior DOE Management Liaisons and with HSS and IN to facilitate smooth Board operation, in compliance with Federal and departmental requirements;
- Facilitating the education of Board members in compliance with Federal agency and institutional requirements;
- Reviewing and approving statements of work for proposed human terrain mapping (HTM) projects prior to project initiation and coordinating with the CDOEIRB, and if necessary, the PI and/or sponsor, to verify that the data to be used will be de-identified (as defined in this SOP);
- Concurring on the plan for any corrective actions, following significant adverse events, unanticipated problems (including a finding of a suspected data breach involving loss or compromise of personally identifiable information (PII)), complaints about the research, suspension or termination of CDOEIRB approval of research, known or potential incidents of non-compliance.

DOE (CDOEIRB) Management Team

The DOE HSP program manager, the NNSA HSP program manager, the FWP program manager (HS-14), the IRB coordinator of the FWP (HS-14), and a representative from IN-10 will serve as the CDOEIRB management team, which has the following responsibilities:

- Serving as the DOE points of contact for the CDOEIRB;
- Addressing issues that arise with regard to the CDOEIRB operation;
- Making recommendations to their senior DOE management liaisons regarding funding and scope of Board activities;

- With input from the CDOEIRB chair, making recommendations to the IO on CDOEIRB composition and membership, including the CDOEIRB manager. This may include adding or removing positions on the Board, depending on the expertise needed and available funding.
- Jointly with the chair, making recommendations to the IO on board member re-appointments after their initial 3-year term.
- Facilitating the education of Board members in compliance with Federal agency and institutional requirements;
- Assisting in the resolution of significant unanticipated problems, adverse events, and noncompliance issues;
- Approving SOPs and any revisions to SOPs; and
- Attending meetings as non-voting, ex-officio representatives.

CDOEIRB Administrative Team

The CDOEIRB administrative team consists of the CDOEIRB chair, vice chair, and CDOEIRB manager.

Chair

The chairperson (chair) is responsible for providing professional leadership and ensuring that the Board carries out its responsibilities. The chair does not vote except in the case of a tie in the membership vote. Chair responsibilities include but may not be limited to the following:

- Jointly with the CDOEIRB management team, making recommendations to the IO regarding board composition and membership;
- Jointly with the CDOEIRB management team, making recommendations to the IO regarding member re-appointments after the initial 3-year term;
- Determining the type of review required (Full Board, Expedited, or Exempt);
- Conducting or delegating expedited reviews;
- Performing chair functions at meetings;
- In consultation with the administrative team, making and communicating determinations regarding conflict of interest;
- Establishing CDOEIRB authorization agreements (IAA) with collaborating (institutional or site) IRBs as appropriate;

- Making initial determinations regarding adverse events, unanticipated problems, and serious or continuing non-compliance;
- Communicating and collaborating with the IO, the CDOEIRB management team, PIs, and/or chairs or members of other IRBs as appropriate (i.e., regarding adverse events, unanticipated problems, and serious or continuing non-compliance);
- Setting the meeting agenda;
- Ensuring the timely review of research protocols; and
- Making a determination (either based on a review by the administrative team or by other Board members) as to whether HTM data received by the PI following DOE approval and project initiation meets DOE criteria for de-identification.

Vice Chair

The CDOEIRB vice chair has the following responsibilities:

- Acting as chair in the chair's absence; and
- Assisting with Board activities, as requested by the chair.

CDOEIRB Manager

The CDOEIRB manager is a voting member. The associate CDOEIRB manager does not vote (unless the CDOEIRB manager is not present at the meeting) but assists the CDOEIRB manager with accomplishing the following responsibilities:

- Serving as primary point of contact (POC) for the CDOEIRB for CDOEIRB members, PIs, and other institutional IRBs;
- Verifying that members have completed required training;
- Assisting the chair and vice chair in making a determination about type of review required and who will serve as primary and secondary reviewers;
- Scheduling meetings and related travel of the Board and others as needed;
- Reviewing all submitted materials for completeness and distributing materials to Board members;
- Generating minutes of meetings;
- Generating and providing all correspondence to CDOEIRB members, PIs, and other involved institutions, as appropriate;

- Maintaining the electronic submission and management system (IRBNet); and
- Maintaining all CDOEIRB records, including training records.

Members

Members' responsibilities are as follows:

- Completing initial DOE-required training, [*Collaborative Institutional Training Initiative \(CITI\)*](#) following appointment;
- Completing refresher CITI training every three years, as required by DOE;
- Attending scheduled meetings;
- Reviewing all materials distributed by the CDOEIRB manager prior to scheduled meetings;
- Participating as primary or secondary reviewers or conducting expedited reviews when requested by the chair, vice chair, or CDOEIRB manager; and
- Performing other CDOEIRB-related activities when requested by the chair, vice chair, or CDOEIRB manager.

Principal Investigators

Principal investigators' (PIs') primary responsibilities are to protect the rights and welfare of human research subjects and comply with all applicable provisions of Federal law, any special requirements of the DOE, and any requirements set by the CDOEIRB. PIs must be familiar with the ethical principles of human subjects' research and the requirements of Federal regulations, DOE directives, and applicable state laws. PIs have the following responsibilities:

- Submitting required materials to the CDOEIRB for review and approval in a timely manner;
- Justifying the need to involve human subjects in research;
- Ensuring that all risks to subjects associated with the protocol are understood and clearly communicated and that each potential subject clearly understands the nature of the research;
- Providing a copy of the signed CDOEIRB-approved informed consent document to each participant at the time of consent unless the CDOEIRB has specifically waived this requirement;
- Ensuring that all signed consent documents are retained in accordance with the terms of DOE's contract, grant, or cooperative agreement or DOE's applicable records retention schedules, if DOE is not the funding source;

- Ensuring that subject privacy and data confidentiality are protected insofar as allowed by law and providing evidence of compliance with DOE requirements for the protection of PII;
- Promptly reporting any proposed changes in previously approved research to the CDOEIRB, and not initiating changes without approval by the CDOEIRB;
- Reporting progress of approved research to the CDOEIRB as often as, and in the manner prescribed by, the CDOEIRB, but not less than annually;
- Promptly reporting to the CDOEIRB any adverse events or unanticipated problems involving risks to subjects or others;
- Notifying the CDOEIRB when the project is complete or needs to be inactivated;
- Notifying the Food and Drug Administration (FDA) and the Board whenever it is anticipated that an investigational new drug (IND) or device exemption (IDE) will be required;
- Ensuring that research is conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA) requirements when required;
- Providing evidence of professional credentials (CV or resume), and initial and refresher training in human subjects protection (through CITI or comparable training provider) for all members of the research team who interact with subjects and/or have access to PII prior to commencement of research activities; and
- Prior to initiation of HTM projects, ensuring: 1) approval by DOE Headquarters [[see DOE Order 443.1B, Section 4a\(2\)](#)]; and 2) that the CDOEIRB has been provided with written verification that only de-identified data, as defined in this SOP] will be used. After project initiation and before beginning work, following the DOE-approved procedures to ensure appropriate CDOEIRB review and approval of any datasets to be used.

CHAPTER 4: CDOEIRB STRUCTURE

Membership

The CDOEIRB will comply with the membership requirements of 10 CFR Part 745.107. The CDOEIRB will be composed of at least five members with various backgrounds to promote complete and adequate review of human subject research activities. Its membership will be sufficiently qualified through the experience, expertise, and diversity of its members, including consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

The CDOEIRB membership will be assessed annually at the beginning of each fiscal year to ensure that the Board is responsive to the areas of research under its purview and that the requirements of 10 CFR Part 745.107 are fully satisfied. Membership of the CDOEIRB will include the following:

- Equitable and reasonable gender representation;
- At least one member whose primary concern is with scientific matters;
- At least one member whose primary concern is with nonscientific matters; and
- At least one member who has not been employed by DOE or its contractors on a full or part-time basis;

Additional members may include the following:

- One member from each of three established DOE/NNSA site IRBs;
- Three (non-voting) alternates, each from a different established DOE/NNSA site IRB not represented by the DOE/NNSA site IRBs noted above;
- One member from each of two FWP medical screening providers;
- Two (non-voting) alternates, each from a different FWP medical screening provider than those represented by the members noted above;
- Two current or former DOE/NNSA workers, each from a different DOE/NNSA site, if possible;
- Two (non-voting) alternates who are current or former DOE/NNSA workers and are from different sites, if possible, than the voting current or former members on the Board;

- Two members derived from the community proximate to a DOE/NNSA organization, site, or facility that have never been employed by DOE/NNSA and do not have immediate family members who are former or current DOE/NNSA organization, site, or facility employees; these individuals should be considered leaders in the community;
- Two (non-voting) alternates derived from the community proximate to a DOE/NNSA organization, site, or facility that have never been employed by DOE/NNSA and do not have immediate family members who are former or current DOE/NNSA organization, site, or facility employees; these individuals should be considered leaders in the community; and
- One expert in the protection of personally identifiable information.

The CDOEIRB may invite individuals with competence in special areas to assist in the review of studies that require their specific area of expertise. These individuals will leave the room before final discussions and will not have a vote.

Members will not participate in initial or continuing review of any project in which they have a conflict of interest.

Non-voting Members

Each of the three (voting) members from established DOE/NNSA site IRBs will be assigned an alternate (non-voting) member from a different DOE site (as mentioned above). Each member representing an FWP medical screening provider will have an alternate member from a different FWP medical screening provider. Each worker representative will be assigned a worker representative alternate, ideally from a different DOE/NNSA site. Each community representative will be assigned a community representative alternate from a different community. The alternate member may participate in voting if the primary member is unavailable. When each voting member representing DOE/NNSA site IRB(s), the FWP, workers, and the community rotates off the CDOEIRB, the alternate will have the option of taking his/her place if approved by the Board.

Selection and Appointment of Members and Chair

Recommendations for Membership: Recommendations for CDOEIRB membership, including alternates and the positions of chair and vice chair, may be made to the IO by any voting or non-voting member of the Board and by DOE/NNSA officials associated with the CDOEIRB.

Potential members will be asked to provide a resume to the CDOEIRB manager, who will share the information with the chair and the CDOEIRB management team. The CDOEIRB chair and management team will make recommendations to the IO, who will determine the final board composition/membership. Only the chair and vice chair positions require prior IRB experience.

Appointment: Board members will receive a letter of invitation from the IO.

Chair and Vice Chair Terms: The chair and vice chair will serve three-year terms. The vice chair will act in the chair's absence and may assume the role of chair after the chair vacates that

position if approved by two-thirds of the eligible voting Board members. Ideally, the chair and vice chair positions will overlap to preserve continuity on the Board.

Board Members and Alternates Terms: Board members and alternates will serve three-year terms. Terms will end in January 2013 and every three years thereafter.

Alternates may succeed to their respective primary position if desired and approved by the IO, at which time, a new alternate may be appointed.

Additional Terms: Additional terms may be served by any member of the Board, if desired, and if re-appointed by the chair and the management team. It is recommended that no more than two consecutive three-year terms be served by any one member, including the chair and vice chair. It is also recommended that members with alternates serve only one term, so as to ensure adequate representation from all DOE sites.

Liability Insurance for Members: DOE, through the Oak Ridge Institute for Science and Education (ORISE), will provide liability insurance for members who otherwise do not have such insurance. It is assumed that members who are employees of DOE laboratories or other organizations are provided with liability insurance through their organizations.

Resignation/Termination of Members

Members may resign from the CDOEIRB at any time, but fulfilling existing terms is encouraged. In the event of a member's resignation before fulfilling the existing term, three months' notification in writing is requested, along with the reason for discontinuing membership.

Termination by the IO of a member from the CDOEIRB prior to expiration of his or her term requires documented "just cause" to show that continuation or renewal of a member's term would be detrimental to the Board. Just cause for removal may include, but is not limited to, unexcused absences for more than 50 percent of the meetings in a year, misconduct, unresolved conflict of interest, failure to complete required training (see below), or a consistent pattern of failure to complete work as assigned or requested by the chair, vice chair, or CDOEIRB manager.

Member Training

Members and alternates are required to successfully complete CITI training following appointment to the Board, with refresher training required every three years thereafter for active members and alternates. Successful completion requires 80 percent accuracy. CITI training records will be maintained for individual members by the CDOEIRB manager(s). Maintenance of other relevant training records, such as attendance at Public Responsibility in Medicine and Research (PRIM&R) and local seminars is the responsibility of individual members.

Time is also allocated on the agenda during each meeting to educate members and to address current issues and pending changes in regulations. The CDOEIRB chair or members may use this time to disseminate other pertinent or educational information.

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CHAPTER 5: REVIEW AND APPROVAL

It is DOE policy that all research involving human subjects that falls under the purview of the CDOEIRB be reviewed and approved by the CDOEIRB prior to the commencement of research/screening activities.

Initial Review of New Studies

The CDOEIRB shall be notified by the PI of all new proposals that fall within the scope of the CDOEIRB. Awareness of this responsibility is developed through specified job duties and mandatory training in human subjects' protection within the PI's institution and outreach and educational programs provided by DOE SC and the CDOEIRB.

Proposal Review Package – The following documents are the minimum required to conduct an initial CDOEIRB review. PIs will be notified by the CDOEIRB manager(s) of any other documents that may be required to complete the proposal review package. All submissions must have consecutively numbered pages to facilitate review and comment regarding the protocol.

- A completed Review Request (Application) form;
- The complete research/funding application. This documentation should include provisions for the protection of human subjects in accordance with all applicable laws and regulations, and any related paperwork (e.g., an activity-specific Standard Operating Procedure, manufacturer's specification sheets, safety reports, etc.);
- A proposed informed consent form that includes all required elements;
- Any proposed advertisement or recruitment materials;
- Copies of approvals from any collaborating institutions' IRBs;
- Policies and procedures for the protection of PII (see Attachment I) – these may be an integral part of the research protocol but should address how the PI will comply with all DOE PII requirements;
- Any HIPAA-related release forms or data use agreements, if applicable; and
- For FWP projects, a protocol handbook during initial CDOEIRB review.

The chair, with input from the vice chair and/or the CDOEIRB manager, will review the application to determine if: 1) the proposed activity requires review and approval by the CDOEIRB, as well as the level of review required; or 2) whether to exempt a protocol from CDOEIRB review. When the CDOEIRB's approval of a protocol is final, the PI will provide a copy with "tracked changes" and a clean/final copy of all revised documents as approved.

Levels of Review

The length of time required to review an application generally depends on the review category into which a given application falls, but may also be impacted by the PI's timely response to requests by the CDOEIRB for additional supporting information. Federal regulation 10 CFR 745.109 allows for three levels of review: (1) exempt, (2) expedited, and (3) full Board. The level of potential risk to the subjects determines the level of review required. The higher the risk, the greater the rigor of review. The CDOEIRB manager will make a recommendation to the chair regarding level of review. Recommendations made by the PI, DOE site, or other institutional IRBs may also be considered. The chair will make the final determination regarding the level of review. Once the chair has made a determination, the CDOEIRB manager will inform the PI regarding the level of review and the general expected time required by the CDOEIRB for such review.

Exempt Review

Certain low-risk research activities are [exempt](#) from full Board review, as listed in 10 CFR Part 745.101(b); however, the chair or vice chair must conduct a preliminary review to determine whether the research meets the criteria for exemption. The chair or vice chair may engage one or more CDOEIRB members in such a review. The final determination shall be made by the chair, in consultation with the vice chair. Exempted proposals will be posted on IRBNet to provide Board members with the option of reviewing and posting their comments. Exempted studies will also be included on the next full Board meeting agenda under "Actions Taken." Annually, the CDOEIRB manager will contact the PI to determine whether the project is still ongoing, and if so, whether any changes in scope are anticipated.

Expedited Review

[Expedited](#) review may be conducted by the chair or others appointed by the chair such as the vice chair, CDOEIRB manager or by a designated, experienced, and eligible voting member, or a group of experienced and eligible voting members designated by the chair. Following an expedited review, the reviewer may recommend that the chair approve a proposal, ask for modifications, or refer it to the full Board.

To be considered for expedited review, proposed research must meet two conditions:

- (1) It must present no more than *minimal risk* to subjects; and
- (2) It must fit into one of the [identified research categories](#), as listed in 10 CFR Part 745.110.

Expedited review may also be used for [minor changes](#) to approved research and for continuation reviews of protocols previously approved at a convened meeting, if the CDOEIRB has determined and documented at the convened meeting that that the research involves no greater than minimal risk and no additional risks have been identified.

The requirements for approval of a protocol under the expedited review mechanism are the same as those that apply to a full Board review (e.g., sound scientific protocol, proper informed consent procedures, minimization of research risks, etc.).

When the expedited review procedure is used, Board members are informed via IRBNet (or by other electronic means) and by including those projects on the agenda for the Board's next meeting, under "Actions Taken."

Proposed research cannot be disapproved under [expedited review procedures](#) and must instead be submitted for full board review.

Full Board Review

Protocols that do not meet federal requirements for exemption or expedited review require [review at a convened meeting](#) by a valid quorum of CDOEIRB members. To be approved, proposed research must receive the approval of a majority of those voting members present (a valid quorum must exist at the time the vote is taken). Alternates in attendance at the meeting may not vote unless the primary member is not there, has a conflict, or for other reasons recused himself/herself. As noted in Chapter 3, the chair also does not vote, except in the case of a tie among voting members. Prior to the Board voting, the CDOEIRB chair will ask that representatives with direct programmatic oversight of the project leave the room. As an example, for NNSA projects, the NNSA HSPP manager would leave the room, but the DOE HSPP manager would remain.

Conflict of Interest and Confidentiality

The term "conflict of interest" in this context refers to a set of conditions in which an investigator's judgment concerning a primary interest (e.g., subject welfare, integrity of research) could be biased by a secondary interest (e.g., personal, professional, or financial gain). Conflicts of interest are particularly important to consider in biomedical and behavioral research because of the impact such conflicts can have on human health. The conduct and review of research must be managed carefully to ensure that neither individual nor institutional financial interests result in danger to subjects.

A conflict of interest exists when investigators, CDOEIRB members or consultants and their immediate family members, including spouses, life partners, children, parents, or other dependents, can be shown to have any financial incentive or personal or professional interests that could cause them to lose their objectivity (or create the appearance thereof) in the conduct or review of research that may, in turn, compromise the validity and integrity of that research and negatively impact the public's trust in DOE's ability to protect human research subjects.

The appearance of a conflict may be just as serious and potentially damaging as a confirmed conflict. Reports of conflicts based on appearances can undermine public trust in irreparable ways even when mitigating facts of a situation are brought to light. Apparent conflicts, therefore, should be evaluated and managed with the same vigor as known conflicts.

Investigators, CDOEIRB members, and consultants to the CDOEIRB are required to reveal any real or apparent conflict of interest that may apply to the work they are conducting or reviewing. Conflict of interest takes many forms. Investigators, CDOEIRB members, and DOE management and staff should be aware of the types that exist and report them promptly to the CDOEIRB. In all instances the CDOEIRB has the authority to make a final determination and take appropriate action, particularly when the rights and welfare of subjects might be impacted.

Investigators

Investigators are required to describe any potential financial or personal conflicts of interest in their application for CDOEIRB review. They may initiate discussions with the CDOEIRB administrative team prior to completing the application or submit the information to the CDOEIRB. In either case, the chair will inform the investigator when the CDOEIRB determines that a conflict exists that may undermine the investigator's objectivity, or create the appearance thereof, in the conduct of that research. When the CDOEIRB determines that a conflict exists, it will defer approval until the conflict has been eliminated or resolved. The CDOEIRB may take the following action(s):

- Require modifications to the protocol;
- Require documentation that the conflict of interest has been eliminated or resolved;
- Require assignment of an alternate investigator; and
- Deny approval if the conflict cannot be resolved.

In most instances, modifications or changes to mitigate a conflict of interest must be approved by the convened Board. The convened Board may, at the time of original review, authorize the CDOEIRB administrative team to approve minor modifications under expedited review procedures. The investigator and CDOEIRB members will be copied on the results of that review.

CDOEIRB Members and Consultants

A conflict of interest exists when an CDOEIRB member, consultant, and/or their immediate family member, defined as a spouse, life partner, child, parent, or other dependent, meets any of the following criteria:

- Receives any financial compensation directly related to the research, of any amount;
- Serves as an investigator or advisor on the study under review;
- Has a personal relationship or conflict with any investigator on the protocol;
- Is involved in the design, conduct, or reporting of the research;

- Has ownership interest, stock options, or other financial interest related to the research, of any value;
- Has an equity interest in the company sponsoring the research;
- Has a proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement or royalties from such rights whose value may be affected by the outcome of the research;
- Holds, or has held within the last 12 months, a significant or influencing position in the company sponsoring the research;
- Has a financial interest in a company that is in direct competition with the sponsor/protocol under review; and
- Has any other interest that would interfere with their decision-making process.

CDOEIRB Members

CDOEIRB members are required to notify the chair or other member of the administrative team that a conflict of interest exists prior to reviewing a protocol. They may accomplish this by contacting any member of the CDOEIRB administrative team prior to the convened meeting or by declaring the conflict at a convened meeting where conflict of interest is addressed as a standing agenda item. In either case, the CDOEIRB chair will notify the CDOEIRB at the convened meeting before the protocol review. CDOEIRB members with a confirmed conflict of interest must leave the room (cannot participate in the discussion, vote, or be counted toward quorum for the review of the protocol with which they have a conflict of interest).

Consultants

When consultants are invited to participate in the review of a protocol, a member of the CDOEIRB administrative team will explain DOE conflict of interest requirements, which include the consultant's responsibility for reporting any potential conflict of interest to the CDOEIRB chair or other member of the CDOEIRB administrative team. If the CDOEIRB administrative team determines that no conflict of interest exists, the consultant may provide information, pose questions to the investigator, and participate fully in the discussions (though a consultant may never vote). If a conflict of interest exists, consultants will not be invited to participate in the CDOEIRB review in any manner.

Primary/Secondary Reviewers

At the chair's discretion, a member of the CDOEIRB may be assigned as a primary/secondary reviewer for protocols requiring full Board or expedited review. Reviewers will perform an in-depth review of all documentation and submit their comments in writing for distribution at the meeting. Other CDOEIRB members will also receive and review the protocol documents. The

primary reviewer should have expertise in the area of the protocol being reviewed, but the secondary reviewer should not to ensure protocols are understandable to all.

Informed Consent

PIs are required to provide informed consent documents that address all the elements of informed consent as prescribed in 10 CFR Part 745.116, and all elements required by DOE, including those required for the FWP. Also, PIs are responsible for ensuring that legally effective informed consent documents comply with the following requirements:

- Be obtained using a consent form that has been reviewed and approved by the appropriate IRBs within the previous 12 months or less;
- Be obtained from the subject or the subject's legally authorized representative;
- Be in nontechnical language (ideally at an eighth-grade reading level) understandable to the subject or his/her representative;
- Clearly state that participation is voluntary and that the subject may withdraw at any time without penalty or loss of their rights; and
- Be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subject should or should not participate;
- Not include [exculpatory language](#) through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights or language that releases or appears to release the PI, the sponsor, the institution or its agents from liability for negligence.

Waiver or Alteration of Informed Consent

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or may waive the requirement to obtain informed consent provided the IRB finds and documents in the project records and meeting minutes that the requirements of 10 CFR Part 745.116(d) are met:

- The research presents no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information following their participation (e.g., a fact sheet).

A waiver of informed consent may be requested in the case of records-based studies where the study participants will not be contacted and the primary risk from the study is loss of privacy. Procedures must be in place to protect the privacy of the data and to protect any PII. Requests

for a waiver or alteration of informed consent must be initiated by the PI with the submission of the protocol, citing criteria from 10 CFR Part 745 and how the conditions of his/her protocol qualify under each criterion.

Documentation of Consent (10 CFR Part 745.117)

Except as otherwise waived or altered, informed consent will be documented by the use of the written consent form approved by the IRB and signed by the subject or the subjects' legally authorized representative. The consent form may be either of the following:

- A written consent document that embodies the required elements of informed consent required in 10 CFR Part 745.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator will give either the subject or the representative adequate opportunity to read it before it is signed.
- A "short form" written consent document stating that the elements of consent have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there will be a witness to the oral presentation. The IRB will approve a written summary of the information being presented. The short form will be signed by the subject and/or the subject's legal representative and both will receive a copy of the summary information.

Subjects will be given a copy of the consent document for their keeping and future reference.

Waiver of Documentation of Informed Consent

An IRB may waive the requirement for the investigator to obtain a signed consent form [10 CFR Part 745.117(c)] for some or all subjects if it finds either of the following to be true:

- The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a break of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.
- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

Requests for a waiver of documentation of informed consent must be initiated by the PI with the submission of the protocol, citing the criteria in 10 CFR Part 745.117(c) and how the conditions of his/her protocol qualify for each criterion. When the documentation requirement is waived, the Board may require the PI to provide subjects with a written statement regarding research.

Disposition of a Protocol Following CDOEIRB Review

When the CDOEIRB reviews a proposed protocol, it has four options:

- **Approve:** Protocol is approved as submitted, or approved with recommended revisions.

- **Approve with conditions:** (see below): Protocol requires modifications or PI must furnish additional information, prior to final approval by the CDOEIRB.
- **Defer:** Protocol needs major revision or rework before the CDOEIRB can complete review or the Board has unresolved questions and the PI is not available to address them.
- **Disapprove:** Protocol does not meet the minimum criteria required for approval.

To approve a research study, the CDOEIRB must ensure that all the following requirements have been satisfied:

- Risks to subjects are minimized and reasonable in relation to anticipated benefits;
- Selection of subjects is equitable;
- Participation is voluntary, and informed consent will be sought and appropriately documented, unless the need for obtaining or documenting informed consent has been specifically waived;
- Adequate provisions are made to protect subject privacy and confidentiality of data;
- When any subjects are likely to be vulnerable to coercion or undue influence, additional safeguards are included to protect the rights and welfare of those vulnerable subjects; and
- All special DOE/NNSA imposed requirements have been satisfied.

Conditional Approval

If the CDOEIRB grants conditional approval pending changes to the proposal, it must delegate authority to the administrative team (and/or other individual(s) with appropriate expertise or qualifications) and note the delegation in the minutes. The required changes must be completed before the administrative team will grant final approval of the proposal. Alternatively, the CDOEIRB may approve, but impose certain restrictions or conditions on the researchers or on the conduct of the research. **In all conditional approval cases, the PI will be given a limited time period in which to respond to the satisfaction of the Board.** For continuing reviews, the response must be reviewed and approved prior to the protocol's current expiration date. If the response is not approved prior to the expiration date, a memo is sent to the PI that approval has lapsed and that no work may be performed until CDOEIRB approval has been obtained.

Three Steps Required for Conditional Approval

- (1) CDOEIRB specifies conditions for approval in writing to the PI;
- (2) PI meets conditions set by the CDOEIRB and provides documentation to the CDOEIRB within a reasonable time as established by the Board; and

- (3) The administrative team verifies that conditions have been met. If verification cannot be made, the proposal cannot be approved and all research activities involving human subjects, biological specimens, or information generated from human subjects must cease until the protocol receives full, unconditional approval.

Defer

When the CDOEIRB determines at a convened meeting that the information provided to them is inadequate to conduct a comprehensive review, or there are unresolved issues regarding the research, the protocol will be deferred pending an appropriate response from the PI. The PI will be informed at that time that activities involving the recruitment or use of subjects may not begin until the protocol has been fully approved. For continuing reviews, work may continue until the protocol expiration date. Major changes require approval by the convened Board at the next scheduled meeting. In some instances, the CDOEIRB may also vote to meet by phone, as allowed by [OHRP](#), as long as the voting members have: 1) received all pertinent material prior to the meeting, and 2) can actively and equally participate in the discussion of all protocols. Minutes of such meetings must clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements

Disapprove

If a study is disapproved, the CDOEIRB will notify the PI and institution in writing and specify the reason(s) for disapproval so the investigator has an opportunity to respond in person or in writing. Investigators have the right to petition the CDOEIRB to reconsider disapproved proposals, with or without modifications. Reconsideration by the full Board may not occur until the next convened meeting. No research may be conducted on a protocol that has been disapproved by the CDOEIRB.

Appeal Process

If a protocol presented at a convened meeting is deferred, disapproved, or requires modifications, the CDOEIRB notifies the PI in writing regarding the issues that need to be addressed for approval.

In cases where there is disagreement between the CDOEIRB and the PI regarding the nature and extent of the requested changes and these disagreements cannot be resolved amicably in an informal manner, the PI and/or the CDOEIRB may appeal to the institutional official for a resolution of the matter. The institutional official may organize a meeting to help facilitate discussion between the CDOEIRB and the PI. The final determination, however, will be made by the CDOEIRB, reflecting the Board's autonomy and responsibilities to assure that the risks to human participants involved in research under its purview are minimized and reasonable in relation to the anticipated benefits and to protect the rights and welfare of study participants in accordance with applicable Federal regulations, state laws, DOE directives, and existing ethical principles.

Approval Period

When the CDOEIRB approves a study, it must also establish a schedule for continuing review. The maximum approval period of 12 months is granted to studies that are determined to be no greater than minimal risk. Studies that have potential for greater than minimal risk are evaluated on a case-by-case basis, and review frequency determined by considering factors such as the health and vulnerability of subjects involved, previously reported adverse events, and investigator/group experience with the proposed work.

Notice of Approval

When all conditions for approval have been satisfied, the CDOEIRB manager will prepare an approval letter notifying the PI of the date of CDOEIRB approval and the date that approval expires. This notice includes the requirements and conditions of approval.

Documentation

Investigators cannot initiate research until they have received documented approval by the CDOEIRB of the protocol and all related forms.

Cooperative Research

[Cooperative research](#) projects involving more than one institution and potentially more than one IRB are permitted under 10 CFR Part 745.114. With the approval of DOE, an institution participating in a cooperative project may enter into a joint review arrangement, may rely upon the review of another institution's qualified IRB, or may make similar arrangements to avoid duplication of effort. When conducting cooperative research, each participating institution is responsible specifically for safeguarding the rights and welfare of the human subjects involved, and an IRB authorization agreement (<http://www.hhs.gov/ohrp/assurances>) must be in place. From DOE's viewpoint, however, the CDOEIRB will remain the IRB of record for all projects under its purview, and no other IRB within or outside the DOE system may take on that role. However, if an FWP provider's IRB, for example, typically also reviews the project protocol and would like to make arrangements to rely on the CDOEIRB's review to avoid duplication of effort that would be acceptable to DOE, provided an IRB authorization agreement between the organizations was established.

International Projects

International projects will be reported to the appropriate HSP program manager prior to initiation and will be conducted in conformance with all applicable regulations (e.g., DOE Order 443.1B and 10 CFR Part 745.101(h)).

CHAPTER 6: POST-APPROVAL EVENTS AND ACTIONS

Continuing Review

Federal regulation 10 CFR Part 745.109(e) requires that approved protocols be periodically reviewed to ensure the continuing protection of human subjects over the course of the research. The scheduling of these reviews should be appropriate to the level of risk involved in the study but not less than once every 12 months. At the time of initial review, the CDOEIRB will make a determination regarding the risks associated with the research protocols. Risks associated with the research will be categorized as no more than minimal, minor increase over minimal or major increase over minimal based on the absolute interpretation of minimal risk. The PI is notified 90 and 60 days in advance of the scheduled date of continuing review of each protocol through IRBNet. As with the initial review of new protocols, the continuing review may be conducted either by the full Board or by an expedited mechanism, depending on the level of risk involved in the research and as outlined in 10 CFR Part 745. The PI will be notified of the level of review required. The application for Continuing Review is available through IRBNet, and on the CDOEIRB webpage. The CDOEIRB will require that, as part of the application package, the PI submit a copy of a redacted signed consent form.

The CDOEIRB may determine that some projects need verification from outside sources that no material changes have occurred since the last review. Requiring independent verification may be based on a routine audit plan or any legitimate concern that may include, but is not limited to the following: a history of investigator non-compliance, complaints from institutional IRBs or subjects that appear not to be adequately addressed by the key research personnel, studies where key research personnel have disclosed or failed to disclose significant conflicts, and/or studies that exhibit high risk profiles. The details of the independent verification will be worked out on a case-by-case basis but may include conducting an audit before reporting findings.

A protocol is considered expired and out of compliance with the terms and conditions of CDOEIRB approval if the CDOEIRB has not re-approved the protocol prior to the protocol's expiration date. All activities involving subjects must stop until the protocol has been appropriately reinstated, unless the CDOEIRB determines that it is in the best interest of the individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration date. Retroactive approval is not allowed under any circumstances.

Amendments/Modifications to an Approved Protocol

The PI will submit a completed Amendment/Modification Request form for all proposed modifications or amendments to an approved protocol through IRBNet to initiate CDOEIRB review and approval prior to their implementation. The review of modifications to an existing protocol may be conducted by either the full Board or the expedited mechanism depending on the level of risk involved and the scope of the proposed changes. In general, modifications to

project personnel and solicitation materials, such as flyers, will be processed administratively by an acknowledgement letter. Final determination of the level of review required for each modification will be determined by the CDOEIRB chair. Changes to an approved protocol shall not be implemented without CDOEIRB approval.

Acknowledging CDOEIRB Receipt of Supplemental Information Received from PIs

Periodically, PIs may submit miscellaneous documents, such as annual reports, copies of project-related presentations, etc., that have not been specifically requested by the CDOEIRB but are relevant to the project. In such situations, the CDOEIRB will keep the document(s) on file and respond to the investigator with the following: "Receipt acknowledged. No CDOEIRB action needed."

Project Completion/Termination

When a study is completed, the PI must notify the CDOEIRB and submit a final report by uploading the completed closure report form to IRBNet. The closure report will be acknowledged by the administrative team. The project closure will be listed in the next meeting agenda.

Deviations from Approved Protocol

The PI may not deviate from an approved protocol without written CDOEIRB approval, except when such deviation is necessary to eliminate an immediate hazard to a study subject.

Any individual noting a deviation from an approved protocol is responsible for reporting the deviation or concern to the CDOEIRB. The CDOEIRB will then review the protocol and any relevant documentation and assess the deviation according to two main criteria:

- Potential or actual harm to the subject; and
- Potential or actual effect on the integrity of the study data that affects the risk/benefit ratio of the research.

The CDOEIRB will determine whether the incident is a serious violation (a subject was harmed, the potential for harm was created, or the violation compromised the integrity of the study) or non-serious (violation did not harm or potentially harm a subject and does not compromise study integrity).

The CDOEIRB will also determine whether further corrective action is warranted:

- If the protocol violation is deemed serious, the CDOEIRB will suspend the study; and
- If the protocol violation is deemed non-serious, correspondence will be sent from the chair of the CDOEIRB to the PI and the designated institutional representative of the PI's parent institution, directing investigation of the incident (if not already accomplished) and corrective actions.

All findings and conclusions of the CDOEIRB will be documented in the protocol file. All the actions outlined above will be conducted in conjunction with all engaged IRBs.

Suspension or Termination of CDOEIRB Approval

In accordance with DOE requirements 10 CFR Part 745.113, the CDOEIRB has the authority to place on administrative hold, suspend, or terminate approval of research that is not being conducted in accordance with the terms and conditions of the CDOEIRB approval (including the requirements for continuing review), or has been associated with unexpected or serious harm to subjects.

Suspension of CDOEIRB approval is “a temporary withdrawal of CDOEIRB approval for some or all research procedures or a permanent withdrawal of approval for some research procedures.” Studies that have been suspended still require continuing review. A suspended study may be re-opened after the problem triggering the suspension has been resolved.

Termination of CDOEIRB approval is defined as “a permanent withdrawal of CDOEIRB approval for all research procedures.” Terminated protocols are considered closed and no longer require continuing review.”

Any suspension or termination of CDOEIRB approval will be reported promptly to the PI and to his/her line management via a letter that will clearly describe the action and the reasons for the action taken by the CDOEIRB. The CDOEIRB administrative team will also be responsible for reporting to the management team. Reporting to OHRP may also be required (<http://www.hhs.gov/ohrp/compliance/reports/>). Issues not resolved within 30 working days will be reported to the senior DOE official and the research sponsor.

- (1) The chair has the authority to suspend a protocol in the situation of a deviation that is serious; and
- (2) The advice and recommendations of the full CDOEIRB will be addressed once the subjects are no longer at risk.

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CHAPTER 7: UNANTICIPATED PROBLEMS, ADVERSE EVENTS, AND INSTANCES OF NON-COMPLIANCE

When unanticipated problems, adverse events, or instances of non-compliance occur, they must be systematically evaluated, corrected, and reported, as appropriate to the situation.

Unanticipated Problems

The phrase *unanticipated problems* involving risks to subjects or others is included, but not defined, in 10 CFR Part 745. During the design of research, investigators carefully consider all possible outcomes that human volunteers may experience in conjunction with the planned protocol. This process forms the basis from which estimates of risk are derived and mitigating actions are planned to minimize the risk. Typically each of these potential events is included in the protocol narrative; some of these events may in fact be deleterious to the research participant, but not unanticipated. OHRP has published guidance to assist in the identification of unanticipated problems. In general, to be classified as an unanticipated problem, any incident, experience, or outcome should meet all three of the following criteria:

- (1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the CDOEIRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- (2) Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- (3) Likely to place subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

When the event is determined to be an unanticipated problem, as defined by the three criteria, it must be reported as required by 10 CFR Part 745.103(a) and 10 CFR Part 745.103(b)(5). Unanticipated problems can include loss or compromise of protected health information (PHI) or PII, with a loss of privacy or confidentiality to a research participant or others.

Adverse Events

Likewise, the term *adverse event* is included, but not defined, in 10 CFR Part 745. In OHRP guidance, the term in general is used very broadly and includes any event meeting the following definition:

Any unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subjects participation in the research, whether or not considered related to the subject's participation in the research.

Adverse events may encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

Noncompliance/Violations/Complaints

All reports of non-compliance, alleged violations of human subjects regulations, and complaints from research subjects will be investigated by the CDOEIRB. Substantiated allegations will be forwarded to the CDOEIRB chair for appropriate action as outlined below.

The CDOEIRB chair must immediately report the following to the senior DOE official, the DOE management team, and OHRP:

- Any serious or continuing noncompliance with the regulations or requirements of the CDOEIRB; and
- Any suspension or termination of CDOEIRB approval for research.

For DOE-funded research reviewed by the CDOEIRB that is conducted by other institution(s), the PI must report to his/her institution's IRB and the CDOEIRB all unanticipated problems, adverse events, and other instances of noncompliance, violation, or complaint within 48 hours, even if there is no obvious causal relationship between the study activities and the event. If there is any possibility of loss or compromise of PII or serious harm to a participant, the PI must report to his/her institution's IRB and the CDOEIRB **immediately**. The CDOEIRB administrative team is responsible for immediately notifying the CDOEIRB management team, who will need to concur on the plan for any remaining corrective actions.

The following minimum information must be included:

- (1) Appropriate identifying information for the research protocol, such as the title, investigator's name, and the CDOEIRB project number;
- (2) A detailed description of the incident, experience, or outcome;
- (3) An explanation of the basis for determining that the incident, experience, or outcome represents an unanticipated problem or adverse event; and
- (4) A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem or adverse event.

The CDOEIRB has authority, under Federal regulations at 10 CFR Part 745.109(a), to require, as a condition of continued approval by the CDOEIRB, submission of more detailed information

about any adverse event or unanticipated problem occurring in a research protocol for which it has CDOEIRB jurisdiction.

Any proposed changes to a research study in response to an adverse event or unanticipated problem must be reviewed and approved by the CDOEIRB and the CDOEIRB management team before being implemented, except when necessary to eliminate apparent immediate hazards to subjects. If the changes are more than minor, the changes must be reviewed and approved by a convened meeting of the CDOEIRB [10 CFR Part 745.103(b)(4) and 10 CFR Part 745.110(a)].

Under some circumstances, incidents must be reported to OHRP
http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html:

- (1) Any unanticipated problems involving risks to subjects or others;
- (2) Any serious or continuing noncompliance with HHS policy or the requirements of determinations of the CDOEIRB;
- (3) Any suspension or termination of CDOEIRB approval.

The CDOEIRB administrative team will coordinate reporting the unanticipated problem and/or adverse event to OHRP, communicating with the investigator's institutional IRB (if applicable), devising a remediation plan, and all other related follow-up activities required of the investigator. The remediation plan must be shared with and concurred on by the DOE management team. Depending on the nature of the unanticipated problem and/or adverse event, the CDOEIRB may determine that the project:

- (1) may continue while corrective actions are being taken;
- (2) must be temporarily suspended until the problem is resolved and/or the protocol rewritten;
or
- (3) must be terminated. Studies terminated by the CDOEIRB must be reported to OHRP.

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CHAPTER 8: MONITORING

Research Conduct

During the course of the research, the PI must comply with all CDOEIRB decisions, directives, conditions of approval, and the responsibilities described in these guidelines. The CDOEIRB may need to contact the PI or (with approval of the participant) the participant, to evaluate the project's compliance with requirements.

Monitoring Evaluations

The CDOEIRB has the responsibility to monitor and evaluate both the CDOEIRB itself and PIs to assure that the CDOEIRB review and approval process, as well as the PI's research activities, are in compliance with the applicable regulatory and procedural requirements and conditions of CDOEIRB approval. The CDOEIRB will conduct comprehensive self-evaluation after three years and at least every three years thereafter using the OHRP Self Assessment Tool, and will also be reviewed during that time by an external team organized by the DOE management team, using the OHRP Quality Assurance Consultation model, to ensure compliance with Federal and DOE requirements to assess effectiveness of the program.

The CDOEIRB will also annually evaluate a subset of the research activities under its purview (as described below) using the requirements of this SOP as well as the applicable DOE and Federal requirements.

PI Evaluation

During the course of the research, the PI must comply with all CDOEIRB decisions, directives, conditions of approval, and the responsibilities described in these guidelines. The CDOEIRB may contact subjects directly or monitor the research to evaluate the PI's conduct and compliance with requirements.

Each fiscal year, the CDOEIRB chair will determine which research activities will be evaluated by the CDOEIRB. The selection should be based on relative risk and complexity of the research, and those programs that have demonstrated negative performance in the past and/or have more than minimal risk designation should be reviewed more frequently.

The CDOEIRB chair is encouraged to coordinate evaluation efforts with the DOE management team and the PI's home institution to minimize duplicative efforts and disruption to the PI research activities.

For each evaluation that is selected, the chair will appoint two Board members to the PI evaluation team. The members of the team shall have no conflict of interest, and at least one member should have previous evaluation experience.

The team will evaluate compliance with federal and DOE requirements using on-site document reviews, interviews with the PI, staff, and subjects, or a combination as needed to assure a complete review. The results of the evaluation will be forwarded to the CDOEIRB chair for disposition and corrective actions.

During the interactions with the PIs, the CDOEIRB team will also ask for feedback on how the PIs believe interactions with the CDOEIRB are working and whether the PIs have any suggested improvements for the CDOEIRB.

NOTE: If the review indicates a non-compliance or violation of the applicable requirements, the evaluation team must immediately notify the CDOEIRB chair for further investigation and possible reporting to the DOE management team.

Suggested program elements include:

- (1) Review of study documentation including, but not limited to, determining that unanticipated problems, adverse events, or other instances of non-compliance are reported, protocol amendments are filed with the CDOEIRB, etc.;
- (2) Review of the consent process, including documents signed by enrolled subjects;
- (3) Review of processes used to assure PII protections are in place and effective;
- (4) Evaluation of training records for research staff; and
- (5) Other subject areas deemed appropriate by the chair.

CHAPTER 9: MEETINGS

Scheduled Meetings

The Board shall convene at least twice within each 12-month period and will meet in person or by teleconference. Phone meetings are considered acceptable by [OHRP](#), as long as the voting members have: 1) received all pertinent material prior to the meeting, and 2) can actively and equally participate in the discussion of all protocols. Minutes of such meetings must clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements

Meetings may be held more frequently as necessary to ensure that the Board meets its responsibilities in accordance with federal and DOE-specific requirements.

The CDOEIRB manager will prepare a preliminary agenda for each meeting. After approval by the chair and DOE management team, the CDOEIRB manager will distribute the agenda and all relevant meeting materials to CDOEIRB members at least two weeks prior to the meeting. A final agenda will be distributed at the meeting. Investigators who fail to submit their materials by the required submission date will be scheduled for the next available meeting.

Minutes

The CDOEIRB manager will take the minutes and submit them to the chair for approval. Final review by the Board, including any noted modifications, will occur at the beginning of the next full Board meeting. Any corrections, modifications, or additions to the minutes will be reported in the next set of meeting minutes. Copies of the minutes will also be sent to the CDOEIRB management team and the senior DOE management liaisons.

Quorum and Voting

A quorum is defined as a simple majority of eligible CDOEIRB voting members, including at least one nonscientific member. Should the quorum fail during a meeting (e.g., loss of a majority through recusal of members with conflicting interests or early departures, or absence of a nonscientific member), the CDOEIRB may not take officially binding actions or votes unless the quorum can be restored. All voting is conducted in closed session, and voting privileges shall be limited to CDOEIRB voting members present at the meeting. Proxy votes are not accepted. The outcome of Board votes is recorded by the CDOEIRB manager; a majority vote is required for any CDOEIRB determination.

No member may participate in the CDOEIRB vote or review of any protocol in which the member has a real or perceived interest or conflicting interest, except to provide information requested by the CDOEIRB. A CDOEIRB member with any conflict of interest must recuse himself or herself from both the discussion of the project and voting. Such action will be noted in the meeting minutes. Recusals could result in loss of a quorum, in which case voting cannot

take place until a quorum has been re-established. If a quorum cannot be re-established, the project or projects must be deferred until the next meeting.

CHAPTER 10: RECORDKEEPING

CDOEIRB Records

All official CDOEIRB records will be stored in IRBNet. Any hard copies will be stored in the CDOEIRB manager's office in locked file cabinets for a minimum of three years after completion of the study, consistent with the requirements of 10 CFR Part 745.115. After that time, all records will be archived and stored in a secured area for the period specified by DOE record retention schedules.

Protocol Records

The CDOEIRB manager will assign each protocol a unique, sequential number that indicates the fiscal year and order of receipt. Official CDOEIRB records for each protocol include the following:

- All documentation reviewed by the CDOEIRB, including the proposal/funding application and scientific evaluations, if any, that accompany the proposal, any subject recruitment material, questionnaires, a list of any published documents, progress reports submitted by investigators, and reports of any injuries to subjects;
- All correspondence related to the protocol, including e-mail exchanges;
- A list of all telephonic communication related to the protocol with a brief summary of the content of each phone call;
- Copies of any press releases related to the protocol that are initiated by the PI;
- Notes from protocol review sessions including reviewer written comments; and
- Approved consent forms, including a copy of a redacted, signed consent form (to be submitted with the continuing review application).

Note: The PI retains all signed consent forms.

Meeting Minutes

Minutes [10 CFR Part 745.115(a)(2)] of CDOEIRB meetings shall be taken in sufficient detail to show the following:

- Attendance, including voting members and alternates, invited experts, and any guests present; members absent; and late arrivals or early departures by voting members and/or their alternates;
- Actions taken by the CDOEIRB (including listings of exempt and expedited reviews);

- The vote on these actions, including the number of members voting for, against, and abstaining;
- The basis for requiring changes or disapproval of proposed protocols;
- A written summary of the discussion of controverted issues and the Board's action; and
- Reports of unanticipated problems or adverse events and the action taken by the Board.

Other Official Records

The CDOEIRB manager will maintain the following records, in addition to protocol records and meeting minutes, in compliance with 10 CFR Part 745.115:

- As required by 10 CFR Part 745.103(b)(3), a current membership list that lists members and their areas of expertise, as well as archived rosters;
- Board members' curriculum vitae (CV), at time of appointment and reappointment to the Board;
- Written procedures for the CDOEIRB and investigators in the same detail as described in 10 CFR Part 745.103(b)(4) and 10 CFR Part 745.103(b)(5);
- Records of continuing review activities;
- Correspondence between the CDOEIRB and the investigators and their local site and institutional IRBs, where appropriate;
- Statements of significant new findings provided to subjects, as required by 10 CFR Part 745.116(b)(5); and
- Reports of unanticipated problems and adverse events and their resolution.

Training Records

Members shall keep documentation of training, or records of completion of training, as required by the Board. Proof of required training must be furnished to the CDOEIRB manager, who will maintain a record of training for each Board member and report to the administrative and management teams if a Board member is out of compliance.

PI Records

The PI must retain all research-related records that originate with the PI or the research team for the length of time as required by law, terms of DOE contract, grant, or cooperative agreement, or as stated in the Federal Register.

CHAPTER 11: REFERENCES

The following programs were established to address adverse health effects resulting from occupational beryllium exposure among workers in DOE and DOE-contractor facilities:

- The final rule to establish a [Chronic Beryllium Disease Prevention Program; Worker Health and Safety Program; Final Rule](#) published in February 2006, 10 CFR Part 850 and 10 CFR Part 851;
- The Former Worker Medical Screening Program, as mandated by [the National Defense Authorization Act of 1993 \(P.L. 102-484\)](#); and
- [The Energy Employees Occupational Illness Compensation Program](#) Act of 2000.

Authority for this Standard Operating Procedure is contained in the following documents:

- [10 CFR Part 745, Protection of Human Subjects](#);
- [45 CFR Part 46, Protection of Human Subjects, Subparts B, C, D, and E](#);
- [Department of Energy Order DOE O 443.1B Protection of Human Research Subjects](#);
- [Human Terrain Mapping Data Review Process/Standard Operating Procedure](#);
- [Human Terrain Mapping or Not Human Terrain Mapping](#); and
- [Best Practices for Reviewing Classified Human Subjects' Research at DOE Sites](#).

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CHAPTER 12: DEFINITIONS

Appropriate Program Manager - The DOE HSP program manager and when an NNSA element is involved, the NNSA HSP program manager.

Adverse Event - Any unfavorable medical occurrence in a human subject, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Atomic Energy Act of 1954 - Passed to promote the peaceful uses of nuclear energy through private enterprise and to implement President Eisenhower's Atoms for Peace Program. The Act allowed the Atomic Energy Commission to license private companies to use nuclear materials and build and operate nuclear power plants. This Act amended the Atomic Energy Act of 1946, which had placed complete power of atomic energy development in the hands of the Atomic Energy Commission.

Code of Federal Regulations (CFR) - Published in the Federal Register, a publication of the Federal government that codifies the general and permanent rules for executive departments and agencies. There are 50 titles that represent broad areas subject to Federal regulation. The CFR is updated once each calendar year and is issued on a quarterly basis.

Conditional Approval - Approval of a protocol contingent upon the PI successfully addressing a set of specified concerns identified during any type of protocol review.

Conflict of Interest - Any affiliation or personal, professional, or financial connection with the institution or person submitting a protocol that might create the appearance of impropriety that could undermine confidence in the individual.

De-identified Data - A data set that has no, or limited, identifiers and for which a person with current knowledge of generally accepted scientific principles determines that the risk that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient, has been reduced to the extent practicable. A graded approach must be used in balancing the de-identification of the datasets and the usability of the dataset to accomplish the needed research.

DOE HQ – Department of Energy Headquarters

Engaged in Human subjects' research – Awardee institutions are automatically considered to be "engaged" in human subjects' research whenever they receive a direct award from DOE or other organization to support such research, even where all activities involving human subjects are carried out by a subcontractor or collaborator. The awardee institution is also responsible for ensuring that all collaborating institutions engaged in the research hold an OHRP-approved assurance prior to their initiation of the research.

Exculpatory Language – Wording in a consent document in which a volunteer research subject is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence. Informed consent may not contain any exculpatory language. Subjects may not be asked to waive, or appear to waive, any of their legal rights, nor may they be asked to release the investigator, sponsor, or institution (or its agents) from liability for negligence.

Federal-wide Assurance – The Federal Policy (Common Rule) for the protection of human subjects requires that each institute “engaged” in Federally-supported human research file an “assurance” of protection for human subjects. The assurance formalizes the institution’s commitment to protect human subjects. The requirement to file an assurance includes both “awardee” and collaborating “performance site” institutions.

HIPAA – Health Insurance Portability and Accountability Act of 1996, Public Law 104-191, a foundation of Federal protections for the privacy of protected health information.

Human Subject– A living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.

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

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for collection of the information to constitute research involving human subjects.

Human Terrain Mapping - Research and data gathering activities primarily conducted for military or intelligence purposes to understand the - human terrain, the social, ethnographic, cultural, and political elements of the people among whom the U.S. Armed Forces are operating and/or in countries prone to political instability. This work includes observations, questionnaires, and interviews of groups of individuals, as well as modeling, and analysis of collected data, and may become the basis for U.S. military actions in such locations. In addition to Human Terrain Mapping (HTM), such activities are often referred to as human social culture behavior (HSCB) and human terrain systems (HTS) studies. It is DOE policy that HTM activities will be managed as HSR.

Informed Consent – A person’s voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or undergo a diagnostic, therapeutic, or preventive procedure. It is obtained after providing the subject with the basic elements of informed consent as set forth in 45 CFR Part 46 and 10 CFR Part 745. Informed consent documents shall include disclosure of all potential risks and related consequences or adverse effects, as well as any benefits that may occur as a result of such participation. In giving informed consent, participants may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

Internet research is any human subjects’ research conducted using the [Internet](#). On the internet are two types of information: *publicly available* and *for authorized use only*.

Publicly Available: Information is publicly available when it is lawfully made available to the general public from: (1) Federal, state, or local government records; (2) Widely distributed media, including information that has been published or broadcast for public consumption, is accessible online to the public, or is available to the public by subscription or purchase; or (3) Disclosures to the general public that are required to be made by federal, state, or local law. Publicly available does not mean “without restriction” (see note below).

For Authorized Use Only: Information that is restricted to authorized users and governed by specific data protection rules.

Note: All internet research, regardless of information type, must comply with the appropriate DOE directives, such as level of security/classification and protection of personally identifiable information (PII). Only information obtained with due authorizations and that complies with applicable requirements will be approved by DOE IRBs/HSPP. The applicable DOE site IRB is the only entity authorized to approve the information to be used. If the DOE site does not manage or operate its IRB, then the Central DOE IRB shall be the responsible IRB.

Legally Authorized Representative – An individual, judicial or other body authorized under applicable law to give consent on behalf of a prospective subject for the subject’s participation in the procedure(s) involved in the research.

Minimal Risk – The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Noncompliance – Failure of a person, group, or institution to act in accordance with Federal and DOE requirements.

The Office for Human Research Protection (OHRP) – The Department of Health and Human Services oversight body that provides guidance and oversight to organizations overseeing and conducting research and to their IRBs.

Ongoing Study/Project – A study/project previously reviewed and approved by the CDOEIRB.

Principal Investigator (PI) – The scientist or other individual designated by his or her site who is responsible for the overall direction of the project.

Private Information – This includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record). Such information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for collection of the information to constitute research involving human subjects.

Protected Health Information (PHI) – This means identifying information about an individual in oral or recorded form, if the information:

- relates to the physical or mental health of the individual, including information that consists of the medical history of the individual’s family;
- relates to the providing of health care to the individual, including the identification of a person as a provider of health care to the individual;
- is a plan of service within the meaning of the Long-Term Care Act, 1994 for the individual;
- relates to payments or eligibility for health care with respect to the individual;
- relates to the donation by the individual of any body part or bodily substance of the individual or is derived from the testing or examination of any such body part or bodily substance;
- is the individual’s health number; or
- identifies an individual’s substitute decision-maker.

Personally Identifiable Information (PII) – Any information collected or maintained about an individual, including but not limited to, education, financial transactions, medical history, and criminal or employment history, and information that can be used to distinguish or trace an individual’s identity, such as his/her name, Social Security number, date and place of birth, mother’s maiden name, biometric data, and any other personal information that is linked or linkable to a specific individual.

Information regarding Federal and DOE requirements for the protection of PII of human research subjects and DOE employees is included in Attachment I.

Quorum – A simple majority of Board members, including at least one nonscientific member.

Research – A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this document, whether or not they are conducted or supported under a program that is considered research for other purposes.

Serious Adverse Event – Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:

- (1) Results in death;
- (2) Is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- (3) Requires inpatient hospitalization or prolongation of existing hospitalization;
- (4) Results in a persistent or significant disability/incapacity;
- (5) Results in a congenital anomaly/birth defect; and
- (6) Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition. Examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Serious Noncompliance – Failure of a person, group, or institution to act in accordance with Federal and DOE requirements, and/or requirements in this SOP, such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject’s willingness to participate in research; or damage or compromise the scientific integrity of research data.

Unanticipated Adverse Event – Any adverse event occurring in one or more subjects in a research protocol, the nature, severity, or frequency of which is not consistent with either

- (1) the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol related documents, such as the CDOEIRB-approved research protocol, any applicable investigator brochure, and the current CDOEIRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
- (2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

Unanticipated Problem – In general, to be categorized as an unanticipated problem, any incident, experience, or outcome should meet all three of the following criteria:

- (1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the CDOEIRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied
- (2) Related or possibly related to the participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)

Likely to place subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Attachment I.

DOE Institutional Review Board Template for Reviewing Human Subjects' Research Protocols that Utilize Personally Identifiable Information

The following items must be addressed in all protocols:

1. Keeping PII confidential.
2. Releasing PII only under a procedure approved by the responsible IRB(s) and DOE, where required.
3. Using PII only for purposes of the Former Worker Medical Screening Program, assisting participants filing claims under the Energy Employees Occupational Illness Compensation Program (EEOICP), or with the consent of the participant.
4. Handling and marking documents containing PII as "containing PII or PHI".
5. Establishing administrative, technical, and physical safeguards to prevent unauthorized use or disclosure of PII.
6. Making no further use or disclosure of the PII except when approved by the responsible IRB(s) and DOE, where applicable, and then only under the following circumstances: (a) in an emergency affecting the health or safety of any individual; (b) for use in another research project under these same conditions and with DOE written authorization; (c) for disclosure to a person authorized by the DOE program office for the purpose of an audit related to the project; (d) when required by law; or (e) with the consent of the participant.
7. Protecting PII data stored on removable media (CD, DVD, USB flash drives, etc.) using encryption products that are Federal Information Processing Standards (FIPS) 140-2, *Security Requirements for Cryptographic Modules*, certified.
8. Using passwords to protect PII used in conjunction with FIPS 140-2 certified encryption that meet the current DOE password requirements.
9. Sending removable media containing PII, as required, by express overnight service with signature and tracking capability, and shipping hard copy documents double wrapped
10. Encrypting data files containing PII that are being sent by e-mail with FIPS 140-2 certified encryption products.
11. Sending passwords that are used to encrypt data files containing PII separately from the encrypted data file, i.e., separate e-mail, telephone call, separate letter.
12. Using FIPS 140-2 certified encryption methods for Web sites established for the submission of information that includes PII.

13. Using two-factor authentication for logon access control for remote access to systems and databases that contain PII (two-factor authentication is contained in the National Institute of Standards and Technology (NIST) Special Publication 800-63 Version 1.0.2, *Electronic Verification Guide*, found at http://csrc.nist.gov/publications/nistpubs/800-63/SP800-63V1_0_2.pdf).
14. Reporting the loss or suspected loss of PII immediately upon discovery to (1) the DOE funding office program manager, and (2) the applicable IRBs (as designated by the DOE program manager); if the DOE program manager is unreachable, immediately notify the DOE-CIRC (1-866-941-2472, www.doecirc.energy.gov).

Attachment II. CDOEIRB Membership Roster

Central DOE Institutional Review Board

Membership Roster - May 2012

CDOEIRB Manager: Becky Hawkins, AAS, CIM
Associate CDOEIRB Manager: Darcy Mallon, BA, CIP

MEMBER NAME	AFFILIATION	EXPERTISE	ALTERNATE
Angela L. Baumann, R.N., M.S., D.O.	Physician for Human Subject Research Program (HSRP) and Voluntary Asst Prof Anesthesiology, SUNY Stony Brook	Anesthesiology/Bioethics	N/A
Robert Bistline, Ph.D.	Retired (Formerly Senior Scientist, DOE Rocky Flats)	Radiation Biology/Occupational Health	N/A
Maureen Cadorette, BSN, MPH, Ph.D.	Johns Hopkins University (Coordinator for Former Worker Program project for Los Alamos and Sandia NM workers)	Nursing and Environmental Health Sciences (FWP Representative)	
Michael Colligan, Ph.D.	Retired NIOSH Psychologist/Former NIOSH IRB Chair	Psychology	N/A
Ann-Marie Dake, M.A., CIP	Lawrence Livermore National Laboratory Human Subjects Protection Program Manager	Bioethics/English (DOE Site IRB Representative)	N/A
David Deubner, M.D., M.P.H.	Brush-Wellman -Occupational Physician	Occupational Medicine	N/A
Betsy Ellis, Ph.D.	Oak Ridge Associated Universities – Site-wide IRB Chair and epidemiologist	Epidemiology	N/A
Kathy Ertell, RN, MS, CIH, CIP	Pacific Northwest National Laboratory – Human Subjects Protection Program Manager	Nursing /Industrial Hygiene (DOE Site IRB Representative)	Gail Van Gorp
Gary Foster	Former Worker (Oak Ridge)	Engineering (Worker Representative)	Robin McLaurin
Don Hagenruber, J.D.	Retired (Formerly Attorney with DOE's National Renewable Energy Laboratory, Oak Ridge National Laboratory, and Oak Ridge Institute for Science and Education)	Lawyer	N/A
*Linda Haskell, MPH	<i>Boston University (Coordinator for the FWP project for former LLNL, Sandia CA, and LBNL workers)</i>	<i>Public Health (FWP Representative)</i>	N/A
Becky Hawkins AAS, CIM	Oak Ridge Institute for Science and Education	CDOEIRB Manager	Darcy Mallon
John Knezovich, Ph.D.	Lawrence Livermore National Laboratory (LLNL) – Director, Strategic University Relations and LLNL IRB Chair	Chemical Ecology (Vice Chair)	N/A
Tim Ledbetter, Ph.D.	Chaplain with Tri-cities Chaplaincy	Clergy (Community Member)	Holly Romig

		Also Community Member on PNNL IRB	
<i>Robin McLaurin, B.S.</i>	<i>Current Worker (Pantex)</i>	<i>Worker Advocacy; Employee Concerns</i>	<i>N/A</i>
<i>*Darcy Mallon, B.A., CIP</i>	<i>Brookhaven National Laboratory</i>	<i>CDOEIRB Associate Manager</i>	<i>N/A</i>
Jim Morris, Ph.D.	Research Scientist, Pacific Northwest National Laboratory (PNNL); PNNL IRB Chair	Microbiology/Immunology (Chair)	N/A
Bill Nebo, MA	Retired Senior Pastor	Divinity (Community Member) Also Community Member on LLNL IRB	Rick Swarts
Patricia Quinn, BA	CPWR – The Center for Construction Research and Training (Coordinator for FWP project for former building trades employees)	English (FWP Representative)	Linda Haskell
Terry Reser, BA, CIP	Sandia National Laboratory – Human Subjects Protection Program Manager	English (DOE Site IRB Representative)	Dena Tomchak
<i>*Holly Romig, MS, LMFT</i>	<i>Retired</i>	<i>Social Work (Community Member)</i>	<i>N/A</i>
Kenneth Silver, DSc, SM	Professor/Researcher, East Tennessee State University/Environ. Health Science	Environmental Health Science	N/A
Mike Simmons	Former Worker (Rocky Flats)	Safety and Health (Worker Representative)	Loretta Valerio
<i>*Frederick (Rick) Swarts, Ph.D.</i>	<i>Assistant Secretary-General, World Association of Non-governmental Organizations</i>	<i>Ethics/Biology (Community Member)</i>	<i>N/A</i>
<i>*Dena Tomchak, Certificate of Applied Science</i>	<i>Idaho National Laboratory – Human Subjects Protection Program Manager</i>	<i>Applied Science/Bioethics (DOE Site IRB Representative)</i>	<i>N/A</i>
<i>*Loretta Valerio</i>	<i>Former Worker (LANL)</i>	<i>Worker Advocacy/Employee Concerns</i>	<i>N/A</i>
Ainsley Weston, Ph.D.	NIOSH/Division of Respiratory Disease Studies	Carcinogen Biochemistry/Toxicology	N/A
<i>*Gail Van Gorp, MS, CIH</i>	<i>Argonne National Laboratory - Industrial Hygienist and Human Subjects Manager</i>	<i>Industrial Hygiene (DOE Site IRB Representative)</i>	<i>N/A</i>

**Alternate Members*

Attachment III. References

10 CFR Part 745, *Protection of Human Subjects*, Department of Energy

10 CFR Part 745.103, *Assuring compliance with this policy—research conducted or supported by any Federal department or agency*

10 CFR Part 745.109, *IRB Review of Research*

10 CFR Part 745.110, *Expedited Review Procedures for Certain Kinds of Research Involving no More Than Minimal Risk, and for Minor Changes in Approved Research*

10 CFR Part 745.115, *IRB Records*

10 CFR Part 745.116, *General Requirements for Informed Consent*

45 CFR Part 46, *Protection of Human Subjects*, Public Welfare, Department Of Health and Human Services

DOE Order 443.1B, *Protection of Human Research Subjects*, March 17, 2011

FIPS 140-2, *Security Requirements for Cryptographic Modules*, Federal Information Processing Standards Publication, December 3, 2002

NIST Special Publication 800-63, Version 1.0.2, *Electronic Authentication Guideline*, National Institute of Standards and Technology, April 2006

The Nuremberg Code, Reprinted from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10*, Vol. 2, pp. 181-182. Washington, D.C.: U.S Government Printing Office, 1949

The Declaration of Helsinki, World Medical Association (WMA), October 2008

The Belmont Report, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979

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