Standard Operating Procedure

Central DOE Institutional Review Board (CDOEIRB)

December 2015

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Revision Log

Standard Operating Procedure

Central DOE Institutional Review Board

Revision No.	Date	Changes Description	Page Modified	Signature of Approval Official
Original	June 4, 2010	Issued Procedure	None	All Management and Administrative Team Members and Institutional Official
Revision 1	November 30, 2011	Modified to incorporate updates to ensure consistency with revised human subjects protection order (DOE Order 443.1B)	All Chapters and Appendices	All Management and Administrative Team Members and Institutional Official
Revision 2	October 2013	Modified to formally recognize changes made to Board membership (smaller board, including no associate IRB manager position), to move responsibility for review of human terrain mapping projects for sites with no internal IRB to the CDOEIRB-C, and also to specifically address a category of research, intentional manipulation of the human environment.	Chapters 1, 3, 4, and attachments	Management Team and Chair
Revision 3	July 2014	Replaced IRBNet with IRB7, updated Board membership, clarified scope (to include review of protocols from sites that do not have an internal IRB that choose to defer to the CDOEIRB, e.g., SRS), and updated the flowchart in Attachment IV	Chapters 1, 5, 6, and Attachments II an IV	Management Team and Chair
Revision 4	December 2015	Added IRB7 (EPS) procedures, Attachment V and VI, made terminology consistent	All chapters and appendices	Team and Chair

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Central DOE Institutional Review Board

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Acronyms

AU	DOE Office of Environment, Health, Safety and Security
Be	Beryllium
BeLPT	Beryllium Lymphocyte Proliferation Test
CBeIRB	DOE's Central Beryllium (Be) IRB
CDOEIRB	Central Department of Energy Institutional Review Board
CITI	Collaborative Institutional Training Initiative
CFR	Code of Federal Regulations
CV	curriculum vitae or resume
DHHS	U.S. Department of Health and Human Services
DOE	Department of Energy
EPS	Electronic protocol system
FDA	Food and Drug Administration
FWA	Federal-wide Assurance
FWP	Former Worker Medical Screening Program
HIPAA	Health Insurance Portability and Accountability Act
HSP	Human Subjects Protection Program
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
NNSA	National Nuclear Security Administration
OHRP	HHS Office for Human Research Protections
ORISE	Oak Ridge Institute for Science and Education
PHI	Protected Health Information
PII	Personally Identifiable Information
PI	Principal Investigator
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. To carry out its duties, the Board operates in accordance with these standard operating procedures (SOPs) but with autonomy in its review and deliberative process.

History, Background, and Scope

The CDOEIRB was established in January 2010 by four DOE Headquarters organizations: the Office of Science (SC), the Office of Environment, Health, Safety and Security (AU), the National Nuclear Security Administration (NNSA), and the Office of Intelligence and Counterintelligence (IN). At present, SC, AU, and NNSA co-fund and oversee the CDOEIRB.

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 Department of Labor managed Energy Employees Occupational Illness Compensation Program.

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.
- Human subjects research in which multiple DOE laboratories/sites are engaged.
- Human subjects research conducted by DOE sites/laboratories that do not have their own internal IRB and choose to rely on the CDOEIRB.

- A portion of the human subjects research involving manipulation of the human environment that is funded by DOE and/or funded by DOE and conducted by outside organizations.*

- The Former Worker Medical Screening Program (FWP), including the beryllium sensitization screening component.**

* DOE requires that all projects that involve manipulation of the human environment, for example, through installation of devices in homes and/or through introduction of gases/chemicals to trace airflow in occupied residential, commercial, or public settings, be managed as human subjects research. Specifically, DOE requires initial review by the CDOEIRB to determine whether the individuals included in the research, whether voluntarily or involuntarily, will be properly informed and protected. Even if the IRB does not see such research as meeting the literal definition of human subjects research (as stated in DOE Order 443.1b), DOE expects that the IRB will review the project (see Attachment IV) initially and annually thereafter and that the project will be subject to the reporting requirements of DOE Order 443.1B (adverse event reporting, annual reporting to the human subjects research database, etc.).

** 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 AU 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 beryllium lymphocyte proliferation test (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 study protocols, informational materials, and consent forms, using a checklist available in the electronic protocol system (EPS), to determine whether the DOE requirements have been met.

Several emerging and/or currently unidentified issues and topics may present challenges that are serious enough to warrant review/oversight by the CDOEIRB. The DOE management team will make a collective determination on a case-by-case basis regarding those for which the CDOEIRB will be the lead DOE 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-50[1] 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 Human Subjects Protection (HSP) Program manager, SC-23, and/or the NNSA HSP[2] program manager, NNSA-S50.

[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 Belmont Report[4]
- The Declaration of Helsinki

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.

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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 subparts of 45 CFR Part 46 (Protection of Vulnerable Subjects), DOE Order 443.1B requires compliance with these additional subparts.

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.

CDOEIRB 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? Note: Generalizable knowledge means knowledge that can be applied to populations or situations beyond those studied. It should be viewed in terms of its contribution to knowledge within the researchers' specific community. So for example, a project of relevance to a particular group at Sandia National Laboratory would be generalizable if: a) the information could be used in other situations/for other purposes within that same group at Sandia National Laboratory; or b) the information would be useful outside of that particular group at Sandia National Laboratory.

Regulatory review requirement	Suggested questions for IRB discussion
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 principal investigator (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?
4. Informed consent is obtained from research subjects or their legally authorized representative(s). 5. Informed consent will be appropriately documented in accordance with, and to the extent required by, 10 CFR Part 745.116.	a) Does the informed consent document include the eight required elements (see below)? b) Is the consent document in a language they understand and conveyed in a manner they understand? c) Who will obtain informed consent (PI, nurse, other) and in what setting? d) If appropriate, is there a children's assent? e) Is the IRB requested to waive or alter any informed consent requirement?
6. The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.	a) What is the nature and scope of foreseeable risks to the subjects? b) Does the research design minimize risks to subjects? c) Would use of a data and safety monitoring board or other research oversight process enhance subject safety?
7. Subject privacy and confidentiality are maximized.	a) Will personally identifiable research data be protected to the extent possible from access or use? b) Are any special privacy and confidentiality issues properly addressed, e.g., use of genetic information? c) Should a data management plan be required? d) Should a certificate of confidentiality be requested?
8. If vulnerable populations are involved, additional safeguards have been included.	a) Are children, prisoners, pregnant women, mentally disabled persons, or other disadvantaged persons involved in the research? b) DOE also considers current and former worker participants a vulnerable population and thus asks that its reviewers consider whether appropriate safeguards have been provided.
Additional considerations	

Regulatory review requirement	Suggested questions for IRB discussion
1. Ionizing radiation	a) If ionizing radiation is used in this protocol, is it medically indicated or for research use only? b) Is there need for review by a radiation safety committee?
2. Cooperative research	a) Is this domestic/international cooperative research? b) If so, are Federalwide Assurances (FWA)s or other assurances required for the sites involved? c) Is there a Cooperative Research and Development Agreement?
3. FDA-regulated research	a) Is an investigational device exemption (IDE) in place/needed? An IDE allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. Is an FDA-regulated investigational drug (IND) involved? Note: If there is a question as to whether a project falls under the oversight of the FDA, the DOE Management Team can help with addressing this question.

Informed Consent

Additional Background on Requirements

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 fifth-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;
- Be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subject should or should not participate; and

- 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

The CDOEIRB may approve a consent procedure that alters some or all of the elements of informed consent or may waive the requirement to obtain informed consent or to provide documentation of informed consent, provided the CDOEIRB 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 CDOEIRB and signed by the subject or the subject's 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 CDOEIRB 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

The CDOEIRB 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 breach 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 the research.

Eight Required Elements of Informed Consent[5]

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.

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

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.

Consent Process

General Information

Delays in IRB approval commonly result from the submission of an inadequate consent form. The following guidelines are meant to assist you with the basic format of your consent form.

- Fifth-grade reading level—The primary goal of a consent form is to provide all required information about a study in language and format that are easily comprehensible and presented at the most likely level of understanding of the subject population. For many studies, the consent form should be written at a fifth-grade reading level. Everyday vocabulary and simple sentence structure should be used throughout the form.

- Lay language—Unless the subjects are themselves medical professionals, scientific or technical terms should either be replaced with or defined in lay language. For example, "blood draw" is preferable to "venipuncture" and "x-ray" to "radiograph."

- Non-legalistic language—Legalistic sounding language such as "You hereby agree," "You certify that," "You, the undersigned, do acknowledge that," should not be used. Also, any phrases similar to the following should not be used: "You understand that," "You realize that," "You have been told that," "It has been explained to me that." Not only do these phrases not ensure a subject's comprehension but they lend the appearance of a legal document to the consent form.

- Consistent use of person—The person in which the form is written should be used consistently throughout. The IRB recommends that the form be written in the second person of the subject, that is, "You have been asked to participate in a research study."

- Page numbering and date—As a record-keeping aid for the study subjects, the IRB members/staff, and the investigators, each page of the consent form should be numbered (preferably "1 of 2," "2 of 2"). In addition, the lower corner of each page of the consent form should include the date of this version of the consent form.

- Correct spelling and grammar—The entire form should be carefully proofread for correct spelling and grammar before it is submitted to the IRB for review.

As described in the Belmont Report, consent must be (1) informed, (2) understood, and (3) voluntary. These are the hallmarks of consent and they provide respect for research subjects by honoring their autonomy. Informed consent is not just a form or a signature but a process of information exchange that includes subject recruitment materials, verbal instructions, written materials, and question and answer sessions. The IRB and investigators share responsibility for

ensuring that the informed consent process is adequate. Rather than an endpoint, the Consent Form should be the basis for a meaningful exchange between the investigator and the subject.

The Consent Form, or information sheet (an unsigned consent document), serves as a written summary of the exact information that is presented to a prospective subject. The investigator is responsible for ensuring that informed consent is obtained from each research subject before the subject participates in the research study. It also serves as a useful reference for both the subject and the investigator.

Obtaining Consent

Investigators should give careful consideration to the process whereby consent is obtained. This should include considerations of how, when, and by whom consent will be obtained. Considerations regarding any special subject population should be addressed, as well.

Children

Federal law defines children as "persons who have not attained the legal age for consent . . . under the applicable law of the jurisdiction." The legal age of consent varies from state to state. When a child is the subject of research, the IRB must determine whether adequate provisions are made for soliciting the assent of the child, as well as the permission of the child's parent or court-appointed guardian. Assent and permission are defined as follows:

Assent—a child's affirmative agreement to participate in research. Failure to object, absent affirmative agreement, should not be construed as assent. In general, children under the age of 7 are considered incapable of providing assent. Children between the ages of 7 and 12 are generally considered capable of providing assent, depending on the nature of the research and the individual child's maturity and psychological state. The assent process for children in this age group should be simplified so it is comprehensible to the child. Children who are at least 13 years old can generally provide assent in a full and meaningful way.

The child's assent is required in all research where the subject has the capacity to comprehend aspects of the study. The assent process assures an element of understanding, cooperation, and a feeling of inclusion on the part of the child and also illustrates the investigator's respect for the rights and dignity of the child in the context of research. Investigators should remember that a child's mere refusal to object to participation in research should not be construed as assent. Out of respect for children as developing persons, they should be asked whether or not they wish to participate in the research, particularly if (1) the research does not involve interventions likely to benefit them and (2) the children can comprehend and appreciate what it means to be a volunteer for the benefit of others.

Parental permission—Current regulations tend to avoid the term "consent" when one person grants approval for another to participate in research. Parents or legal guardians therefore grant "permission" for children to participate in research (45 CFR 46.408). The permission form is, in essence, a consent document and should follow all applicable requirements for informed consent as outlined in this manual.

Whenever possible, the permission of both parents should be obtained; however, current Federal regulations do not require permission from both parents in all research situations. In general, the risk to the child and the prospect of direct benefit for the child as a research subject determine whether single parental/guardian permission may be permitted. If the research involves no greater than minimal risk or greater than minimal risk but presenting the prospect of direct benefit to the child, permission of only one parent is sufficient [45 CFR 46.404]. If the research involves greater than minimal risk and no prospect of direct benefit to the child, consent of both parents must be obtained unless one parent is deceased, unknown, incompetent, not reasonably available, or when only one parent has the legal responsibility for the care and custody of the child [45 CFR 46.408(b)]. Investigators should obtain written permission from the parent/guardian prior to contacting a child for participation in research.

Non-English Speaking Subjects

If the study will include non-English speaking subjects, investigators should discuss the use of translators in the consent process and a copy of the translated Consent Form or information sheet should be submitted with the application.

Subjects Unable to Provide Consent for Themselves

For studies involving subjects who cannot give signed or even verbal consent for themselves (e.g., young children, mentally handicapped persons, unconscious patients), the IRB may waive this requirement if sufficient justification for use of the particular subject group is presented and if appropriate measures for obtaining consent from a legally authorized representative or a relative and/or subject advocate are followed. OHRP has reminded the IRBs of the mandate for obtaining legally effective informed consent prospectively from each research subject or the subject's legally authorized representative.

Alternatives

This section should discuss any alternatives to participation in the study. This can be a short statement, but it should make clear the possible choices (e.g., no participation, some or all of the protocol treatment but without participation in the study, etc.) that are available if the individual chooses not to participate in the study. If the study involves only normal, healthy volunteers, the only alternative is to decline participation in the study.

Financial Considerations

Costs/Financial Considerations

When participation in the study may result in any costs whatsoever to the subjects, clear information must be provided in the consent form regarding these costs. If there are no costs to the subject, this should be clearly stated as well.

If any real or potential financial conflicts of interest have been identified regarding the research activity, that information, as it affects the subject's decision to participate, should be included.

Reimbursement/Payment

When referring to money that subjects will receive in return for participation in a study, either "reimbursement" or "payment" may be used. However, the term "compensation" should not be used because it is used on consent forms to designate compensation for injury. Investigators should avoid connotations of undue influence to participate or that the subject is being employed by the investigator. Rather, the sense should be that subjects will be reimbursed for their time, travel expenses, and the inconvenience of being a research subject.

This section should state the total dollar amount that the subject will be paid for participation in the study and should give any other relevant information, such as prorating, if a subject does not complete the study, or bonus payment at the end of the study. If appropriate, a payment schedule should be included in this section. Subjects should not be required to complete the entire study in order to be reimbursed, and bonus payments for study completion should be modest.

Subjects should be informed how payment will be made (e.g., in cash, by check) and when they will be paid (e.g., immediately after the interview, approximately 6 weeks after individual completion of the study). It is important that this information be clear and complete.

Payments for research participation in excess of $600 per calendar year are considered taxable income. If subjects will be paid more than $600, the Reimbursement section should explain that the institution will request the subject's Social Security number in order to report this income to the IRS.

If there will be no payment or reimbursement to subjects for study participation, this information should be stated in this section.

Questions

This section should provide contact information for the subject in case of questions about the study. The principal investigator's name and phone number must be included in this section, as subjects often wish to contact the person who is supervising the project. The IRB Chair's and Administrator's names and contact information should also be included. Blank lines to be filled in later may be included for additional contact persons. If the person explaining the study and obtaining consent is not the principal investigator, the blank lines in this section may be filled in with that person's name and telephone number, if different, at the time consent is obtained.

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.

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,* Subparts 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 Federalwide Assurance (FWA) and CDOEIRB registrations 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 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 Administrator, who does not have a term limit;
- Terminating, with input from the chair and the management team, members for cause; and
- Making a determination on any requests for exceptions to the requirements outlined in these SOPs.

Senior AU Management Liaison

AU will name a senior management liaison to the CDOEIRB, who will be responsible for:

- Ensuring appropriate allocation of funding/resources from AU for the CDOEIRB, which will be co-funded by SC and NNSA;

- Working with the DOE IO to determine scope of CDOEIRB activities; and

- Attending meetings as a non-voting, ex-officio representative and/or designating an individual from their organizations to serve in that capacity. During meetings, the senior AU management liaison may share information on the background and context of DOE program(s) but will not contribute to the CDOEIRB's deliberations about any particular study.

Human Subjects Protection 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 AU 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;

- Advising the CDOEIRB on DOE-specific expectations for projects involving intentional manipulation of the human environment; and

- 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, or known or potential incidents of non-compliance.

DOE (CDOEIRB) Management Team

The DOE HSP program manager, the NNSA HSP program manager, and the FWP program manager (AU-14) are responsible for:

- Completing initial DOE-required training, Collaborative Institutional Training Initiative (CITI), and completing refresher CITI training every 3 years;

- Serving as DOE points of contact for the CDOEIRB;

- Addressing issues that arise with regard to the operations of the CDOEIRB;

- Making recommendations to their senior management regarding funding and scope of Board activities;

- With input from the chair, making recommendations to the IO on CDOEIRB composition and membership, including the CDOEIRB Administrator. This may include adding or

removing positions on the Board, depending on the expertise needed and available funding.

- With input from the chair, making recommendations to the IO on Board member re-appointments after their initial 3-year term;
- Assisting in the resolution of significant unanticipated problems, adverse events, and noncompliance issues;
- Approving SOPs and any guidance documents, in consultation with the IO; and
- Attending meetings as non-voting, ex-officio representatives.

CDOEIRB Administrative Team

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

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:

- Providing input to the CDOEIRB management team and IO regarding Board composition and membership;
- Providing input to the CDOEIRB management team and 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;
- Concurring on CDOEIRB authorization agreements (IAA) with collaborating (institutional or site) IRBs, which are signed for the CDOEIRB by the IO;
- Making initial determinations regarding adverse events, unanticipated problems, and serious or continuing non-compliance;
- Communicating and collaborating with the IO, the CDOEIRB management team, principal investigators (PI)s, 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; and
- Ensuring the timely review of research protocols.

Vice Chair

The vice chair have the following responsibilities:

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

CDOEIRB Administrator

The CDOEIRB Administrator is a non-voting member and has the following responsibilities:

- Serving as primary point of contact for the CDOEIRB for CDOEIRB members, PIs, and other institutional IRBs;
- Verifying that members and PIs have completed required training;
- Assisting with determinations about type of review required and who will serve as primary and secondary reviewers;
- Notifying the DOE/NNSA HSP program manager(s) of all research that will involve participation of the DOE and/or contractor workforce as human research subjects, upon receipt of a PI request for CDOEIRB review;
- 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 EPS; and
- Maintaining all CDOEIRB records, including training records.

Member

A member's responsibilities are as follows:

- Completing initial DOE-required training, CITI, following appointment;
- Completing refresher CITI training every 3 years, as required by DOE;
- Informing the chair or member of the administrative team if they have a conflict of interest with a proposed or ongoing study;
- Reviewing all materials distributed by the CDOEIRB Administrator prior to scheduled meetings;
- Participating as primary or secondary reviewer or conducting expedited reviews when requested by the chair, vice chair, or CDOEIRB Administrator;
- Attending scheduled meetings; and
- Performing other CDOEIRB-related activities when requested by the chair, vice chair, or CDOEIRB Administrator.

Principal Investigator

Principal investigator's 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 must comply with CDOEIRB decisions, directives, and conditions of approval and have responsibilities including:

- 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;

- Ensuring that research is conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA) requirements, when required;

- Promptly reporting any proposed changes in previously approved research to the CDOEIRB and not initiating changes without approval by the CDOEIRB, except when such changes are necessary to eliminate an immediate hazard to a study subject;

- 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, in accordance with DOE Order 443.1B;

- 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 investigational device exemption (IDE) will be required; and

- Providing evidence of professional credentials (curriculum vitae (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.

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:

- One chair and at least five members with varying backgrounds;
- 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 non-scientific matters; and
- At least one member who has not been employed by DOE or its contractors on a full or part-time basis (unaffiliated).

Additional members may include the following:

- One member from an FWP medical screening provider;
- One (non-voting) alternate from a different FWP medical screening provider than the one represented by the member noted above;
- One current or former DOE/NNSA worker;
- One (non-voting) alternate who is a current or former DOE/NNSA worker and is from a different site, if possible, than the voting current or former member on the Board;
- One member derived from the community proximate to a DOE/NNSA organization, site, or facility who has never been employed by DOE/NNSA and does not have immediate

family members who are former or current DOE/NNSA organization, site, or facility employees; this individual should be considered a leader in the community;

- One (non-voting) alternate derived from the community proximate to a DOE/NNSA organization, site, or facility who has never been employed by DOE/NNSA and does not have immediate family members who are former or current DOE/NNSA organization, site, or facility employees; this individual should be considered a leader in the community; and

- One expert in the protection of personally identifiable information.

Scientist members are members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline. Scientist members are recruited from among active or retired professionals and also from the community.

Non-scientist members are members whose training, background, and occupation would incline them to review research activities from a standpoint outside of any biomedical or behavioral scientific discipline. They may be recruited from among active or retired professionals and also from the community.

Unaffiliated representatives may be scientists or non-scientists, but at least one should be a non-scientist who represents the general perspective of participants; is sensitive to community attitudes in promoting respect of research participants regardless of race, gender, and cultural background; and safeguards the rights and welfare of human subjects. To be eligible for participation on the IRB, neither the member nor any member of his/her immediate family may otherwise have a direct affiliation (employee, contractor, student in a fellowship, volunteer at the institution, or business unrelated to the IRB) with the institution.

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 non-voting or alternate members may vote if the primary member is unavailable. When each voting member representing the FWP, workers, or the community rotates off the CDOEIRB, the alternate will have the option of taking his/her place, if approved by the Board.

Use of Consultants

If the Board chair determines that consultants or experts are required to advise the Board in its review of a study, such an expert or consultant will be recruited and will receive copies of the

research study package. Their presence at the meeting as a non-voting attendee or their written comments on the study package will be invited, whichever is more appropriate. Their opinions will be considered by the Board in reaching its decision on the study.

Compensation of Consultants: An honorarium is given to consultants when they are asked to travel to attend a meeting or participate in a teleconference.

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 IRB Administrator 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 Administrator, who will share the information with the chair and the CDOEIRB management team. The chair and management team will make recommendations to the DOE 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 DOE IO.

Chair and Vice Chair Terms: The chair and vice chair will serve 3-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 the DOE IO. 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 3-year terms. Terms will end January 14, 2019 and every 3 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 3-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.

Compensation of IRB Members: An honorarium is given to unaffiliated IRB members when they are asked to do a primary or designated review, training, travel, or attend a meeting in person or by teleconference.

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, a 3-months notification in writing is requested, along with the reason for discontinuing membership.

Termination of a member by the DOE IO 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, or a consistent pattern of failure to complete work as assigned or requested by the chair, vice chair, or CDOEIRB Administrator.

Member Training

Members and alternates are required to successfully complete CITI training following appointment to the Board. Successful completion requires 80 percent accuracy. CITI training records will be maintained for individual members by the CDOEIRB Administrator. Maintenance of other relevant training records, such as attendance at Public Responsibility in Medicine and Research (PRIM&R) conferences 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 chair or members may use this time to disseminate other pertinent or educational information.

Refresher training

The applicable refresher training is required every 3 years for active members and alternates. The EPS will send out notification starting 90 days before expiration.

CHAPTER 5:
INITIAL 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 PI shall notify the CDOEIRB of all new studies 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.

The steps for initial review are described in detail below. All submissions must have consecutively numbered pages to facilitate review and comment regarding the protocol.

PI Develops Draft Research Protocol

The PI develops a draft protocol to conduct research that will involve human subjects or their personal data. The protocol must reflect what will actually occur in the research. The institution is legally responsible (as are researchers and their supervisors) for research conducted at or sponsored by the institution or using the institution's proprietary information. Once the CDOEIRB has approved a protocol, the research team is required to follow that protocol and to seek CDOEIRB approval for any proposed change before implementing the change, except when such change is necessary to eliminate an immediate hazard to a study subject. The protocol itself becomes a vital part of official documentation. Should anyone question the research, the approved protocol is powerful evidence that the project has sufficient value to justify the risks or inconveniences involved.

If a proposed study is determined to be human subjects research, the PI must familiarize himself or herself with the information in this manual and must be able to demonstrate that s/he is familiar with:

- His or her responsibilities as a PI, and
- The IRB procedures described here.

The PI and/or his or her manager review the proposed research and validate the following:

- Necessity of involving human subjects.
- Scientific merit of the protocol.
- Appropriateness of conducting the proposed study at the institution (or using the institution's funds).
- Source of funding for the protocol.
- Safety issues, including potential hazards to research personnel and subjects.

- Expertise and experience of members of the research team.
- Availability of departmental resources for the proposed work.
- Scientific processes involved to minimize potential risk to human subjects.

PI Submits Review Package to IRB in the Electronic Protocol System (EPS)

For the CDOEIRB to conduct a review, the PI must submit their package in the EPS. The review package must include the following:

- Protocol/Application including provisions for the protection of human subjects in accordance with all applicable laws and regulations
- Other documents for review may include, but are not limited to, the following:
    - Informed Consent or Information sheet that includes all required elements (see 10 CFR 745.116) and is written in language understandable by the subject population.
    - HIPAA release
    - Data use agreement
    - Recruitment materials
    - Advertisements/Outreach materials (flyer, e-mail, phone script, etc.)
    - Surveys/Interview Scripts/Questionnaires
    - Data collection tools
    - Any external IRB approval letters
    - Policy and procedure for protection of PII

CDOEIRB Administrator Pre-Reviews Submitted Materials

Upon receipt of the protocol package, the CDOEIRB Administrator:

- Reviews package for missing information and items that need clarification.
- Verifies that the package contains all required components.
- Gathers enough information to determine whether the proposed project meets the definition of "human subjects research" as defined in the DOE Order 443.1B.
- Suggests the level of review required for the study considering the risk/benefit analysis.
- Notifies the chair and the program managers at DOE and NNSA by email of any proposed human subjects research that involves the following:
    - an institution without an established IRB;
    - a foreign country;
    - the potential for significant controversy;
    - vulnerable subjects;
    - the generation or use of classified or sensitive unclassified information; or
    - the potential to constitute human terrain mapping (HTM).
- Documents the email sent to the program managers in the EPS.
- Assigns a designated reviewer for expedited review or adds the review to the agenda for the next meeting of the Full Board.

- Distributes complete protocol package to all members participating in the Full Board review. Ideally, IRB members receive the review materials 2 weeks prior to a scheduled meeting.

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 Administrator 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 Administrator will inform the PI regarding the level of review and the general expected time required by the CDOEIRB for such review.

Full Board Procedure

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. At the chair's discretion, a member of the CDOEIRB may be assigned as a primary/secondary reviewer for protocols requiring Full Board 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.

During the protocol review, the CDOEIRB Administrator documents the deliberations, any issues identified, and any conditions that reviewers determine must be met in order to approve the study. The PI may be invited to, or may request to, attend the review or reviewers may call the PI during the review for clarification or additional information as needed. However, the PI cannot participate in or attend the deliberations of the Board. The chair or CDOEIRB Administrator also asks for and records the total vote of all eligible voting 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 chair may ask that representatives with direct programmatic oversight of the project leave the room.

CDOEIRB Determination

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

- **Approve**: Protocol is approved as submitted.

- **Approve with conditions or require modifications to secure approval**: Protocol is approved by the CDOEIRB, with certain specified conditions, which must be met (and accepted by the CDOEIRB or its administrative team on behalf the CDOEIRB), prior to initiation of work. Alternatively, the protocol requires modifications or PI must furnish additional information prior to the CDOEIRB considering the protocol for approval. In both cases, the PI must submit corrected materials via the EPS to the CDOEIRB for review.

- **Defer:** Protocol needs major work or lacks sufficient information for the CDOEIRB to complete its review.

- **Disapprove**: Protocol does not meet the minimum criteria required for approval.

Approve

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.

Approve with Conditions or Require Modifications to Secure Approval

Study requires additional clarification or changes to secure final CDOEIRB approval. The board, at its discretion, may require that the investigator respond to requested modifications within a specified period. If the response is not received from the PI within the specified time, the application will be considered withdrawn and will be administratively terminated.

In a full board vote, the IRB must indicate whether the response to CDOEIRB's requested modifications can be reviewed and approved via the administrative team (consisting of the chair, vice chair, and administrator) or must be returned for review and approval by the convened board. For projects that are approved with conditions, the date of the vote to approve shall be deemed the date of the Full Board convened meeting.

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.

Defer

When a study has too many issues to be approved, the CDOEIRB may defer the determination. The Board must identify why the proposed work is not approvable in its current form and what issues need to be resolved before the CDOEIRB can proceed. Until the PI provides that information and/or revises the submitted materials, the Board can take no further action, and no activity may begin on the study. Deferring a study is rare, but when it occurs, the PI can either revise the submission package or abandon the project. There is no set time limit for the PI to respond, but one may be imposed on a case by case basis.

Disapprove

Only the convened CDOEIRB can disapprove a study, and this study-specific decision may not be modified by any other agency or entity.

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 studies, with or without modifications. A PI may submit a new study on the same research topic, without prejudice, if the CDOEIRB's reasons for disapproval in the first instance are fully addressed.

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.

Notice of CDOEIRB Determination to PI

The CDOEIRB Administrator creates the applicable determination letter and issues it to the PI in the EPS. The CDOEIRB Administrator must verify completion of all required training before the final approval letter for a non-exempt study letter can be issued.

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 is 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. If the Board deems it necessary to review a protocol prior to the 12-month maximum, such a determination will be explained in the approval letter sent to the PI.

Documentation

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

Appeal Process

If a protocol presented at a convened meeting is 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 IO, through the management team, for a resolution of the matter. The management team and/or IO 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.

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 IAA between the organizations was established.

Other Considerations:

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)).

Research on human subjects must adequately protect the rights and welfare of the subjects regardless of where that research is conducted. All DOE-funded or DOE site/laboratory-conducted human subjects research that would be subject to U.S. Federal regulations and DOE requirements if conducted wholly within the United States, must comply with these requirements even if conducted in other countries.

In addition to IRB review and approval, human subjects research conducted outside the United States may involve international and country-specific requirements, including review by the appropriate local equivalent of an IRB. The DHHS OHRP provides an International Compilation of Human Research Standards. This comprehensive work is updated annually and is a good resource that the CDOEIRB should refer to when reviewing projects conducted in other countries.

Research conducted outside the United States can also involve a number of additional challenges:

- The IRB must ensure that the proposed research is acceptable in the local setting where it is to be conducted.
- Local community/ethical concerns, subject population, and institutional policies and values must be taken into account in addition to the requirements noted above.
- The protocol, informed consent document, and instructions to the foreign IRB (or equivalent) members must be written in the appropriate language and translated into English (for review by the IRB).
- Minutes of the foreign IRB meeting, including approval, must be translated into English and forwarded to the IRB.
- PIs must be knowledgeable about and sensitive to issues, such as the expectations of the local volunteer population, the practices of the local collaborating experimenter(s), the meaning of informed consent, and possible coercion and enticement activities. Also, the IRB is required to notify DOE about any study that has a foreign component.

To avoid potential delays in IRB review, PIs who are considering international research should contact the CDOEIRB Administrator as early as possible in the planning stage to discuss whether additional requirements apply and any attendant time constraints.

Projects Involving Toxic or Potentially Harmful Agents

Using human subjects in research that involves exposure to potentially toxic materials or potentially harmful physical agents (lasers, electromagnetic or particle radiation, noise, heat, chemical tracers, etc.) requires careful consideration. To allow the IRB to fully evaluate the risks and benefits of the proposed work, PIs must submit information documenting the expected exposure of subjects to these agents and must have their dose calculations independently reviewed and validated. Any qualified independent party can perform this review, and the PI is responsible for any cost associated with such validation.

The documentation should provide enough information for the IRB to assess the adequacy of the independent validation and must include the following:

- The assumptions used regarding subjects, agent(s) and quantity, route of exposure, and frequency or duration of exposure
- The calculations that yield the estimated dose, and, whenever possible, quantitative risk associated with the exposure
- Reference to any applicable community or occupational standards
- A statement that the reviewer has no direct involvement in the research
- A brief (2- to 4-sentence) summary of the qualifications of the reviewer
- If the proposed subjects are employees at the institutions or a collaborating institution and the proposed exposure is to chemical agents involving inhalation only for which there is an existing OSHA Permissible Exposure Limit or American Conference of Governmental Industrial Hygienists Threshold Limit Value the analysis may be based on exposure rather than absorbed dose.

Internet Research

Internet research is any human subjects research conducted using the Internet. Such research may include two types of information:

- **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 terms of use and/or data protection rules.

Note: All internet research, regardless of whether information is directly retrieved and/or aggregated for the purpose of the research, must comply with the appropriate DOE directives, such as level of security/classification and protection of PII. Only information obtained with due authorizations and that complies with applicable requirements will be approved.

Vulnerable Populations

Pregnant Women, Human Fetuses, or Neonates

Research involving pregnant women, human fetuses, or neonates that is not otherwise approvable under Subpart B may be approved after special review by DHHS (45 CFR 46.207). DHHS will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if:

- the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

- the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (science, medicine, ethics, law) and following an opportunity for public review and comment, has determined either: (1) that the research in fact satisfies the conditions for IRB approval; or (2) that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; the research will be conducted in accord with sound ethical principles; and informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts.

Prisoners

U.S. Department of Health and Human Services regulations at 45 CFR 46, Subpart C, detail special additional protections for research involving prisoners who, because of their incarceration, may have a limited ability to make truly voluntary and uncoerced decisions about whether or not to participate as subjects in research.

A prisoner is defined as any individual involuntarily confined or detained in a penal institution.

To review research involving prisoners covered by the DHHS regulations, IRBs must:

- have a majority of its members not otherwise associated with the prison (45 CFR 46.304(a); and
- include a prisoner or a prisoner representative with appropriate background and experience to serve in this capacity, unless the research has already been reviewed by an IRB that included a prisoner or prisoner representative (45 CFR 46.304(b)).

Children

U.S. Department of Health and Human Services regulations at 45 CFR part 46, Subpart D, and FDA regulations at 21 CFR Part 50, Subpart D, require that special protections be provided for research involving children. Under the regulations, children are defined as persons who have not attained the “legal age” (in their jurisdiction) for consent to treatments or procedures that may be involved in the research, under applicable law of the jurisdiction in which the research will be conducted

Note: Additional protections for vulnerable populations are described in 45 CFR 46, Subparts B, C, and D.

Using Workers as Subjects

All personnel (employees, contractors, students) are vulnerable to pressures to appear cooperative with regard to projects conducted by their managers and/or co-workers. Additionally, when the subject pool consists entirely of people who are or may be familiar with the study, the validity of the data may be in question.

The basic ethical principles that form the basis of U.S. Federal Laws governing human subjects research are very clear on this topic: subject selection cannot be based solely on the subject’s

ready availability or malleability. Accordingly, if research plans include recruitment of fellow workers from within the PI's group, justification will need to be included. The following suggestions may reduce the possibility of unintended coercion and concerns about objectivity, while still permitting these individuals to participate as subjects in research:

- IRB-approved advertisements must be posted throughout the site to recruit subjects from a broad base of employees, contractors, and students
- Personal solicitations of co-workers by investigators or fellow co-workers should be avoided
- A statement should be included about why this is not a sample of convenience
- Recruitment materials should include how objectivity and validity of the data will be ensured
- Specific steps should be included about how potential coercion will be minimized.

Investigator Self-Experimentation

The CDOEIRB discourages investigators from conducting research on themselves, unless clearly justified and approved by the CDOEIRB and the PI's management. While researchers may be aware of the risks of self-experimentation, they may also be more willing to accept risks that are ill-advised. Application for review with the IRB allows a neutral third party to raise concerns and/or propose measures to promote the welfare of researchers.

HIPAA

The HIPAA governs the way certain health information is collected, maintained, used, and disclosed. It establishes a set of safeguards on certain types of protected health information (PHI). This law affects researchers when proposed research either:

- creates or generates PHI, or
- requires access to and/or use of PHI.

For more information, visit the DHHS HIPAA website or contact the CDOEIRB Administrator.

The HIPAA Privacy Rule protects the confidentiality of personally identifiable data generated as a result of health care services and includes the requirement that authorization be obtained in most cases before this type of data can be used for research purposes. The Privacy Rule also requires that research plans involving this type of data be reviewed and approval by an IRB or Privacy Board.

Datasets

- Research using de-identified datasets that are obtained from a commercial or governmental source is not considered human subject research, is not governed by 10 CFR 745 or 21 CFR 50&56, and review by the CDOEIRB is not required.
- All other research involving datasets, whether identified or de-identified, requires CDOEIRB review.

Future Use of Data

Researchers must also consider whether the data generated in the study might be used in future research. If so, that likelihood needs to be communicated to potential subjects in the consent agreement. Otherwise, if researchers later identify a need to use study data for something outside the scope of the original study or it was not noted in the consent, they may need to go back and get new consent from subjects before using that data.

Deception or Withholding Information

The intent of informed consent is comprehensive, honest, and understandable disclosure of all elements of the subject's participation in research. However, some research necessitates that PIs withhold information about the real purpose of the study or intentionally give subjects false information about some aspect of the research in order to prevent subject bias. As a result, subjects cannot give fully informed consent prospectively.

Generally, minor deception, such as withholding the real purpose of a minimal risk study is acceptable, provided that (a) the research involves no more than minimal risk and (b) subjects are debriefed afterward.

The PI must justify the reasons for deceiving or withholding information from subjects and provide a debriefing script or copy of the information that subjects will receive after participation. The debriefing should occur as early as feasible, preferably at the conclusion of the subject's participation, but no later than at the conclusion of the data collection. After debriefing, subjects should be allowed to withdraw their data.

Expedited Review Procedure

During the pre-review, the CDOEIRB Administrator documents any issues identified and any conditions that must be met in order to approve the study. Expedited review may be conducted by the chair or others appointed by the chair such as the vice chair; CDOEIRB Administrator or by a designated, experienced, and eligible voting member; or a group of experienced and eligible voting members designated by the chair. The CDOERIB Administrator may contact the PI for clarification or additional information as needed. Following an expedited review, the reviewer may recommend that the chair approve a study, 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 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 the EPS.

Note: A study cannot be disapproved by the Expedited Review Process and would require Full Board review.

CDOEIRB Determination

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

- **Approve:** Protocol is approved as submitted.
- **Approve with conditions or require modifications to secure approval**: Protocol is approved by the CDOEIRB, with certain specified conditions, which must be met (and accepted by the CDOEIRB or its administrative team on behalf the CDOEIRB), prior to initiation of work. Alternatively, the protocol requires modifications or PI must furnish additional information prior to the CDOEIRB considering the protocol for approval. In both cases, the PI must submit corrected materials via the EPS to the CDOEIRB for review.
- **Defer:** Protocol needs major work or lacks sufficient information for the CDOEIRB to complete its review.

Notice of CDOEIRB Determination to PI

The CDOEIRB Administrator creates the applicable determination letter and issues it to the PI in the EPS. The CDOEIRB Administrator must verify completion of all required training before the final approval letter for a non-exempt study letter can be issued. Expedited studies will also be included on the next Full Board meeting agenda under “Actions Taken.”

Exempt Review Procedure

Certain low-risk research activities are exempt from Full Board review, as listed in 10 CFR Part 745.101(b). Following a review by the Administrative Team and determination by the chair that the research is exempt human subjects research, the chair may ask that the Administrative Team review the proposed research or may designate another member of the CDOEIRB to conduct the review. The final determination shall be made by the chair, in consultation with the vice chair.

Notice of CDOEIRB Determination to PI

If the chair determines that the research is exempt from Federal requirements governing human subjects research, the CDOEIRB Administrator creates an exemption determination letter and issues it to the PI in the EPS. Exempted studies will also be included on the next Full Board meeting agenda under “Actions Taken.” Annually, the CDOEIRB Administrator will contact the

PI to determine whether the project is still ongoing, and if so, whether any changes in scope are anticipated.

Other Considerations When Determining Whether Proposed Research May be Exempt

Anonymous Data

Data are considered to be anonymous when there is no possible way to identify the participants from the data collected. Data are not anonymous if anyone or any procedure, such as accessing a computer database, will identify the subject. In most instances, the omission of specific identifiers, such as name, social security number, or patient number, is sufficient to qualify a study as anonymous. Sometimes an investigator may preserve a subject's anonymity while still retaining data on individual characteristics such as age, gender, ethnic origin, occupation, or diagnosis. Anonymity is possible only when studying large samples or populations. When the number of potential participants is small and/or the research setting is identified, anonymity can be threatened or compromised even when identifiers have been removed from the data.

Archived pathology or diagnostic specimens that are considered residual biological material and destined to be destroyed can be used in research. They are considered exempt from IRB review if there are no patient identifiers linked to the specimen and if the data are not intended to be used in the diagnosis or treatment of a patient. If either of these conditions does not apply, then consent of the research subject is required and the study will require IRB review.

Use or collection of anonymous human biological specimens for research efforts focused on understanding, diagnosing, and treating genetic diseases will require review by the IRB. There are additional ethical concerns for genetic research (e.g., the potential for discrimination with regards to employment or insurability) that may not apply for other types of research with biological specimens. Please contact the IRB Administrator for additional information.

Existing Data

The term "existing" refers to the time period that the data or materials were obtained. "Existing" refers to material or tissue that was "archived" or "on the shelf" prior to approval for the funding of the research. If the data/specimens are collected after approval of the funding, then the data/specimens are not preexisting or "archived," the protocol will require IRB review, and the investigator may be required to obtain written informed consent.

Specimens received as extra material or extra specimens requested from a physician conducting a clinical procedure are not preexisting or "archived" and thus require written informed consent from the subject and review by the IRB. If there is a link to the patient's identity and a possibility that the patient may be contacted in the future, an informed consent document is required. Furthermore, informed consent is required if there is a link to the patient's identity and a possibility that the research may result in commercial or economic value.

Use of existing human biological specimens for genetic research will require review by the IRB. There are additional ethical concerns for genetic research that may not apply for other types of research with biological specimens. Please contact the IRB Administrator for additional information.

Sensitive Survey Research

Sensitive surveys or questionnaires are seldom exempt from IRB review. A sensitive survey includes questions about illegal activities or highly personal aspects of the subjects' behavior, life experiences, or attitudes. Examples include chemical substance abuse, sexual activity or attitudes, sexual abuse, criminal behavior, sensitive demographic data, detailed health history, etc. The potential for provoking a negative emotional reaction from subjects, their families, or the community is a principal determining factor of sensitive survey research.

Potential for Breaches of Confidentiality

Additional consideration for exemption includes determining if there is a risk associated with a possible breach of confidentiality (i.e., accidental disclosure of drug use to law enforcement personnel). In surveys with potential psychological risk, review for exemption includes risks associated with surveys about sensitive topics as well as those resulting from a breach of confidentiality. When confidentiality is an issue, the presence or absence of subject identifiers may be a decisive factor.

Use of Consent Forms

A Notice of Exemption does not necessarily exempt investigators from the requirement of obtaining written informed consent from subjects. Most research involving surveys, questionnaires, or otherwise interacting with subjects will require the use of a consent form. For studies where there are no subject identifiers (i.e., when anonymous data are collected), an information sheet or cover sheet is usually required.

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 a 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 (e.g., spouse, colleague, or friend) 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 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 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.

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: 1) no more than minimal, 2) minor increase over minimal, or 3) 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 the EPS. 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 the EPS.

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.

Continuing Review Procedure

The CDOEIRB can proceed with its review of a study before receiving confirmation that all necessary training has been completed.

The steps for continuing review and approval are described in detail below.

When conducting continuing review and evaluating whether research continues to satisfy the criteria for CDOEIRB approval of research, the IRB should pay particular attention to the following aspects of the research:

- Risks to subjects are minimized and reasonable in relation to anticipated benefits.
- Selection of subjects is equitable.
- Participation is voluntary. Informed consent will be sought from each subject, if applicable, and will be appropriately documented.
- 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. (See 45 CFR 46, Subparts B, C, and D.)

PI Submits Continuing Review Package to IRB in the EPS

For the CDOEIRB to conduct a review, the PI must submit a continuing review package in the EPS. The review package must include the following:

- Continuing Review Application including provisions for the protection of human subjects in accordance with all applicable laws and regulations.
- Informed Consent or Information sheet that includes all required elements (see 10 CFR 745.116) and is written in language understandable by the subject population.
- Any document in which changes are being requested.
- When applicable, any external IRB approval letters.

CDOEIRB Administrator Pre-Reviews Submitted Materials

Upon receipt of the continuing review package, the CDOEIRB Administrator:

- Reviews package for missing information and items that need clarification.
- Verifies that the package contains all required components.
- Verifies the study's risk/benefit analysis remains unchanged.
- Assigns a designated reviewer for Expedited review or adds the review to the agenda for the next meeting of the Full Board.
- Distributes complete protocol package to all members participating in the Full Board review. Ideally, CDOEIRB members receive the review materials 2 weeks prior to a scheduled meeting or assigns a designated reviewer if the project is determined to be expedited.

Full Board Procedure for Continuing Review

IRB Full Board Reviews Continuing Review Package

During the protocol review, the CDOEIRB Administrator documents the deliberations, any issues identified, and any conditions that reviewers determine must be met in order to approve

the study. The PI may be invited to, or may request to, attend the review, or reviewers may call the PI during the review for clarification or additional information as needed. However, the PI cannot participate in or attend the deliberations of the Board. The chair or CDOEIRB Administrator also asks for and records the total vote of all eligible voting members.

If the Full Board determines that the risks of a study is no more than minimal, the Board may change the level of review to expedited, and it will not need future review by the Full Board.

Typically, minor modifications are handled by Expedited review unless the level of risk to the participants has increased for projects that were reviewed by the Full Board

Major modifications for studies reviewed by the Full Board must be returned to the Full Board for review.

CDOEIRB Determination

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

- **Approve**: Protocol is approved as submitted.
- **Approve with conditions or require modifications to secure approval**: Protocol requires modifications or PI must furnish additional information prior to final approval by the CDOEIRB. Protocol is approved by the CDOEIRB, with certain specified conditions, which must be met (and accepted by the CDOEIRB or its administrative team) prior to initiation of work. Alternatively, the protocol requires modifications or PI must furnish additional information prior to the CDOEIRB considering the protocol for approval. In both cases, the PI must submit corrected materials via the EPS for further review by the CDOEIRB.
- **Defer:** Protocol needs major work or lacks sufficient information for the CDOEIRB to complete its review.
- **Disapprove**: Protocol does not meet the minimum criteria required for approval.

Notice of CDOEIRB Determination to PI

The CDOEIRB Administrator creates the applicable determination letter and issues it to the PI in the EPS. The IRB administrator must verify completion of all required training before the final approval letter for a non-exempt study letter can be issued.

Expedited Procedure for Continuing Review

CDOEIRB Administrative Team Assigns a Designated Reviewer

During the pre-review, the CDOEIRB administrative team documents any issues identified and any conditions that must be met in order to approve the continuation of the study. The administrative team may contact the PI for clarification or additional information as needed. At

the administrative team's discretion, an additional CDOEIRB member may be designated to assist in the review.

The Designated Reviewer Approves or Defers Proposed Package

The designated reviewer completes the non-committee review and determines the expedited or exempt category or determines that Full Board review is required.

Note: A continuing review package cannot be disapproved by the Expedited Review Process and requires Full Board review.

CDOEIRB Determination

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

- **Approve**: Protocol is approved as submitted.
- **Approve with conditions or require modifications to secure approval**: Protocol is approved by the CDOEIRB, with certain specified conditions, which must be met (and approved by the Board), prior to initiation of work. Alternatively, the protocol requires modifications or PI must furnish additional information prior to the CDOEIRB considering the protocol for approval. In both cases, the PI must submit corrected materials via the EPS to the CDOEIRB for review.
- **Defer:** Protocol needs major work or lacks sufficient information for the CDOEIRB to complete its review.

Notice of CDOEIRB Determination to PI

The CDOEIRB Administrator creates the applicable determination letter and issues it to the PI in the EPS. The CDOEIRB Administrator must verify completion of all required training before the final approval letter for a non-exempt study letter can be issued.

Modifications to an Approved Protocol

The PI will submit a completed Modification Request form for all proposed modifications to an approved protocol through the EPS 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 chair. Changes to an approved protocol shall not be implemented without CDOEIRB approval, except when such changes are necessary to eliminate an immediate hazard to a study subject.

Procedure for Modification

The steps for making a modification and approval are described in detail below.

PI Submits Modification Package to IRB in the EPS

For the CDOEIRB to conduct a review, the PI must submit a modification package in the EPS. The package must include the following:

- The application including provisions for the protection of human subjects in accordance with all applicable laws and regulations.
- Any new documents or documents in which changes are being requested.

The CDOEIRB Administrative Team Pre-Reviews Proposed Study Package

During the pre-review, the CDOEIRB administrative team documents any issues identified and any conditions that must be met in order to approve the modification. The administrative team may contact the PI for clarification or additional information as needed. At the administrative team's discretion, an additional CDOEIRB member may be designated to assist in the review.

The CDOEIRB administrative team/designated reviewer evaluates the following requirements for approval to ensure that:

- Risks to subjects remain minimized and reasonable in relation to anticipated benefits.
- Selection of subjects continues to be equitable.
- Provisions are still adequate to protect subject privacy and confidentiality of data.

When any subjects are likely to be vulnerable to coercion or undue influence, additional safeguards continue to be included to protect the rights and welfare of those vulnerable subjects. (See 45 CFR 46, Subparts B, C, and D.)

Depending on the determination made by the CDOEIRB administrative team/designated reviewer, the modification is either assigned to a Full Board review or reviewed by the Expedited procedure.

Full Board Procedure for Modification

Typically minor modifications are handled by Expedited review unless the level of risk to the participants has increased for projects that were reviewed by the Full Board.

Major modifications for studies reviewed by the Full Board must be returned to the Full Board for review.

Expedited Procedure for Modification

For projects that were reviewed by the expedited procedure, review of major and minor modifications can be expedited.

The CDOEIRB Administrator creates the applicable determination letter and issues it to the PI in the EPS. The CDOEIRB Administrator must verify completion of all required training before the final approval letter for a non-exempt study letter can be issued.

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 has 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 in the EPS within 30 days. 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 member of the project team 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;

- 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 IO and the research sponsor. Note that:

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 (3) 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.

Unanticipated problems can include loss or compromise of PHI or PII, with a loss of privacy or confidentiality to a research participant or others.

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).

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 subject's 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. Significant adverse events, or adverse events that are unexpected and substantively impact the human subjects, must be reported to the IRB and to DOE.

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 chair for appropriate action as outlined below.

The chair must immediately report the following to the IO and to the DOE management team, and the DOE management team will be responsible for reporting to 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, significant adverse events, and other instances of noncompliance, violation, or complaint within 48 hours. .

If there is any possibility of loss or compromise of PII or serious harm to a participant, the PI must immediately report to his/her institution's IRB and the CDOEIRB. 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.

CDOEIRB Follow-up with Regard to Unanticipated Problems and Significant Adverse Events and Noncompliances

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, through DOE: 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; and

3) Any suspension or termination of CDOEIRB approval.

The CDOEIRB administrative team will coordinate reporting the unanticipated problem to DOE, 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(s), the participant(s), 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 3 years and at least every 3 years thereafter using DOE-approved self-assessment tools that include an evaluation of compliance with the Federal regulations and DOE-specific requirements. The CDOEIRB 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 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 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 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 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 Board will follow the Rules of Order (Attachment V).

The CDOEIRB Administrator will prepare a preliminary agenda for each meeting. After approval by the chair and DOE management team, the CDOEIRB Administrator will distribute the agenda and all relevant meeting materials to CDOEIRB members at least 2 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.

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 in order to ensure protocols are understandable to all. A reviewer document is available in the EPS.

Minutes

The CDOEIRB Administrator 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.

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 or unaffiliated 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 Administrator; 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 review of the project or projects must be deferred until the next meeting.

CHAPTER 10:
RECORDKEEPING

CDOEIRB Records

All official CDOEIRB records will be stored in the EPS. Any hard copies will be stored in the CDOEIRB Administrator's office, which is in a secure area, for a minimum of 3 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 Administrator 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 study protocol and scientific evaluations, if any, that accompany the study protocol, 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;
- 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 (to be submitted with the continuing review application).

Note: The PI retains all signed consent forms.

Meeting Minutes

The CDOEIRB Administrator records the minutes of each convened meeting of the IRB. Minutes will be posted electronically for review as soon as possible following each meeting. Minutes are reviewed by the Board at the next Full Board meeting. Any corrections, modifications, or additions to the minutes will be reported in the next set of 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 or recusing;
- 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 Administrator 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' 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 Administrator, 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 other requirements as determined by the IRB. .

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*;
- OHRP Guidance on Engagement of Institutions in Human Subjects Research, December 23, 1999;
- OHRP Guidance on Reporting Incidents to OHRP, May 27, 2005;
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, January 15, 2007;

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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. A significant adverse event is one that is unexpected and substantively impacts the human subjects. For example, an expected, but mild, headache that clears up in a few hours would not be considered significant, but an unexpected migraine that prevents an individual from driving would be. Expected mild nausea for a couple of hours after taking the dose would not be considered significant, while unexpected nausea lasting days on end and interfering with eating would be. Note that significant adverse events are not typically considered unanticipated problems (and thus do not have to be reported to OHRP). They are, however, reportable to the DOE/NNSA HSP Program Managers.

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 dataset 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 – Typically occurs when the involvement of an institution's employees or agents includes any of the following: a) receipt of an award for the conduct of HSR, even where such activities are conducted by employees or agents of another institution; b) intervention by performing invasive or noninvasive procedures, such as drawing blood or using physical sensors; c) intervention by manipulating the environment (e.g., controlling environmental light, sound, or temperature, presenting sensory stimuli, or orchestrating environmental events or social interactions); d) interaction with human subjects (e.g., requesting that an individual provide a specimen); e) obtaining informed consent; f) obtaining biological specimens or identifiable private information from any source for the research; or g) analyzing identifiable private information and/or specimens. (From OHRP's Guidance on Engagement of Institutions in Human Subjects Research (December 23, 1999) http://www.hhs.gov/ohrp/policy/engage08.html).

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 (FWA) – 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.

Generalizable – Information/research findings that can be applied to populations or situations beyond that studied.

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 (whether professional or student) conducting research obtains: a) data through intervention or interaction with the individual, or b) identifiable private information.

> *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subjects' 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 which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, 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 obtaining the information to constitute research involving human subjects.

Human Subjects Research – Any activity meeting the definitions of both: 1) research; and 2) human subject, as defined in this section.

Identifiable Private Information – Any information that would allow an investigator to readily ascertain the identity of an individual, using: 1) information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place; and/or 2) information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public. The following are examples of types of information considered identifiable private information by OHRP:

- Name;
- Facial images;
- Social security number; and
- Voice recordings.

Therefore, any research involving the above is considered human subjects research.

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 – 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/HSP. 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 CDOEIRB shall be the responsible IRB.

Institutional Review Board (IRB) – The generic term used in all regulations for the local body that reviews and approves human subjects research.

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 researcher who is designated by his or her site senior management and 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. (DOE O 443.1B)

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

Study Review Package – The minimal information required by the CDOERB from the PI in order to conduct a review of proposed research.

Quorum – A simple majority of Board members, but not less than five CDOEIRB members, including at least one non-scientist, one scientist, and one unaffiliated member (DOE Policy). The Chair is counted in the quorum.

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. *Generalizable knowledge* is information/research findings that can be applied to people or situations beyond that studied (e.g., to the same population in a different situation or other populations.)

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.

Unaffiliated Member – To be eligible for participation on the IRB, neither the member nor any member of his/her immediate family may otherwise have a direct affiliation (employee, contractor, student in a fellowship, volunteer at the institution, or business unrelated to the IRB) with the institution.

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); 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.

Vulnerable Populations – Populations identified in Subparts B, C, and D of 45 CFR Part 46: pregnant women, children, and prisoners. Also, as a matter of policy, DOE considers its current and former workers to be a vulnerable population (Attachment VII) and subject to some of these provisions, as approved by the management, in consultation with the IO.

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 meets 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 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 Joint Cybersecurity Coordination Center (1-866-941-2472, jc3hq@hq.doe.gov, http://www.energy.gov/cio/office-chief-information-officer/services/incident-management/jc3-incident-reporting).

Attachment II. CDOEIRB Membership Roster - January 2016

Central DOE Institutional Review Board

CDOEIRB Administrator: Lindsay Motz

MEMBER NAME	***AFFILIATION***	***EXPERTISE***	***ALTERNATE***
Teeb Al-Sammarai, MD	White House Intern with DOE	Internal Medicine	N/A
Eula Bingham, Ph.D.	Professor Emerita, University of Cincinnati	Environmental Health/FWP	N/A—she is an alternate to Ed Mee
Chris Byrne, MA	Lawrence Berkeley Lab (LBL)	IRB Manager/Chair from LBL	N/A
Stewart Curtis, MD	Idaho National Laboratory	Occupational Medicine	*Teeb Al-Sammarai*
Elizabeth (Betsy) Ellis, Ph.D.	Oak Ridge Associated Universities – Site-wide IRB Chair and epidemiologist	Epidemiology	N/A
Susan Erlich, J.D.	Former Judge	Law	N/A
Don Hagengruber, 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
Tim Ledbetter, Ph.D.	TBD	Minister; Significant prior experience serving on an IRB	N/A
Ed Mee	Former Worker (ORNL)	Pipefitting (FWP Representative)	*Eula Bingham*
Michael Montopoli, MD	Self	Occupational Medicine	*Teeb Al-Sammarai*
Jim Morris, Ph.D.	Retired (Research Scientist, Pacific Northwest National Laboratory (PNNL); PNNL IRB Chair)	Microbiology/Immunology (Chair)	N/A
Kenneth Silver, DSc, SM	Professor/Researcher, East Tennessee State University/ Environmental Health Science	Environmental Health Science	N/A
Frederick (Rick) Swarts, Ph.D.	Academic Dean, Bridgeport International Academy	Ethics/Biology (Community Member)	*Susan Ehrlich*
Loretta Valerio	Former Worker (Los Alamos National Laboratory)	Worker Advocacy/Employee Concerns	N/A
Ainsley Weston, Ph.D.	National Institute of Occupational Safety and Health/Division of Respiratory Disease Studies	Carcinogen Biochemistry/Toxicology	N/A

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

Attachment IV. DOE Requirements for Research Involving Modification of Environment Letter

Department of Energy
Washington, DC 20585
April 25, 2013

Dear Laboratory Institutional Officials:

The purpose of this communication is to clarify the DOE requirements for research involving intentional modification of an individual's or a group of individuals' environment, for example through installation of devices in homes and/or through introduction of gases/chemicals to trace airflow in occupied residential, commercial, or public settings.

It is DOE policy that any such DOE-funded or DOE laboratory-managed or conducted projects will be managed as human subjects research and thus will be subject to the requirements of DOE Order 443.1B. Such projects must be reviewed and approved by the Central DOE Institutional Review Board (IRB), a DOE laboratory IRB, or (if conducted by a university) a university IRB with an approved Federalwide Assurance of compliance, prior to the initiation of the research and after consultation with the appropriate Human Subjects Protection (HSP) program manager.

Much of this work is funded by the DOE Office of Energy Efficiency or is work-for-others sponsored by the Department of Homeland Security and other federal agencies. Please feel free to contact me or the HSP program managers with any questions:

Elizabeth (Libby) White, DOE HSP Program Manager:
elizabeth.white@science.doe.gov; 301-903-7693

John Ordaz, NNSA HSP Program Manager:
john.ordaz@nnsa.doe.gov; 202-586-0142

Sincerely,

Elizabeth White

Elizabeth (Libby) White
DOE HSP Program Manager, SC-23.2

John Ordaz
NNSA HSP Manager, NA-SH-10

Sharlene C. Weatherwax, Ph.D.
DOE Institutional Official for
Human Subjects Research
Associate Director of Science for
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cc:
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Mary Fields, HS-10
Isaf Al-Nabulsi, HS-10
DOE Laboratory IRB Chairs
DOE Laboratory IRB Managers
Central DOE IRB Chair and Co-Managers
Managers, DOE Site Offices

Attachment V. IRB Rules of Order[6]

1. Basic Rules

a. All members are equal and their rights are equal. Those rights are:
   - To attend meetings on time
   - To make motions
   - To speak in debate
   - To vote

b. A quorum must be present to do business:
   - A quorum is a simple majority of IRB members; at least one member whose primary concerns are in non-scientific areas must be present
   - Members who do not vote (abstain) are counted toward the quorum

c. The majority rules:
   - A majority means the majority of members present
   - The minority has the right to be heard
   - Once a decision has been made by the majority, the minority must then respect and abide by the decision

d. Silence is consent:
   - Members who do not vote (abstain) agree to go along with the decision of the majority by their silence

e. A two-thirds vote is required whenever:
   - The rights of members are limited or taken away
   - Something that has already been decided is being changed

f. One question at a time and one speaker at a time:
   - No motion is in order which does not directly relate to the question under consideration
   - Once a member has been recognized by the chair, he/she has the floor and may not be interrupted

g. Debatable motions must receive full debate:
   - Debatable motions may not be voted on as long as members wish to debate it
   - Exception: debate can be suspended by a two-thirds vote of members present

2. Duties of Chair

a. Be on time and start on time.
b. Follow the agenda and keep on schedule.
c. Be in control of the floor:
   - "Assign" the floor by recognizing members who wish to speak
   - Remind those who interrupt that the floor has been assigned to another
   - Discourage private conversations during the meeting

[6] Adapted from "Robert's Rules in Plain English," by Doris P. Zimmerman, Harper Collins, 1997.

- Be impartial in calling on members to speak

d. Direct deliberations to focus on essential review concerns.
e. Facilitate consensus on critical issues by eliciting individual votes.[7]
f. Restate the main motion before taking a vote.
g. Lead the Board to develop clear instructions to IRB staff for correspondence to investigators.
h. Use general consent when possible (e.g., "If there is no objection, …").
i. Allow the withdrawal of motions by general consent.

3. Types of Motions

a. Main motions:
    - Cannot interrupt a member who has been assigned the floor
    - Require a second, unless the motion is from a committee
    - Can be debated
    - Can be amended
    - Require a majority vote
b. Secondary motions:
    - Can be made while the main motion is on the floor and before it has been decided
    - Three classes: subsidiary motions; privileged motions; incidental motions
c. Process:
    - The floor is assigned to the primary or secondary reviewer
    - The primary or secondary reviewer presents the proposal and the issues
    - A motion for disposition of the proposal is made (the motion is "on the floor")
    - The motion is seconded
    - The chair states the motion (the motion is "pending")
    - Debate is held "one speaker at a time"
    - The chair may open the floor to general discussion[8]
    - The chair puts the question to a vote
    - Votes are taken by a show of hands
    - The chair announces the vote
d. Other points:
    - The maker of a motion has first right to speak to it
    - A member can vote against his/her own motion, but cannot speak against it
    - A member can modify his/her own motion before it is stated by the chair
    - A member can amend his/her own motion after it has been stated by the chair
    - A member can withdraw his/her own motion up to the time it is stated by the chair, and after that with the group's permission (e.g., general consent)

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[7] See "Division of a Question," Item 6.d.

[8] This modifies Robert's Rules to allow free discussion without the Chair needing to assign the floor to individual members before they could speak.

- Motions that repeat the same question on the same day, or that conflict with an already adopted motion, are out of order

4. Subsidiary Motions

a. Subsidiary motions relate directly to the main motion on the floor.
b. They have rank among each other: a motion of higher rank can be made at the time when a motion of lower rank is on the floor or pending; the motion of higher rank takes precedence:
    - Previous Question (call for the vote) – Highest Rank
    - Limit or Extend
    - Main Motion – Limits of Debate
    - Amend Lowest Rank
c. **Amend**: Changes the wording of a motion to make it more clear, complete or more acceptable before the motion is voted upon.
    - An amendment must be germane to the motion on the floor
    - A member must obtain the floor to offer an amendment
    - An amendment must be seconded
    - An amendment is debatable if it is made to a debatable motion
    - A primary amendment can be amended; the secondary amendment cannot
    - An amendment requires a majority vote even when applied to a motion that requires a two-thirds vote
    - Adopting an amendment does not adopt the motion
    - Amendments that are the same as a negative vote on the motion are out of order
d. **Limit Debate**: Exercises special control over the debate by reducing the number and length of speeches allowed or by requiring that debate be limited to a period of time after which the vote must be taken.
    - Can be used with any motion
    - Must be seconded
    - Is not debatable
    - Can be amended but only regarding the number and/or length of speeches or when the vote will be taken
    - Requires a two-thirds vote
e. **Previous Question**: Used to cut off debate and bring the group to an immediate vote on a pending motion.
    - Can be applied to any pending question
    - It is out of order when a member has the floor
    - It cannot be debated
    - Requires a two-thirds vote

5. Privileged Motions

a. Privileged motions are not related to the business on the floor but to the rights of members and the organization.

b. **Recess**: Proposes a short intermission in the meeting.
    - It must be seconded
    - It cannot be debated
    - It can be amended only as to length or time or recess
    - It requires a majority vote
c. **Adjourn**: Closes the meeting.
    - It must be seconded
    - It cannot be debated
    - It cannot be amended
    - It requires a majority vote
d. The Chair can move for recess or adjournment by general consent.

6. Incidental Motions

a. Have no rank among themselves and may be applied to any main motion; usually decided as they arise, they are usually not debatable and can only rarely be amended.
b. **Point of Order**: To raise the possibility that rules of order are not being followed.
c. **Point of Information**: To obtain additional information on the subject being considered.
d. **Division of a Question**: Used when a motion contains several parts, and the group wishes to vote on each part separately:
    - It requires a second
    - It requires a majority vote

7. Restorative Motions

a. Allows the group to change its mind on previously adopted motions.
b. **Rescind**: Used to quash or nullify a previously adopted motion:
    - It requires a second
    - It requires a two-thirds vote
    - It is not in order if action has already been taken as a result of adoption of the motion
c. **Reconsider**: Used to reconsider the vote on a previously adopted motion:
    - Can only be made by someone who voted on the prevailing side
    - Must be made on the same day that the vote to be reconsidered was taken
    - It requires a second
    - It may be debated, and it opens up to debate the motion to which it is applied
    - It requires only a majority vote

8. Voting

a. All votes on motions for disposition are taken by show of hands; the number in favor, opposed, and abstaining are recorded.
b. To be adopted, a majority of members present at the meeting must vote in favor.
c. The Chair votes only to break a tie vote.

Attachment VI. Policy Memo from DOE IO Considering Current or Former DOE and M&O Contractors Vulnerable Subjects

Department of Energy
Washington, DC 20585

May 22, 2015

Dear Laboratory Institutional Officials:

The purpose of this communication is to remind DOE sites that DOE considers current or former Federal or contractor employees who become subjects of DOE human subjects research (HSR) to be vulnerable subjects. DOE HSR includes all HSR conducted with

DOE funding, at DOE institutions, or by DOE or DOE contractor personnel.

As is stated in the DOE Report, *Creating an Ethical Framework for Studies that Involve the Worker Community*, "when workers are the subjects of research, additional care must be exercised to assure that their participation is truly voluntary and that data collected about individual workers are kept confidential....For consent to be informed, participants must have adequate, understandable descriptions of the study purpose, what is expected of them, and any benefits and risks they may experience. For consent to be voluntary, they must not face coercion or reprisal for their decisions."

Many ongoing projects at DOE sites involving employees as subjects are work-for-others projects that may be sensitive in nature and require that information be close held. It is especially important with these projects to ensure that employees who participate as subjects do so without undue influence or potential repercussions.

Most of your sites already have policies in place to protect employees who become research subjects. New researchers should be informed of these policies and IRBs should be reminded that, in ensuring that the *Criteria for IRB approval of research (as stated in 10 CFR Part 745.111)* are met prior to approving HSR protocols, they should place special emphasis on 10 CFR 745.111 (b) if employees are research subjects.

Section 10 CFR Part 745.111(b) states: "When some or all of the subjects are likely to be vulnerable to coercion or undue influence…additional safeguards have been included in the study to protect the rights and welfare of these subjects."

Please feel free to contact me or the HSP Program Managers with any questions:

Elizabeth (Libby) White, DOE HSP Program Manager:

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Sincerely,

`

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DOE Laboratory IRB Chairs
DOE Laboratory IRB Managers
Central DOE IRB Chair and Vice Chairs
Managers, DOE Site Offices