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Human Subject Research

The INL is a U.S. Department of Energy National Laboratory
operated by Battelle Energy Alliance.

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OVERVIEW

Ethical Principles

The Battelle Energy Alliance, LLC (BEA) Institutional Review Board for Human Subjects Research (IRB) is guided by three ethical principles set forth in the Belmont Report of the National Commission for the Protection of Human Subjects. These principles of respect for persons, beneficence, and justice may also serve as a guide to researchers in formulating their protocols and research procedures. Briefly stated:

1. ***Respect for persons*** means that researchers should obtain the informed consent of all human subjects invited to participate in research. In order to respect subject autonomy, the consent process should include giving subjects full and comprehensible information about the research and provide clear assurance for the subjects' voluntary participation.

2. ***Beneficence***, or concern for the well-being of subjects, means that the risk of harm to subjects should be the least possible, and that the sum of benefits to the subjects and the importance of the knowledge to be gained should so outweigh the remaining risk of harm to the subject as to warrant a decision to allow this risk.

3. ***Justice*** means that the selection of human subjects should be fair and equitable and that the risks and benefits of research should be distributed among subjects in a fair and equitable manner, with particular concern for subjects whose personal status or condition – as children, prisoners, patients, and impoverished persons – places them in a vulnerable or dependent status.

Battelle Energy Alliance, LLC Policy and Procedures

Federal regulations and Idaho National Laboratory (INL) policy require special review of research projects that involves humans as research subjects. These reviews are conducted by the BEA IRB. The IRB is authorized to review and approve human subjects research under a Federal-Wide Assurance (FWA).

Battelle Energy Alliance, LLC Guide to Human Subjects Research

This guide describes the review process and documentation requirements set forth by the aforementioned regulations and policy. Section I includes BEA Standard Policy and Procedures. Section II provides specific information for principal investigators (PI).

SECTION I – STANDARD POLICY AND PROCEDURE

1. INTRODUCTION – WHAT IS HUMAN SUBJECTS RESEARCH?

Human subjects research is "*Research involving a living human being about whom we obtain private information through manipulation or intervention.*" Human subjects research includes a broader range of research than many investigators realize. In addition to traditional biomedical and clinical studies, human subjects research includes studies that:

- *Use humans to test devices, products, or materials* that have been developed through research. Also included is research that uses humans to examine human-machine interfaces.

- *Use data collected through intervention or interaction with individuals.* Intervention includes not only physical procedures (like drawing blood), but also manipulation of a subject's environment. Interaction includes interpersonal contact and other kinds of communication.

- *Use private information that can be readily identified with individuals,* even if the information was not collected specifically for the study in question. Information is private if the individual can reasonably expect it not to be made public or if the information concerns behavior that the individual can reasonably expect not to be observed or recorded.

- *Use bodily materials from a "living individual"* such as cells, blood, urine, tissues, organs, hair, and nail clippings, even if the researcher did not collect these materials. (Such research may be considered exempt from human subjects requirements if materials are unidentifiable). In all cases, the researcher should consult the IRB.

- *Use humans to evaluate environmental alterations,* for example, weatherization options or habitat modifications.

1.1 Purpose of this Manual

This manual is intended to serve as a simple guide to principal investigators, contracts personnel, project administrators, secretaries, and other support staff to help them understand the ethical principals, policies, and procedures that guide the careful assessment and management of human subjects research projects at the INL. This manual includes:

- Section I – Section II – Battelle Energy Alliance Standard Policy and Procedures

- Principal Investigator Information.

1.2 Policies and Guidelines Establishing the Battelle Energy Alliance, LLC IRB

The following policies and guidelines establish an IRB within INL by BEA to review all projects involving humans as research subjects:

- Title 10 CFR Part 745, "Protection of Human Subjects"
- Title 45 CFR Part 46, "Protection of Human Subjects"
- DOE Order 443.1a (dated 12/20/07), "Protection of Human Subjects"
- DOE 4300.2B, "Non-Department of Energy Funded Work (Work for Others)"

Compliance with all applicable government regulations is a stated requirement of these policies and guides. Federal government regulations are described primarily in 10 CFR 745, "Federal Policy for the Protection of Human Subjects; Notices and Rules" (Appendix B), referred to as the "Common Rule," and in directives from the U. S. Department of Energy's (DOE's) Idaho Operations Office. DOE Order 443.1a (Appendix C) (dated 12/20/07) contains the following additional instructions:

A. All research work (DOE funded, other federal agency funded, or non-DOE funded) potentially involving human subjects and conducted at the INL Site, or as part of consolidated site operations, will be reviewed prior to initiation by an IRB Chairman, or his delegate, duly established pursuant to 10 CFR 745. Research involving human subjects being conducted at institutions being funded by the INL may not begin until the INL IRB approves the protocol. Written approval to begin research or subcontract for the use of human subjects under the applicable protocol proposed for this award will be issued from the INL IRB under separate letter to the funded institution and the PI. A copy of this approval will be retained in the INL IRB official files. Non-compliance with any provision of this clause may result in the withholding of funds and/or the termination of the award.

B. Note that research involving records or statistics on individuals, or groups of individuals, is potentially human subjects research. That work determined by the IRB to not be human subjects work will be so certified by the IRB and such certification will accompany all proposals and records on the project. We will be conservative in this determination in order to fully implement DOE policy that the rights and welfare of individuals involved in human subjects research are fully protected.

C. Research work determined to involve human subjects work will receive appropriate IRB review and approval (certification) pursuant to 10 CFR 745 and DOE Order 443.1a (dated 12/20/07).

1.3 Functions and Authority of the IRB

Functions of the IRB can be broadly stated as follows:

- Assure that the rights and welfare of human subjects involved in research projects are adequately protected, and that the risks to the subjects are minimized and are outweighed by the benefits derived from the research.
- Assure that the proposed research is in compliance with appropriate regulations governing research involving human subjects throughout the life of the project.
- Assure proper documentation of actions to be taken with regard to involving human subjects in the research, including obtaining informed consent from the subjects by adequate and appropriate methods. IRB structure and composition are defined in the Common Rule, Section 107.

Authority of the IRB

The IRB has authority to approve, require modifications, or disapprove any research proposal involving human subjects and usually decides in one of the following manners:

A. Approved

B. Granted Conditional Approval, pending modification

C. Disapproved.

1.4 Informed Consent

Informed Consent is the cornerstone of protection for human subject research volunteers. It is a fundamental mechanism to ensure respect for persons by seeking thoughtful consent to a voluntary act and is to be treated as a ***process***, not just a form. Informed Consent is required as part of the proposal package unless waived by the IRB under circumstances that are detailed as part of Appendix D. A sample format of the INL Informed Consent form is included as part of Appendix D, as well. The Informed Consent must be reviewed and approved at least annually and must always be tailored to the work in progress. If applicable, the advertisement for volunteers must be included in the Informed Consent package.

1.5 Definitions

The Common Rule (Section 102) defines a number of terms used in conjunction with regulations governing research involving human subjects that are also applicable to this manual.

"***Research*** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities."

Human Subject means a living individual about whom an investigator conducting research obtains:

1. Data through intervention or interaction with the individual

2. Identifiable private information.

"***Intervention*** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. '***Private information'*** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, information which has been provided for specific purposes by an individual, and information 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."

"***Minimal risk*** means that 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."

"***Certification*** means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance."

2. TYPES OF REVIEW

Research projects involving human subjects may be categorized by the type of review required. They are: Exempt, Expedited, Full Board, and Conditional.

2.1 Exempt

Definition: This research involves human subjects, but is determined to be "Exempt" from federal regulation by the IRB chair or his delegates based on one or more of the following conditions, as stated in the Common Rule, Section 101.

1. "Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of, or the comparison among, instructional techniques, curricula, or classroom management methods."

2. "Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement) survey procedures, interview procedures, or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation."

3. "Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this Section, if: (i) the human subjects are elected or appointed as public officials or candidates for public office; or (ii) federal statutes(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter."

4. "Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available, or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects."

5. "Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or

procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs."

6. "Taste and food quality evaluation and consumer acceptance studies: (i) if wholesome foods without additives are consumed, or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture."

2.2 Expedited Review Procedure[a]

2.2.1 Applicability

1. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

2. The categories in this list apply regardless of the age of subjects, except as noted.

3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. The expedited review procedure may not be used for classified research involving human subjects.

a. An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

5. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

6. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

2.2.2 Research Categories

1. Clinical studies of drugs and medical devices only when condition (A) or (B) is met.

   A. Research on drugs for which an investigational new drug application (21 CFR Part 3212) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   B. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

   A. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

   B. From other adults and children,[b] considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in

b. Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” 45 CFR 45.402(a).

an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

   A. Hair and nail clippings in a non-disfiguring manner

   B. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction

   C. Permanent teeth if routine patient care indicates a need for extraction

   D. Excreta and external secretions (including sweat)

   E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue

   F. Placenta removed at delivery

   G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor

   H. Supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process if accomplished in accordance with accepted prophylactic techniques

   I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings

   J. Sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (i.e., not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy

B. Weighing or testing sensory acuity

C. Magnetic resonance imaging

D. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography

E. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the Health and Human Services (HHS) regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:

A. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related intervention; and (iii) the research remains active only for long-term follow-up of subjects

B. Where no subjects have been enrolled and no additional risks have been identified

C. Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply, but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

All IRB members are informed of projects approved via expedited review and are given the opportunity to request the review materials.

2.3 Full Board Review

Research projects involving human subjects that do not qualify for exemption or expedited review are reviewed at a convened meeting of the IRB in which a quorum of members must be present. For the research to be approved (or disapproved), it must receive the approval (or disapproval) of a majority of those members present at the meeting. Each member fills out an IRB Member Review Form (Appendix E) approving or disapproving the proposed research.

Under Full Board Review, the IRB must determine that all of the following requirements are satisfied:

- Risks to the subjects are minimized.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects, and to the importance of the knowledge that may reasonably be expected to result.
- Selection of subjects is equitable given the issues and potential benefits involved.
- Informed consent will be sought and documented. The content of the informed consent is spelled out in Section 116 of the Common Rule.

Additional information about the content of Informed Consent is presented in Appendix D.

- When appropriate, provision is made for monitoring the data collected to ensure the safety of subjects.
- When appropriate, adequate provisions are made to protect the privacy of subjects and to maintain the confidentiality of data.
- Appropriate additional safeguards are included for subjects likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, and educationally disadvantaged persons.

2.4 Conditional Review

The IRB may grant conditional approval of a proposal with the stipulation that the Principal Investigator (PI) provide revised or new information before the review can be finalized. If the revised information is found acceptable, the IRB Chair (or delegates) will remove the "condition(s)" and notify the PI that the work has been approved under one of the methods stated in the procedures section below.

It's important to remember that project work involving human subjects may not begin until all of the requirements are satisfied and approved by the IRB.

3. PROCEDURES FOR REVIEWING HUMAN SUBJECTS RESEARCH PROJECTS

3.1 Original Submission by PI – Early Notification

NOTE: *The IRB should be notified at the earliest possible moment in the proposal process—in most cases when scope is filed and/or when the Prep/Risk form is initially filled out. Early notification allows adequate time for IRB interaction with the PI to prepare for the review and, assuming approval, time to provide certification to the PI and to Contracts for transmittal to the client. See Flow Chart Appendix I.*

When the IRB determines that a proposal qualifies as "human subjects" research, the PI will be instructed to submit some or all of the following materials (depending on the level of review required) for preliminary review. Any records or data obtained as a result of the study may be inspected by the sponsor, by any relevant governmental agency (e.g., U.S. Department of Energy), by the INL Institutional Review Board, or by the persons conducting this study, provided that such inspectors are legally obligated to protect any identifiable information from public disclosure, except as otherwise authorized or required by law.

Prepare and submit to IRB Administrator a proposal package** that includes two copies of each of the following:

**"Exempt" review requires 1 and 2; "Expedited" and "Full" require 1–5.

1. A signed "Human Subject Proposal Review Recommendation" form

2. A 1–2 page abstract of the proposed research (including a description of risks and benefits)

3. A complete research proposal, including provisions for the protection of human subjects in accordance with DOE Regulations and all other applicable laws and regulations

4. Sample(s) of proposed informed consent form(s) or proposed research subject information form; [see "Research Consent Form" template document]

5. DOE Project Data Summary form [this information may be released to the public by DOE Hqs, so fill in appropriately] (see Appendix K)

6. Any proposed advertisement for human volunteers.
(**NOTE:** *6 only applies if PI will advertise for volunteers.*)

NOTE: Copies of proposal, abstract, and informed consent document should be marked "INL-IRB."

3.2 Exempt Review Procedures

For research projects determined to be exempt from IRB review, the procedures are as follows:

A. The Chair (and/or delegates) reviews the submitted materials, and, if necessary, may consult with the PI, staff with relevant expertise, or other IRB members to help determine that the proposed research qualifies for exemption.

B. The Administrator, by internal memo to the PI, summarizes the actions arising from the review. When required, an HHS 310 Assurance Form, signed by the IRB Chairman, will be sent to the PI and to the cognizant contracts representative for submittal with the proposal.

Proposals to the Department of Health and Human Services (DHHS) and other federal agencies classified as "**Exempt**" typically require an approved HHS 310 Form stating the basis for exemption.

Exempt proposals to industrial clients do not require any forms. The PI may choose to note in the proposal that the work was approved as "**Exempt**" by BEA IRB, which is authorized under DOE to conduct the review.

A. In summary, the Chair (and/or delegates) will copy the declaration of exemption memo and HHS 310 Form (when required) to the PI. The PI is responsible for notifying the proposed client that the work has been reviewed and declared exempt by the IRB. Exempt proposals/projects will be reviewed yearly to confirm the work maintains its exempt status.

B. The IRB documents all internal files.

3.3 Expedited Review Procedures

For research projects that may be reviewed under "***Expedited Review***," the procedures are as follows:

A. The Chair (and/or delegates) reviews the submitted materials and, when necessary, consults with the PI, other board members, or persons with relevant expertise to make a determination that the proposed research qualifies for ***Expedited Review***.

B. The Administrator, by internal memo to the PI, summarizes the actions arising from the review, stating the regulations by which the determination was made. When required, an HHS 310 Form, signed by the IRB Chairman, will be sent to the PI for submittal with the proposal.

C. The PI will notify the proposal client that the work has been reviewed and approved by the IRB.

D. The IRB documents actions to the IRB and to internal files.

If <u>not approved</u>, the decision of disapproval must be followed by a Full Board Review. In this case:

A. The Administrator: Will send a memo to the PI summarizing actions arising from the review, providing the PI an opportunity to revise or submit new information prior to meeting with the IRB to discuss the research.

B. The IRB will send copies of full review package to IRB members in preparation for the Full Board Review.

3.4 Full Board Review Procedures

The procedures for research projects requiring ***Full Board*** review are as follows:

A. The Administrator sends copies of the complete review package to the IRB members at least a week in advance of the meeting.

B. The Administrator invites the PI to give a short presentation and be prepared to answer questions relating to the research. The PI is not present when the IRB votes.

C. The IRB members discuss the risks and benefits to the human subjects and vote to approve/disapprove the proposal via the IRB Member Review form. All discussion and resulting actions of the IRB are summarized in the meeting minutes, which are compiled, recorded, and protected according to federal regulation.

D. The Administrator, by internal memo to the PI, summarizes the actions arising from the review, stating the regulations by which the determination was made. When required, an HHS 310 Form, signed by the IRB Chairman, will be sent to the PI for submittal with the proposal.

E. The PI will notify the proposal client that the work has been reviewed and approved by the IRB.

F. The IRB Administrator documents actions to the IRB and to the internal files.

3.5 Conditional Review Procedures

Conditional Review may result from either Expedited or Full Board Review, with the exception that the IRB has requested revised or additional information. When the revised information is found acceptable, the IRB Chair (or delegates) will remove the “conditions” and notify the PI that the work has been approved under one of the methods stated above. Reporting requirements will depend on the client-type.

NOTE: *in all cases:*

1. *Work that has been determined to include human subjects may not begin until it is reviewed and approved by the IRB.*

2. *The PI will receive a schedule for Continuing Review.*

4. REPORTING IRB REVIEW AND APPROVAL TO CLIENTS (CERTIFICATION)

The PI is responsible for notifying the client upon IRB approval of the research protocol.

5. CONTINUING REVIEW

All active research projects involving human subjects that are not exempt must be reviewed at least annually. The IRB may require more frequent reviews appropriate to the degree of risk to the human subjects. The IRB Administrator will issue a request for review at least one month in advance of the expiration date of the last review. A Continuing Review form (see Appendix H) and current Informed Consent form, signed by the PI, will be required for completion of the review. Depending on the project status, additional information such as a revised Statement of Work may be requested as well.

6. MODIFICATIONS TO APPROVED RESEARCH PROTOCOLS

Actions outside the IRB approved scope of research must not be taken without prior IRB approval, except under emergency conditions.

An emergency exists only when a human subject is confronted by an exceptionally serious or life-threatening situation and when no standard, alternate, acceptable treatment is available. In such a situation, the PI must report to the IRB as soon as possible that the above conditions exist.

Minor changes to previously approved research protocols (during the period of one year or less for which approval is authorized) may be reviewed by the expedited review procedure (with the exceptions previously noted). For all other changes, IRB review and approval are required. Proposed changes are submitted with the same materials as required of the original proposal.

7. NONCOMPLIANCE – REPORTING AND REVIEWING ADVERSE EVENTS

BEA and federal regulations and policies require that significant or continuing noncompliance with those regulations or the requirements or determinations of the IRB will be reported in a timely manner to the IRB, BEA management, and the department/agency supporting the research. Responsibility for reporting noncompliance and adverse events rests with the PI and his/her management. The IRB is responsible for conducting and reporting to DOE and/or the funding client the results of Full Board Reviews of adverse events and items found not in compliance. Actions may result, ranging from temporary suspension of research until the problem is corrected, to cancellation of the research, which is based upon circumstances involved in the adverse event/unanticipated problem.

The federal human subjects protection regulations (45 CFR 46) issued by the HHS Office of Human Research Protections (OHRP) requires prompt reporting of any unanticipated problem (such as loss of data) to the IRB, to appropriate institutional and agency officials, and to OHRP. OHRP guidance recommends that the PI report an unanticipated problem to the IRB within 2 weeks and to OHRP within 6 weeks (or within 1 month of notifying the IRB.

DOE Order 443.1A also requires prompt reporting to the DOE Human Subjects Research Program Manager, SC-23 (and the DOE Human Subjects Research (HSR) Program Manager NA-1 for NA sites) and coordination with and approval from the HSR Program Manager in determining plans to correct any noncompliance or to deal with the unanticipated problem. Noncompliances or unanticipated problems that do not involve PII must be reported within 48 hours.

The definition of “prompt reporting” is different when PII is involved. Federal and DOE requirements require that any incident involving potential loss or compromise of PII must be reported by the PI immediately, and then immediately through the appropriate Departmental Element AND to the DOE Cyber Incident Response Capability (DOE-CIRC). Any PII loss incident must also be reported immediately to the HSR Program Manager.

Additionally, in accordance with federal and DOE requirements, PII transferred from one organization to another as part of a human subject research protocol (when/as authorized by the approving IRB, the responsible DOE Program Office, and the research/screening participant) MUST FIRST BE ENCRYPTED consistent with PII protection requirements stated in DOE M 205.1-7 using a program such as Entrust.

8. COOPERATIVE RESEARCH

In conducting cooperative research, each participating institution is responsible specifically for safeguarding the rights and welfare of the human subjects involved and generally for compliance with the Common Rule. INL takes a conservative approach to cooperative research and asks that any research that may involve human subjects be reviewed by the BEA IRB to ensure that the rights and welfare of the human subjects involved in the research are protected. Where appropriate, the BEA IRB may choose to accept the actions of the cooperating institution.

9. RECORDS

PIs are required to maintain human subject project records for at least three years following Project closure (in particular, the Informed Consent records), THEN TRANSFER TO A Document and Records Service Center or Record Storage for the remainder of the retention.

The IRB maintains the following records in compliance with the Common Rule, Section 115:

- A list of IRB members
- Delegations of Authority
- Written procedures for the IRB and PIs
- Copies of all research proposals reviewed and approved consent forms
- Minutes of IRB meetings
- Records of continuing review activities
- Copies of correspondence between the IRB and the PIs.

SECTION II – PRINCIPAL INVESTIGATOR INFORMATION

1. PRINCIPAL INVESTIGATOR ROLES AND RESPONSIBILITIES

Table 1. Matrix – roles and responsibilities of the principal investigator.

ROLES AND RESPONSIBILITIES	PRINCIPAL INVESTIGATOR
Proposes/agrees on the need to use human subjects in research	X
Notifies IRB of plans for human subjects research proposal	X
Agrees on type of review needed (Exempt, Expedited, Full Board)	X
Prepares proposal, abstract, and sample consent form or information form	X
Obtains Directorate scientific merit approval for all non-exempt proposals	X
Submits proposal and required information to the IRB	X
Participates in Full Board Reviews	X
Modifies proposal/Informed Consent if required by the IRB, IRB Chair, or DOE to meet federal regulations for approval	X
Formally notifies client that IRB has reviewed and approved the research	X
Sends approved proposal on for funding approval	X
Obtains IRB written approval before starting human subjects work	X
Obtains and maintains proper Informed Consent throughout life of the project	X
Follows originally approved procedures or requests IRB approval for changes	X
Reports any injury, unexpected adverse event, unanticipated problem, or noncompliance with the DOE Federal Wide Assurance (FWA)	X
Provides requested input for continuing review approval of projects	X
Retains signed consent forms and research records as required	X
Produces IRB records/forms to respond to human protection audits	X
Notifies IRB of project closure	X

2. PRINCIPAL INVESTIGATOR CHECK LIST

If you think your proposal might possibly involve human subjects, or know for sure that it will, contact the IRB as soon as possible. We can (1) help you determine if it qualifies as human subjects research; (2) give you a good idea of the type of review required; and (3) get you started on the information you'll need for the review. The whole process may be as simple as a phone call and/or fax. Our intent is to turn around "Exempt" in one day, "Expedited" in no more than 2–3 days, and complete a Full Board Review in no more than two weeks. These schedules are all contingent on how quickly we receive complete and accurate information from you. Please let us know the date your proposal is due to the client.

2.1 Principal Investigator Check List – Proposal Process

Prepare and submit to IRB Administrator a proposal package** that includes two copies each of the following:

**"Exempt" review requires #1 & #2; "Expedited" and "Full" require #1–5.

1. A signed "Human Subject Proposal Review Recommendation" form

2. A 1–2 page abstract of the proposed research (including a description of risks and benefits)

3. A complete research proposal, including provisions for the protection of human subjects in accordance with DOE Regulations and all other applicable laws and regulations

4. Sample(s) of proposed informed consent form(s) or proposed research subject information form; [see "Research Consent Form" template document]

5. DOE Project Data Summary form [this information may be released to the public by DOE Hqs, so fill in appropriately] (see Appendix K)

6. Any proposed advertisement for human volunteers.
(NOTE: #6 only applies if PI will advertise for volunteers.)

NOTE: Copies of proposal, abstract, and informed consent document should be marked "INL-IRB."

Remember

- **Human subjects work cannot start until it is IRB approved.**

- **The IRB must be notified of adverse events immediately.**
- **All projects/informed consents require at least annual review.**

If you have any questions, contact the IRB – Call, e-mail, or fax.

Dena Tomchak – Administrator
E-mail – DENA.TOMCHAK@INEL.GOV
Office – 526-1590 Fax – 526-0876

Harold Blackman – Chair
E-mail – HAROLD.BLACKMAN@INEL.GOV
Office – 526-0245 Fax – 526-0425

3. APPENDIXES

Appendix A, Federal Wide Assurance

Appendix B, Federal Policy for the Protection of Human Subjects; Notices and Rules 10 CFR 745 – The "Common Rule"

Appendix C, DOE Order 443.1a (dated 12/20/07)

Appendix D, Informed Consent Requirements and Experimental Subject's Bill of Rights

Appendix E, IRB Member Review Form and Reviewer Considerations

Appendix F, Human Subject Proposal Review Recommendation Form

Appendix G, Continuing Review Document

Appendix H, Battelle Energy Alliance, LLC IRB Members/Administrative Contacts

Appendix I, Human Subjects Research Procedures Flow Chart

Appendix J, Matrix of Roles and Responsibilities

Appendix K, DOE Project Data Summary Form

Appendix A

Terms of the Federal-Wide Assurance

FEDERAL-WIDE ASSURANCE (FWA) FOR THE PROTECTION OF HUMAN SUBJECTS

U. S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP)

A. TERMS OF THE FEDERAL-WIDE ASSURANCE (FWA) FOR INSTITUTIONS WITHIN THE UNITED STATES

1. Human Subjects Research must be guided by Ethical Principles

All of the Institution's human subjects research activities, regardless of whether the research is subject to federal regulations, will be guided by the ethical principles in: (a) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, or (b) other appropriate ethical standards recognized by federal departments and agencies that have adopted the Federal Policy for the Protection of Human Subjects, known as the Common Rule.

2. Applicability

These terms apply whenever the Institution becomes engaged in human subjects research conducted or supported* by any federal department or agency that has adopted the Common Rule, unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. In general, the Institution becomes so engaged whenever (a) the Institution's employees or agents intervene or interact with human subjects for purposes of federally conducted or supported research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of federally conducted or supported research; or (c) the Institution receives a direct federal award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

[*Federally supported is defined throughout the FWA and the Terms of Assurance as the U.S. Government providing any funding or other support.]

3. Compliance with the Federal Policy for the Protection of Human Subjects and Other Applicable Federal, State, Local, or Institutional Laws, Regulations, and Policies

When the Institution becomes engaged in federally conducted or supported human subjects research to which the FWA applies, the Institution and the institutional review boards (IRBs) designated under the Institution's Assurance will comply with the Federal Policy for the Protection of Human Subjects.

The reference in the Code of Federal Regulations is shown below for each department and agency which has adopted the Common Rule:

7 CFR Part 1c	Department of Agriculture
10 CFR Part 745	Department of Energy
14 CFR Part1230	National Aeronautics and Space Administration
15 CFR Part 27	Department of Commerce
16 CFR Part 1028	Consumer Product Safety Commission
22 CFR Part 225	Agency for International Development
24 CFR Part 60	Department of Housing and Urban Development
28 CFR Part 46	Department of Justice
32 CFR Part 219	Department of Defense
34 CFR Part 97	Department of Education
38 CFR Part 16	Department of Veterans Affairs
40 CFR Part 26	Environmental Protection Agency
45 CFR Part 46	Department of Health and Human Services
45 CFR Part 46 (by Executive Order 12333)	Central Intelligence Agency
45 CFR Part 690	National Science Foundation
49 CFR Part 11	Department of Transportation

For any federally conducted or supported human subjects research to which the FWA applies, the Institution will also comply with any additional human subjects regulations and policies of the department or agency which conducts or supports the research and any other applicable federal, state, local, or institutional laws, regulations, and policies. When the Institution is engaged in human subjects research conducted or supported by the Department of Health and Human Services (HHS), the Institution will comply with all subparts of the HHS regulations at Title 45 Code of Federal Regulations part 46 (45 CFR Part 46, subparts A, B, C, and D).

Human subjects research conducted or supported by each federal department or agency listed above will be governed by the regulations as implemented by the respective department or agency. The head of the department or agency retains final judgment as to whether a particular activity conducted or supported by the respective department or agency is covered by the Common Rule. If the Institution needs guidance regarding implementation of the Common Rule and other applicable federal regulations, the Institution should contact appropriate officials at the department or agency conducting or supporting the research. For federally conducted or supported research covered by the FWA, the department or agency that conducts or supports the

research retains final authority for determining whether the Institution complies with the Terms of Assurance. If HHS receives an allegation or indication of noncompliance related to human subjects research that is covered by the FWA and is conducted or supported solely by a Common Rule department or agency other than HHS, HHS will refer the matter to the other department or agency for review and action as appropriate.

NOTE: If the Institution voluntarily extends the Common Rule and/or subparts B, C, and D of the HHS regulations at 45 CFR Part 46 to all research, regardless of support, OHRP will have the authority to ensure that the Institution complies with this commitment for all research to which the FWA applies that is not federally conducted or supported.

4. Written Procedures*

a) The Institution submitting the FWA has established written procedures* for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any department or agency conducting or supporting the research (or designee), any applicable regulatory body, and OHRP of any:

1. Un-anticipated problems involving risks to subjects or others.
2. Serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB(s).
3. Suspension or termination of IRB approval.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

b) The Institution must ensure that the IRB(s) designated under the FWA has established written procedures* for:

1. Conducting IRB initial and continuing review (not less than once per year) of research, and reporting IRB findings to the investigator and the Institution.
2. Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since the previous IRB review.
3. Ensuring prompt reporting to the IRB of proposed changes in a research activity and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subjects.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

[*For HHS-conducted or supported human subjects research, see OHRP guidance on written IRB procedures on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm.]

5. Scope of IRB(s)'s Responsibilities

All human subjects research to which the FWA applies, except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, will be reviewed, prospectively approved, and subject to continuing review at least annually by the designated IRB(s). The IRB(s) will have the authority to approve, require modifications in, or disapprove the covered human subjects research. For research approved by the IRB(s), further appropriate review and approval by any department or agency conducting or supporting the research or by officials of the institution holding the FWA may be required.

6. Informed Consent Requirements

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, informed consent for research to which the FWA applies will be:

a) Sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, Section 116 of the Common Rule.

b) Appropriately documented, in accordance with, and to the extent required by, Section 117 of the Common Rule.

7. Requirement for Assurances for Collaborating Institutions

When the Institution holding the FWA is either (a) the primary awardee under a federal grant, contract, or cooperative agreement supporting research to which the FWA applies: or (b) the coordinating center for federally conducted or supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved or other federally approved assurance for the protection of human subjects.

An institution holding an FWA may collaborate with another institution that does not have an FWA. In such circumstances, a collaborating institution may operate under the FWA with the approval of the department or agency conducting or supporting the research and the institution holding the FWA.

For federally conducted or supported research covered by the FWA, the department or agency that conducts or supports the research retains final authority for determining which institutions are engaged in the research and the need to hold an assurance for the protection of human subjects.

8. Written Agreements with Independent Investigators Who are Not Otherwise Affiliated with the Institution

When the Institution holding the FWA is either (a) the primary awardee under a federal grant, contract, or cooperative agreement supporting research to which the FWA applies; or (b) the

coordinating center for federally conducted or supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating independent investigators engaged in such research operate under an appropriate OHRP-approved or other federally approved assurance for the protection of human subjects.

The engagement in federally conducted or supported human subjects research activities to which the FWA applies by each independent investigator who is not otherwise an employee or agent of the Institution may be covered under the FWA only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB review. OHRP's sample Individual Investigator Agreement (see http://www.hhs.gov/ohrp/humansubjects/assurance/unaflsup.rtf) may be used or adapted for this purpose, or the Institution may develop its own commitment agreement in coordination with the department or agency conducting or supporting the research. Institutions must maintain commitment agreements on file and provide copies upon request to OHRP and any department or agency conducting or supporting the research.

For federally conducted or supported research covered by the FWA, the department or agency that conducts or supports the research retains final authority for determining which independent investigators are engaged in the research and need to be covered by a written commitment agreement with the institution holding the FWA.

9. Institutional Support for the IRB(s)

The Institution will ensure that each IRB designated under the FWA has meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

10. Compliance with the Terms of Assurance

The Institution accepts and will follow items 1–9 above and is responsible for ensuring that (a) the IRB(s) designated under the FWA agree to comply with these terms; and (b) the IRB(s) possess appropriate knowledge of the local research context for all research to which the FWA applies (please refer to the OHRP Guidance on IRB Knowledge of Local Research Context on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm).

Any designation under the FWA of the IRB of another institution or organization must be documented by a written agreement between the Institution holding the FWA and the IRB organization outlining their relationship and include a commitment that the designated IRB will adhere to the requirements of the FWA. OHRP's sample IRB Authorization Agreement may be used for such purpose, or the parties involved may develop their own agreement. This agreement should be kept on file at both institutions/organizations and made available upon request to OHRP and any department or agency conducting or supporting research covered by the FWA.

11. Assurance Training

The OHRP Assurance Training Modules (see http://137.187.172.153/CBTs/Assurance/login.asp) describe the major responsibilities of the Institutional Signatory Official, the Human Protection Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB Chair(s) that must be fulfilled under the FWA. OHRP strongly recommends that the Institutional Signatory Official, the Human Protections Administrator, and the IRB Chair(s) personally complete the relevant OHRP Assurance Training Modules, or comparable training that includes the content of these modules, prior to submitting the FWA.

12. Educational Training

OHRP strongly recommends that the Institution and the designated IRB(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research investigators, IRB members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with, the following: relevant ethical principles; relevant federal regulations; written IRB procedures; OHRP guidance; other applicable guidance; state and local laws; and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that (a) IRB members and staff complete relevant educational training before reviewing human subjects research; and (b) research investigators complete appropriate institutional educational training before conducting human subjects research.

13. Renewal of Assurance

All information provided under the FWA must be renewed or updated at least every 36 months (3 years), even if no changes have occurred, in order to maintain an active FWA. Failure to update this information may result in restriction, suspension, or termination of the Institution's FWA for the protection of human subjects.

B. TERMS OF THE FEDERAL-WIDE ASSURANCE (FWA) FOR INTERNATIONAL (NON-U.S.) INSTITUTIONS

1. Human Subjects Research Must Be Guided by Ethical Principles

All of the Institution’s human subjects research activities, regardless of whether the research is subject to U.S. federal regulations, will be guided by one of the following statements of ethical principles: (a) The World Medical Association's Declaration of Helsinki (as adopted in 1996 or 2000); (b) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; or (c) other appropriate international ethical standards recognized by U.S. federal departments and agencies that have adopted the U.S. Federal Policy for the Protection of Human Subjects, known as the Common Rule.

2. Applicability

These terms apply whenever the Institution becomes engaged in human subjects research conducted or supported* by any U.S. department or agency that has adopted the Common Rule, unless the research is otherwise exempt from the requirements of the Common Rule or a U.S. federal department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. In general, the Institution becomes so engaged whenever (a) the Institution's employees or agents intervene or interact with human subjects for purposes of U.S. federally conducted or supported research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of U.S. federally conducted or supported research; or (c) the Institution receives a direct award to conduct U.S. federally supported human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

If a U.S. federal department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided by the U.S. Federal Policy for the Protection of Human Subjects, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided above, consistent with the requirements of section 101(h) of the U.S. Federal Policy for the Protection of Human Subjects.

[*Federally supported is defined throughout the Assurance document and the Terms of Assurance as the U.S. Government providing any funding or other support.]

3. Compliance with Laws, Regulations, Policies, and Guidelines

When the Institution becomes engaged in U.S. federally conducted or supported human subjects research to which the FWA applies, the Institution and institutional review boards (IRBs) or independent ethics committees (IECs) designated under the FWA at a minimum will comply with one or more of the following:

a) The U.S. Federal Policy for the Protection of Human Subjects (see section 3 of the Terms of the FWA for Institutions within the United States for a list of U.S. federal departments and agencies that have adopted the Common Rule).

b) The Common Rule and subparts B, C, and D of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR Part 46.

c) The U.S. Food and Drug Administration (FDA) regulations at 21 CFR Parts 50 and 56.

d) The May 1, 1996, International Conference on Harmonization E-6 Guidelines for Good Clinical Practice (ICH-GCP-E6), Sections 1 through 4.

e) The 2002 Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects.

f) The 1998 (with 2000, 2002, and 2005 amendments) Medical Research Council of Canada Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans.

g) The 2006 Indian Council of Medical Research Ethical Guidelines for Biomedical Research on Human Subjects.

h) Other standard(s) for the protection of human subjects recognized by U.S. federal departments and agencies which have adopted the U.S. Federal Policy for the Protection of Human Subjects.

All U.S. federally conducted or supported human subjects research to which the FWA applies will also comply with any additional human subjects regulations and policies of the U.S. federal department or agency which conducts or supports the research and any other applicable U.S. federal, international, state, local, or institutional laws, regulations, and policies.

The head of the U.S. federal department or agency retains final judgment as to whether a particular activity conducted or supported by the respective department or agency is covered by the Common Rule. If the Institution needs guidance regarding implementation of the Common Rule and/or other applicable U.S. federal regulations, the Institution should contact appropriate officials at the U.S. federal department or agency conducting or supporting the research. For U.S. federally conducted or supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining whether the Institution complies with the Terms of Assurance. If HHS receives an allegation or indication of noncompliance related to human subjects research that is covered by the FWA and is conducted or supported solely by a Common Rule department or agency other than HHS, HHS will refer the matter to the other U.S. federal department or agency for review and action as appropriate.

4. IRB/IEC Written Procedures*

a) The Institution submitting the FWA has established written procedures* for ensuring prompt reporting to the IRB/IEC, appropriate institutional officials, the head of any U.S. federal department or agency conducting or supporting the research (or designee), any applicable regulatory body, and OHRP of any:

1. Un-anticipated problems involving risks to subjects or others.
2. Serious or continuing noncompliance with the applicable U.S. federal regulations or the requirements or determinations of the IRB(s)/IEC(s).
3. Suspension or termination of IRB/IEC approval.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

b) The Institution must ensure that the IRB(s)/IEC(s) designated under the FWA has established written procedures* for:

1. Conducting IRB/IEC initial and continuing review (not less than once per year), of research, and reporting IRB/IEC findings to the investigator and the Institution.
2. Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since the previous IRB/IEC review.
3. Ensuring prompt reporting to the IRB/IEC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB/IEC approval has already been given, may not be initiated without IRB/IEC review and approval, except when necessary to eliminate apparent immediate hazards to the subjects.

Upon request, the Institution will provide a copy of these written procedures to OHRP and any department or agency conducting or supporting research covered by the FWA.

[*For HHS-conducted or supported human subjects research, see OHRP guidance on written IRB procedures on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.htm.]

5. Scope of IRB(s)/IEC(s)'s Responsibilities

All U.S. federally conducted or supported research to which the FWA applies, except for research exempted or waived in accordance with sections 101(b) or 101(i) of the U.S. Common Rule, will be reviewed, prospectively approved, and subject to continuing review at least annually by the designated IRB(s)/IEC(s). The IRB(s)/IEC(s) shall have authority to approve, require modifications in, or disapprove the covered human subjects research. For research approved by the IRB(s)/IEC(s), further appropriate review and approval by any U.S. federal department or agency conducting or supporting the research or by officials of the institution holding the FWA may be required.

6. Informed Consent Requirements

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the U.S. Common Rule, informed consent for research to which the FWA applies will be:

a) Sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, Section 116 of the U.S. Common Rule.

b) Appropriately documented, in accordance with, and to the extent required by, Section 117 of the U.S. Common Rule.

7. Considerations for Special Class of Subjects

For HHS-conducted or supported human subjects research, the Institution will comply with the HHS regulations at 45 CFR Part 46, subparts B, C, and D, prior to the involvement of pregnant women, fetuses, or neonates; prisoners; or children, respectively. For non-HHS U.S. federally supported human subjects research, the Institution will comply with any human subject

regulations and/or policies of the supporting U.S. federal department or agency for these classes of subjects.

8. Requirement for Assurances for Collaborating Institutions

When the Institution holding the FWA is either (a) the primary awardee under a U.S. federal grant, contract, or cooperative agreement supporting research to which the FWA applies; or (b) the coordinating center for U.S. federally conducted or supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved or other U.S. federally approved assurance for the protection of human subjects.

An institution holding an FWA may collaborate with another institution that does not have an FWA. In such circumstances, a collaborating institution may operate under the FWA with the approval of the U.S. federal department or agency conducting or supporting the research and the institution holding the FWA.

For U.S. federally conducted or supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining which institutions are engaged in the research and need to hold an assurance for the protection of human subjects.

9. Written Agreements with Independent Investigators Who are Not Otherwise Affiliated with the Institution

When the Institution holding the FWA is either (a) the primary awardee under a U.S. federal grant, contract, or cooperative agreement supporting research to which the FWA applies; or (b) the coordinating center for U.S. federally conducted or supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating independent investigators engaged in such research operate under an appropriate OHRP-approved or other U.S. federally approved assurance for the protection of human subjects.

The engagement in U.S. federally conducted or supported human subjects research activities to which the FWA applies by each independent investigator who is not otherwise an employee or agent of the Institution may be covered under the FWA only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB/IEC review. OHRP's sample Individual Investigator Agreement (see http://www.hhs.gov/ohrp/humansubjects/assurance/unaflsup.rtf) may be used or adapted for this purpose, or the Institution may develop its own commitment agreement in coordination with the U.S. federal department or agency conducting or supporting the research. Institutions should maintain commitment agreements on file and provide copies upon request to OHRP or any U.S. federal department or agency conducting or supporting the research.

For U.S. federally conducted or supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining which independent investigators are engaged in the research and need to be covered by a written commitment agreement with the institution holding the FWA.

10. Institutional Support for the IRB(s)/IEC(s)

The Institution will ensure that each IRB(s)/IEC(s) designated under the FWA has meeting space and sufficient staff to support the IRB's/IEC's review and recordkeeping duties.

11. Compliance with the Terms of Assurance

The Institution accepts and will follow items 1–10 above and is responsible for ensuring that (a) the IRB(s)/IEC(s) designated under the FWA agree to comply with these terms, and (b) the IRB(s)/IEC(s) possess appropriate knowledge of the local research context for all research to which the FWA applies (please refer to the OHRP Guidance on IRB Knowledge of Local Research Context on the OHRP website at http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm).

Any designation under the FWA of the IRB/IEC or another institution or organization should be documented by a written agreement between the Institution holding the FWA and the IRB/IEC organization outlining their relationship and include a commitment that the designated IRB/IEC will adhere to the requirements of the FWA. OHRP's sample IRB Authorization Agreement may be used for such purpose, or the parties involved may develop their own agreement. This agreement should be kept on file at both institutions/organizations and made available upon request to OHRP and any U.S. federal department or agency conducting or supporting research covered by the FWA.

12. Assurance Training

The OHRP Assurance Training Modules (see http://137.187.172.153/CBTs/Assurance/login.asp) describe the major responsibilities of the Institutional Signatory Official, the Human Protection Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB/IEC Chair(s) that must be fulfilled under the FWA. OHRP strongly recommends that the Institutional Signatory Official, the Human Protections Administrator, and the IRB/IEC Chair(s) personally complete the relevant OHRP Assurance Training Modules, or comparable training that includes the content of these Modules, prior to submitting the FWA.

13. Educational Training

OHRP strongly recommends that the Institution and the designated IRB(s)/IEC(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research investigators, IRB/IEC members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with, the following: relevant ethical

principles; relevant U.S. regulations; written IRB/IEC procedures; OHRP guidance; other applicable guidance; national, state, and local laws; and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that (a) IRB/IEC members and staff complete relevant educational training before reviewing human subjects research; and (b) research investigators complete appropriate institutional educational training before conducting human subjects research.

14. Renewal of Assurance

All information provided under the FWA should be renewed or updated every 36 months (3 years), even if no changes have occurred, in order to maintain an active FWA. Failure to update this information may result in restriction, suspension, or termination of the Institution's FWA for the protection of human subjects.

Implementation

A. Research Investigator. The responsibilities of the research investigator are as follows:

1. Determination of Human Subject Involvement.

   A. The research investigator shall determine whether research will involve human subjects, as defined in this Assurance.

   B. If the research investigator is uncertain whether research will involve human subjects, the investigator should request a determination from the IRB.

2. Preparation and Submission of Protocol.

   A. Prior to involving human subjects in research, the investigator shall prepare and submit to the IRB a protocol that includes:

      1. A complete description of the proposed research.

      2. Provisions for the protection of human subjects in accordance with this Assurance, the DOE Regulations, and all other applicable laws and regulations.

      3. Sample(s) of proposed informed consent form(s).

   B. The research investigator shall submit the original research protocol and a supplement to the IRB when:

      1. It is proposed to involve human subjects in research that previously lacked definite plans for the involvement of human subjects. Applications for grants, cooperative agreements, or contracts that are submitted for funding or support with the knowledge that subjects may be involved within the period of support, but without definite plans for such involvement, need not be reviewed by the IRB before an award may be made. However, human subjects may not be involved in any project supported by such an award until the project has been reviewed and approved by the IRB in accordance with this Assurance. (NOTE: This provision is intended to cover activities such as institutional grants when selection of specific projects will be the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects involvement will depend upon completion of instruments, prior animal studies, or purification of compounds.)

2. It is proposed to involve human subjects in research that previously had no plans for involvement of human subjects. In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by the IRB.

3. It is proposed to change previously approved research during the period (of one year or less) for which approval is authorized. The research investigator shall not initiate any changes in previously approved research without the approval of the IRB, except when necessary to eliminate apparent immediate hazards to the subject(s).

C. The research investigator is responsible for submitting to the IRB a request for renewal of approval of ongoing research at least one month prior to the expiration date of the approval.

3. Compliance with Decision of the IRB; Obtaining Informed Consent.

A. The research investigator shall comply with the IRB's decisions, conditions, and requirements regarding the research protocol.

B. The research investigator shall obtain and document informed consent prior to involving human subjects in the research, as required by the IRB, and shall retain signed informed consent forms at least three years after termination of the approval period.

4. Reporting. The research investigator shall promptly report to the IRB:

A. Any proposed changes in previously approved research.

B. Any injuries to human subjects, any unanticipated problems that involve risks to human subjects or other, or any serious or continuing noncompliance with the requirements or determinations of the IRB.

B. The Institutional Review Board (IRB).

1. Duties and Authority. The IRB shall review and have authority to approve, require modifications in (as a condition of approval), or disapprove all research covered by this Assurance, or suspend or terminate previous approval of such research, to assure the protection of the rights and welfare of human subjects.

2. Membership.

   A. The IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of the research covered by this Assurance. The IRB shall be sufficiently qualified through the experience, expertise, and diversity of its members, including consideration of race, gender, and 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.

   B. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of BEA's commitments and policies, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.

   C. The IRB shall not consist entirely of members of one profession, and nondiscriminatory efforts shall be made to ensure the IRB does not consist entirely of men or entirely of women.

   D. The IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas.

   E. The IRB shall include at least one member who is not otherwise affiliated with BEA and who is not a member of the immediate family of a person who is affiliated with BEA.

   F. No member may participate in the IRB review of any project in which the member has a conflicting interest, except to provide information requested by the IRB, and the minutes of the IRB meeting shall so reflect.

   G. The IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise in addition to that available on the IRB. These individuals may not vote with the IRB.

   H. The IRB members' names, representative capacities, and relationships (if any) with BEA are set forth in Attachment "A" hereto.

3. Meetings. Except when an expedited review procedure is used, the IRB shall review proposed research at convened meetings at which a majority of the IRB members are present, including at least one member whose primary concerns are in non-scientific areas. In order for research to be approved, it shall receive the

approval of a majority of the members present at the meeting. The IRB shall meet not less than once per year, at the call of the chairperson, after appropriate notice to all members.

4. Continuing Review.

   A. The IRB shall establish and follow a schedule for review of all previously approved research at intervals appropriate to the degree of risk, but not less than once per year. When review intervals of less than one year are required, the IRB's notice of approval to the research investigator shall specify the review interval.

   B. The IRB shall observe or have a third party observe the consent process and the conduct of the research, if the IRB determines such observation should be required as a condition of approval.

   C. The IRB shall require verification from sources other than the investigators that no material changes have occurred since previous review by the IRB, if the IRB determines such verification should be required as a condition of approval.

5. Suspension and Termination of Approval. The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB requirements or that has been associated with unexpected serious harm to subjects.

6. Notice of Actions. The IRB shall notify investigators in writing and maintain records of its decisions to approve or disapprove proposed research, to require modifications as a condition of approval, or to suspend or terminate approval granted previously. If the IRB disapproves research, or suspends or terminates approval, it shall include in its written notification a statement of the reasons for its action and give the investigator an opportunity to respond in person or in writing.

7. Reports to BEA Officials and DOE. The IRB shall report promptly to the Laboratory Director of BEA/INL, DOE, and the supporting federal department or agency (if other than DOE):

   A. Any injuries to human subjects, any unanticipated problems that involve risks to human subjects or others, or any serious or continuing non-compliance with the requirements or determinations of the IRB.

   B. Any suspension or termination of the IRB approval of research.

   C. Any change in the IRB membership.

C. Criteria for Approval of Research. In order to approve research covered by this Assurance, the IRB shall determine that all of the following requirements are satisfied:

1. Risks to subjects are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk, and, wherever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies research.) The IRB shall not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable, taking into account the purposes of the research and the setting in which the research will be conducted.

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, DOE regulations and this Assurance.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by, DOE regulations and this Assurance.

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the research to protect the rights and welfare of those subjects.

D. Informed Consent. The IRB shall require that information given to subjects as part of informed consent is in accordance with DOE regulations and this Assurance, or may waive obtaining informed consent in accordance with DOE regulations and this Assurance, as set forth below.

1. General Requirements for Informed Consent.

A. An investigator shall not involve a human being as a subject in research covered by this Assurance unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative, or the IRB has specifically waived informed consent in accordance with DOE Regulations and this Assurance.

B. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

C. The information given to the subject or the subject's representative shall be in language understandable to the subject or the representative.

D. Informed consent, whether oral or written, may not include exculpatory language through which the subject or the subject's representative waives or appears to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, BEA, or its employees from liability for negligence.

2. Basic Elements of Informed Consent. Except as provided in Paragraph 4 of this Section, in seeking informed consent the following information shall be provided to each subject:

A. 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.

B. A description of any reasonable foreseeable risks or discomforts to the subject.

C. A description of any benefits to the subject or to others that may reasonably be expected from the research.

D. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

E. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

F. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

G. 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.

H. 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.

3. Additional Elements of Informed Consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

A. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.

B. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

C. Any additional costs to the subject that may result from participation in the research.

D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

E. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.

F. The approximate number of subjects involved in the study.

G. Any additional information that would meaningfully add to the protection of the rights and welfare of the subject.

4. Waiver of Informed Consent. The IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in this section, or may waive the requirement to obtain informed consent, provided the IRB finds and documents that:

A. The research involves no more than minimal risk to the subject.

B. The waiver or alteration will not adversely affect the rights and welfare of the subject.

C. The research could not practicably be carried out without the waiver or alteration.

D. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

5. Documentation of Informed Consent.

A. General Requirement for Documentation of Informed Consent. Except as provided in Paragraph C of this Section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

B. Long and Short Forms. Except as provided in Paragraph C of this Section, the consent form may be either of the following:

1. A written consent document that embodies the elements of informed consent required by DOE regulations and this Assurance. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.

2. A “short form” written consent document stating that the elements of informed consent required by DOE Regulations and this Assurance have been presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the “short form.”

C. Waiver of Documentation of Informed Consent. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

1. That 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.

2. That the research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

6. Federal, State, and Local Law. The informed consent requirements set forth above do not pre-empt any applicable federal, state, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

7. Emergency Medical Care. The informed consent requirements set forth above are not intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so, under applicable federal, state, or local law.

E. Expedited Review[c].

Applicability

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- The categories in this list apply regardless of the age of subjects, except as noted.

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

c. An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

- The expedited review procedure may not be used for classified research involving human subjects.

- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review – expedited or convened – utilized by the IRB.

- Categories 1 through 7 pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when Condition A or B is met.

   A. Research on drugs for which an investigational new drug application (21 CFR Part 3212) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   B. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

   A. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week.

   B. From other adults and children[d], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

d. Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 45.402(a).

3. Prospective collection of biological specimens for research purposes by non-invasive means. Examples:

   A. Hair and nail clippings in a non-disfiguring manner.

   B. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.

   C. Permanent teeth if routine patient care indicates a need for extraction.

   D. Excreta and external secretions (including sweat).

   E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue.

   F. Placenta removed at delivery.

   G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor.

   H. Supra and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process if accomplished in accordance with accepted prophylactic techniques.

   I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.

   J. Sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

   A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy.

   B. Weighing or testing sensory acuity.

   C. Magnetic resonance imaging.

D. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography.

E. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:

   A. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related intervention; and (iii) the research remains active only for long-term follow-up of the subjects.

   B. Where no subjects have been enrolled and no additional risks have been identified.

   C. Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Categories 2 through 8 do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Copies of materials used in an expedited review procedure are sent to all IRB members to keep them advised of research proposals that have been approved under this procedure.

F. Cooperative Research. In the conduct of cooperative research projects that are covered by this assurance and involve BEA and one or more other institutions, BEA and the other institution(s) shall each be responsible for safeguarding the rights and welfare of human subjects. With the approval of DOE, BEA may enter into a joint review arrangement, rely upon the review of another institution's qualified IRB, or make similar arrangements to avoid the duplication of effort.

G. Record-keeping.

1. The IRB shall prepare and maintain adequate documentation of the IRB activities, including the following:

   A. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

   B. Minutes of IRB meetings, which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions, including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

   C. Records of continuing review activities.

   D. Copies of all correspondence between the IRB and the investigators.

   E. A list of the IRB members' names, earned degrees, representative capacities, relevant experience, and relationship (if any) with BEA.

   F. This Assurance, any modifications thereto, and any procedures not described therein.

   G. Statements of significant new findings provided to subjects, as required by DOE regulations and this Assurance.

2. The records required by this Assurance shall be retained for at least three years, and records relating to research that is conducted shall be retained for at least three years after completion of the research, then transferred to a Document and Records Service Center or Record Storage for the remainder of the retention. All records shall be accessible for inspection and copying by authorized representatives of DOE at reasonable times and in a reasonable manner.

Appendix B

Federal Policy for the Protection of Human Subjects: Notices and Rules 10 CFR 745 – the "Common Rule"

Electronic access to 10 CFR 745 can be obtained through the INL Research Library and Information Center Home Page, hotlinks, CPI, or by clicking on the hyperlink below:

http://humansubjects.energy.gov/worker-studies/files/cfrtext.pdf

Appendix C

DOE Order 443.1a (Dated 12/20/07)

Electronic access to DOE Order 443.1 and DOE Policy 443.1 can be obtained through the INL Research Library and Information Center Home Page, hotlinks, DOE Directives, Current, New Series Directives, or by clicking on the hyperlink below:

http://www.directives.doe.gov/pdfs/doe/doetext/neword/443/o4431a.html

Appendix D

Essential Elements of the Idaho National Laboratory

RESEARCH SUBJECT INFORMED CONSENT FORM (*SAMPLE)*

(Principal Investigator: This is a basic sample form to help you address all possible situations. Please adapt as appropriate for your research protocol.)

Prospective Research Subject - Read this consent form carefully and ask as many questions as you like before you decide whether you want to participate in this research project.

Project Title:

Project No. INL IRB No.

Sponsor:

Principal Investigator : Phone:

Organization :

Location :

Other Investigators : Phone:

Organization :

Location :

1. Purpose of this Research Study

- Include 3–5 sentences written in a nontechnical language – **"You are being invited to participate in a research study designed to..."**
- Define what is unique or different about this project.
- If possible, indicate population and number of people to be studied. In particular, note if any vulnerable populations (i.e., women, children, the aged, mentally or physically handicapped, institutionalized, fetuses, etc.) will be used in this study.

2. Procedures

- Describe procedures: **"The following is what you will be asked to do..."**
- Identify any procedures that are experimental.
- Define expected duration of subject's participation.

Subject Initials _____ Date _____

- Indicate type and frequency of monitoring during and after the study.
- Describe ownership, use, and disposal of samples taken during the study.

3. Possible Risks or Discomforts

- Describe known or possible risks.
- Indicate special risks to women of childbearing age; if relevant, state that study may involve risks that are currently unforeseeable, e.g., to developing fetus.
- If subject's participation will continue over time, state: ***"any new information developed during the study that may affect your willingness to continue participation will be communicated to you."***

4. Possible Benefits and Compensation

- If the research is not of direct benefit to the participant, explain possible benefits to others.
- Explain any financial compensation involved or state: ***"There is no financial compensation (other than your normal salary) for your participation in this research project."***

5. Available Medical Treatment for Adverse Experiences

"If you are injured as a direct result of taking part in this research study, emergency medical care will be provided by _____medical staff or by transporting you to your personal doctor or medical center. Neither the INL Occupational Medical Program nor the federal government will be able to provide you with long-term medical treatment or financial compensation except as may be provided through whatever remedies are normally available by law."

6. Available Alternative Courses of Treatment

If the procedure involves an experimental treatment, indicate whether other non-experimental (conventional) treatments are available and compare the relative risks (if known) of each.

Subject Initials _____Date _____

7. Confidentiality

"Your identity in this study will be treated as confidential. The results of the study, including laboratory or any other data, may be published for scientific purposes but will not give you name or include any identifiable references to you."

"However, any records or data obtained as a result of your participation in this study may be inspected by the sponsor, by any relevant governmental agency (e.g., U.S. Department of Energy), by the Battelle Energy Alliance, LLC Institutional Review Board, or by the persons conducting this study, provided that such inspectors are legally obligated to protect any identifiable information from public disclosure, except as otherwise authorized or required by law."

8. Termination of Research Study

"You are free to choose whether or not to participate in this study, and there is no penalty or loss of benefits if you decide not to participate. You are also free to leave the study at any time without penalty or loss of benefits, but if you do so, you must notify the Principal Investigator. Your participation in this study may be ended by the Principal Investigator at any time. The sponsor also reserves the right to terminate the study at any time."

9. Available Sources of Information

"Any questions you may have about this study will be answered by the Principal Investigator:

_____ Phone No. _____."

"Any questions you may have about your rights as a research subject will be answered by:

_____ Phone No. _____."

"In case of a research-related emergency, call: Day Emergency No. _____

Night Emergency No. _____."

Subject Initials _____Date _____

10. Authorization

"I have read and understand this consent form, and I volunteer to participate in this research study. I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent does not take away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study. I further understand that nothing in this consent form is intended to pre-empt any applicable federal, state, or local laws regarding informed consent."

Participant Name (Printed or Typed)	Date
Participant Signature	Date
Principal Investigator Signature	Date
Witness Signature	Date

Idaho National Laboratory

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject, I have the following rights:

1. **To be told what the study is trying to find out.**

2. **To be told what will happen to me and whether any of the procedures, drugs, or devices differ from what would be used in standard practice.**

3. **To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes.**

4. **To be told if I can expect any benefit from participating and, if so, what the benefit might be.**

5. **To be told of the other choices I have and how they may be better or worse than being in the study.**

6. **To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study.**

7. **To be told what sort of medical treatment is available if any complications arise.**

8. **To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study.**

9. **To receive a copy of the signed and dated consent form.**

10. **To be free of pressure when considering whether I wish to agree to be in the study.**

If I have other questions, I should ask the researcher or the research assistant. In addition, I may contact the Battelle Energy Alliance, LLC Institutional Review Board for Human Subjects Research (IRB), which is concerned with the protection of volunteers in research projects. I may reach the IRB office by calling Dena Tomchak, 526-1590, 7:00 a.m. to 4:30 p.m., Monday through Friday, by E-mail/Lotus Notes, or in writing.

Appendix E

INL/Battelle Energy Alliance, LLC Institutional Review Board

Member Review Form and Reviewer Considerations

Full Board Review
INL IRB No._____
Date

"Project Title"
Project Investigator:

The rights of the subjects are adequately protected. _____

If No, ***"the rights of the subjects are not adequately protected because"***

a) The Informed Consent is inadequate.

b) Coercion may be possible.

c) Special assurance is needed because of the type of subjects involved.

d) There is insufficient information to make a determination. I need to know:

e) Other reason(s):

The welfare of the subjects is adequately protected. _____

If No, ***"the welfare of the subjects is not adequately protected because"***

a) The risks are greater than the potential benefits.

b) The risks are greater than the importance of the knowledge to be gained.

c) Psychological repercussion is likely due to the possible or real existence of the adverse or degrading nature of the experiment, public reactions, or religious impacts, etc.

d) There is insufficient information to make a determination. I need to know:

e) Other reason(s):

INL IRB No. _____

The subjects are: At Risk _____ At Minimal Risk _____ At No Risk _____

If "At Risk," the possible risks associated with this project (for example, aggravation of anxiety status, preservation of data confidentiality, psychological reactions, etc.) are:

The benefits outweighing the risks are:

To my satisfaction, the Informed Consent Includes:

_____ A clear explanation of the procedures to be followed, including an identification of those which are experimental.

_____ A description of the attendant discomforts and risks.

_____ A description of appropriate alternative procedures that would be advantageous to the subject is applicable.

_____ An offer to answer any inquiries concerning the procedures.

_____ An instruction that the subject is free to withdraw his consent and discontinue participation in the activity at any time.

This project requires progress reports at _____ intervals (at least annually).

I am _____ am not _____ involved in the conduct of this project.

In Accordance with Federal Regulation 10 CFR 745, this project is:

_____Approved

_____Disapproved

_____ _____

Signature Date

(INL IRB Member)

IRB Reviewer Considerations

Evaluation of the Nature and Purpose of the Research

1. What is the purpose/overall objective of the research?

2. Does the proposal contain sufficient background information regarding the results of previous studies, including animal or clinical studies?

3. Is the research controversial and could it potentially generate public concern? If so, should any special recommendations be implemented?

4. Are there any potential legal problems or increased investigator/institutional liability associated with the research? If so, should any special safeguards be suggested?

Evaluation of the Risks

[A risk is a potential injury (harm) associated with the research that a reasonable person in the subject's position would be likely to consider injurious. Risks can be categorized as physical, psychological, sociological, economic, and legal.]

1. What are the potential risks/discomforts/inconveniences associated with the research?

2. What is the overall risk classification: less than minimal, minimal, greater than minimal, or life threatening?

3. What is the estimated probability, severity, average duration, and reversibility of any given harm?

4. Have adequate safeguards been adopted to minimize to the greatest possible extent the probability of occurrence and the magnitude of the risks?

5. What steps will be taken to treat a subject who may suffer an injury?

Evaluation of the Benefits

1. What are the potential benefits to the subject? Are these potential benefits maximized to the greatest possible extent?

2. What are the potential benefits to society (or some subset)? Are these potential benefits maximized to the greatest possible extent?

Evaluation of the Risk/Benefit Relationship

1. Is the potential risk to the subject outweighed or balanced by the potential benefit to the subject and/or by the potential benefit to society?

2. Research involving children, pregnant women and fetuses, prisoners: Is the risk/benefit relationship acceptable according to the requirements of 45 CFR 46 Subparts D, B, or C?

Evaluation of the Subject Populations

1. What are the inclusion/exclusion criteria: sex, age, health status, number of subjects, etc.?

2. Is the proposed subject population appropriate for the goals of the study?

3. Is the selection of subjects as equitable as possible given any restrictions imposed by justifiable inclusion/exclusion criteria?

4. Will any particular physiological, health, psychological, or sociological characteristics of the subject population pose special medical, ethical, or legal problems? Have appropriate steps been taken to minimize these potential problems?

5. Is the inclusion of a vulnerable subject population (children, pregnant women, fetuses, prisoners, elderly persons, mentally incompetent, terminally ill) justified and in compliance with 45 CFR 46?

Evaluation of Subject Recruitment

1. Is the method used to identify a particular subject population ethically and legally acceptable?

2. Is the process used to recruit potential subjects appropriate and free of coercion?

3. Are the advertisements used to recruit subjects acceptable?

Evaluation of the Process of Obtaining Informed Consent

1. Who will solicit informed consent from the subject?

2. Will the timing of and setting for the process of informed consent be conducive to rational and thoughtful decision-making by the subject without coercion?

3. Should subjects be re-educated at periodic intervals and informed consent again solicited?

4. Will the nature of the research or other factors potentially inhibit a subject's desire/ability to withdraw from participation? If so, have appropriate steps been taken to minimize this problem?

5. Will the subjects be physically and mentally competent to give informed consent? If no, is the proposed proxy consent procedure acceptable?

6. Should a subject advocate or other individual be present during the consent process?

7. If a waiver of some or all of the elements of informed consent is requested, does the nature and/or importance of the research justify such a waiver? Is the waiver in compliance with federal regulations?

Evaluation of Research Data Processing and Storage

1. How will the research data be stored and maintained?

2. How sensitive will the research data be?

3. Will the investigator provide information about subjects to other individual and/or agencies? If so, is this ethically and legally acceptable?

4. To what extent would a breach of confidentiality or invasion of privacy constitute a harm to subjects?

5. Are there adequate provisions to protect participants from the risks of breach of confidentiality and invasion of privacy?

6. Should a statutory shield against subpoena of research records be obtained? [available for research on mental disorders and drug and alcohol abuse]

Additional Monitoring

1. Should the research be reviewed by the IRB more often than annually? If so, when and how should this review be accomplished?

Appendix F

Human Subject Proposal Review Recommendation

Principal Investigator: _____

Org: _____ MS: _____ Phone: _____

Project Title: _____

Please indicate whether you think this proposal needs Exempt, Expedited, or Full Review.

To determine whether your project is exempt or not, read the following six statements. Please CIRCLE the numbers of the research categories below that apply to the proposed research.

RESEARCH QUALIFYING FOR EXEMPTION FROM FEDERAL REGULATIONS FOR THE PROTECTION OF HUMAN SUBJECTS

(Quoted from the Code of Federal Regulations, Title 45, Part 46.101)

1. Research conducted in established or commonly accepted educational settings, involving normal education practices, such as (i) research on regular and special education instructional strategies; or (ii) research on the effectiveness of or on the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, **unless** (i) information obtained is recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the subject's responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under Paragraph 2 of this Section, if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statues(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
5. Research and demonstration projects which are conducted by, or subject to the approval of, the department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to

those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed; or (ii) if a food is consumed that contains a food ingredient at or below the level of and for a use found to be safe by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

How many research categories above are circled? _____ If **NONE** are circled, project **DOES NOT** qualify for exempt status.

If you circled any of categories 1 through 6, answer the following questions about human subjects:

	YES	NO
Are any subjects under 18 years of age? (Other than in an established educational setting and involving minimal risk)	____	____
Are any subjects confined in a correctional or detention facility?	____	____
Is pregnancy a pre-requisite for serving as a subject?	____	____
Are fetuses in utero subjects in this research?	____	____
Are any subjects presumed to be not legally competent?	____	____
Are personal records (medical, academic, etc.) used without written consent?	____	____
Are data from subjects (responses, information, specimens) directly or indirectly identifiable?	____	____
Are data damaging to subjects' financial standing, employability, or reputation?	____	____
Is material obtained at autopsy used in the research?	____	____
Will subjects be asked sensitive questions about personal feelings/behavior/interactions/sexual experiences?	____	____
Will alcohol be ingested?	____	____
Will blood/body fluids be drawn?	____	____

Is the answer to any question above YES?
If YES → Project **DOES NOT** quality for exempt status.
If NO → Project qualifies for exempt status.

MANAGER APPROVAL

I have reviewed and approved this proposal for scientific merit.
I concur that this research qualifies for Exempt based on # _____ above.

Signature _____ Date: _____
(PI or PI's manager)

NON-EXEMPT? (EXPEDITED OR FULL)**YES, because proposal is to:

- Collect human data, documents, records, pathological specimens, or diagnostic specimens through intervention or interaction with a human subject, or
- Study existing individually identifiable human data, pathological specimens, or diagnostic specimens, or
- Use existing private information to identify potential human subjects.

  **Requires manager signoff at bottom

EXPEDITED? YES, because research is:

Minimal (OR NO) RISK*, plus one or more of the nine categories (Check off below).
*Minimal risk means potential for harm/discomfort ≤ daily life or the performance of routine physical or psychological exams/tests

Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure[e]

Applicability

1. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

2. The categories in this list apply regardless of the age of subjects, except as noted.

3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. The expedited review procedure may not be used for classified research involving human subjects.

5. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

6. Categories 1 through 7 pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when Condition A or B is met.

    A. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

e. An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

B. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children[f], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

   A. Hair and nail clippings in a non-disfiguring manner.

   B Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.

   C. Permanent teeth if routine patient care indicates a need for extraction.

   D. Excreta and external secretions (including sweat).

   E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue.

   F. Placenta removed at delivery.

   G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor.

   H. Supra and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

   I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.

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f. Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” 45 CFR 46.402(a).

J. Sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

   A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy.

   B. Weighing or testing sensory acuity.

   C. Magnetic resonance imaging.

   D. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography.

   E. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows: where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains

active only for long-term follow-up of subjects; or where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Categories 2 through 8 do not apply, but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

FULL IRB REVIEW? YES, because:
Federal Regulations require FULL Board review for all human subjects research with *GREATER THAN MINIMAL RISK*.

Is this proposal funded? _____

If so, indicate funding source: _____

MANAGER APPROVAL

- I have reviewed and approved this proposal for scientific merit.
- I concur that this research needs to involve human subjects, data, or specimens.

Manager: _____ Org: _____

Date: _____

Appendix G

Continuing Review Document

INL Institutional Review Board for Human Subjects Research Annual Continuing Review Form for INL IRB No:_____

Current Date:

INL IRB Last Approval Date:

Type of IRB Review:

INL-IRB-

Client:

Last Date Informed Consent Approved:

Principal Investigator:

Project Title:

Project Start Date:

End Date:

200X Funding: $ _____ Estimate of funding for actual human subjects costs $ _____

A. Research Project Current Status:

1. What is the present status of your research project?

2. If the research project has been initiated, please summarize the research findings obtained thus far:

   - No. of Human Research Subjects involved in 200X_____
   - No. of Human Research Subjects involved in 200X _____ (planned)
   - Describe the subjects' experiences (e.g., comments, concerns, cooperativeness, etc.) as you enrolled them and as then participated in the research.
   - Were there withdrawals from the research? How many? For what reasons?
   - Were there adverse effects, unanticipated risks, or complaints related to the involvement of the research subjects? If yes, describe the circumstances and corrective actions taken.

3. What changes have occurred in the risk/benefit assessment during the past year?

4. Has there been any new information arising from your research or from changes in the research protocol since the last review of your project that the IRB should know about?

B. Informed Consent Form

Please attach a signed and dated consent form (ICF) that you intend to use during 200X. **ICF's must be resubmitted for approval by the IRB at least once a year and must accurately reflect the current research and involvement of the human subjects.**

C. Future Activities

Describe briefly the scope of activities planned for the next review period:

D. Does your experience to date in this research project warrant any changes in the following (please circle):

1. Informed consent process: Yes/No

2. Confidentiality procedures: Yes/No

3. IRB Reviews: Yes/No

If any are Yes, the IRB will contact you.

Signature:

Principal Investigator: _____ Date: _____

Project No._____

Internal Distribution

Date

To

From Dena Tomchak, IRB Administrator

Subject: INSTITUTIONAL REVIEW BOARD FOR HUMAN SUBJECTS RESEARCH – CONTINUING REVIEW OF ACTIVE PROJECTS

The INL Institutional Review Board for Human Subjects Research is required to perform continuing review of all active research involving human subjects. The following project was reviewed in dd/mm/yyyy.

INL IRB No: INL Project No:

Title:

Principle Investigator:

Client Type:

Client:

Start Date:

End Date:

Action: Please confirm or correct the information, complete the forms indicated below, and send the completed review package to Dena Tomchak, MS 2203, by _____.

This project is:

Active: _____ Not Active: _____

Required Attachments:

____This memo, signed

____Continuing Review Form, signed/dated

____Current Proposal/Prep and Risk

____1997 Informed Consent, signed/dated*

____Annual or last monthly report

Required Attachments:

___This memo signed

___Continuing Review Form (to close out)

___Final report

*Federal Regulation 10 CFR 745 requires annual review/update of the Informed Consent. A sample ICF form now suggested for use by INL is attached. Please use the format and adapt as appropriate to your project.

Signature: _____Date: _____

Principle Investigator

Appendix H

Battelle Energy Alliance, LLC IRB Members/Administrative Contacts

Harold S. Blackman, IRB Chairman, Deputy Associate Laboratory Director,
Battelle Energy Alliance, LLC
MS 3560
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Katherine Moriarty, Attorney, Legal Office
Battelle Energy Alliance, LLC
MS 3899
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Maxine Dakins, Associate Professor
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Mark Holubar, Director Human Resources and Diversity
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MS 3204
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Dena Tomchak, IRB Administrator
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Phone: 526-1590

Dennis Patterson
Battelle Energy Alliance, LLC
MS 3425
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Arantza Zabala, Manager, Workforce Programs
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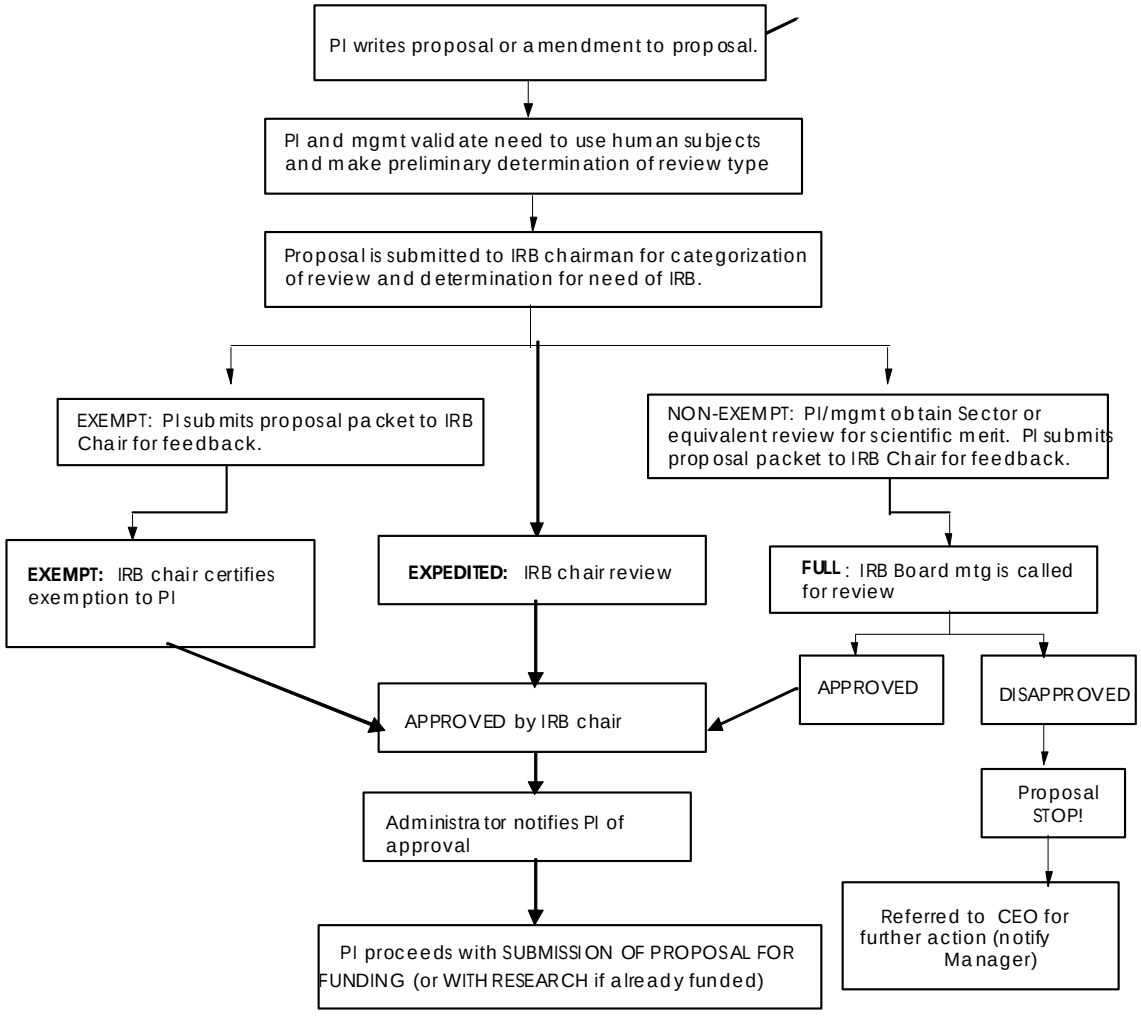
Jeffrey Joe, PI, Human Factors and I&C Systems
Battelle Energy Alliance, LLC
MS 3605
Phone: 526-4297

(01/07/05)

Appendix I

Human Subjects Research Procedures Flow Chart

HUMAN STUDIES REVIEW PROCESS FLOW CHART



Appendix J

Matrix of Roles and Responsibilities

PROJECT TASKS	Principal Investigator	PI's Mgr	Directorate Mgr	IRB Admin	IRB Chair	IRB Board	INL Director	DOE ID	DOE Hqs
Proposes/agrees on the need to use human subjects in research	X	X							
Notifies IRB of plans for human subjects research proposal	X								
Agrees on type of review needed (i.e., Exempt, Expedited, or Full review)	X	X		X	X				
Prepare proposal, abstract, and sample consent form or information form	X								
Obtain Directorate scientific merit approval for all non-Exempt proposals	X	X							
Submit proposal package to IRB for review	X								
Certify proposal is Exempt from review to DOE and to Principal Investigator					X			X	
Perform an Expedited review					X				
Convene IRB meetings				X	X				
Participates in a Full IRB review	X			X	X	X			
Modify proposal and/or consent form as required by IRB, IRB Chair, or DOE	X								
Obtain IRB written approval before starting human subjects work	X								
Formally notify client that IRB has reviewed and approved the research	X								
Send approved proposal on for funding approval.	X								
Obtain and maintains proper informed consent throughout the life of the project	X								
Follow approved procedures or request IRB approval of changes needed	X								
Report any injury, unexpected adverse event, unanticipated problem, or noncompliance with the DOE Single Project Assurance (SPA)	X		X	X	X			X	
Request renewal of approval for continuing research				X					
Provides requested input for continuing review approval of projects	X								
Perform annual reviews of approved human research				X	X	X			
Provide annual status report to DOE Hqs				X					
Provide guidance and education to INL staff and management				X	X	X	X	X	
Present IRB briefings or training as needed				X	X				
Maintain paperwork flow to PI's, IRB, INL officials and DOE				X				X	
Maintain written IRB procedures and update as needed				X					
Retain IRB records as required				X					
Retain signed consent forms and research records as required	X			X					
Produce IRB records/forms as needed to support human protection audits	X			X					
Notifies IRB of project closure	X								

Appendix K

PROJECT DATA SUMMARY
DEPARTMENT OF ENERGY
PROTECTION OF HUMAN SUBJECTS

POLICY: Research activities that involve human subjects and that are funded by the U. S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel, must be approved in accord with 10 CFR Part 745 by an Institutional Review Board (IRB). Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project. The institution must complete this form for each research activity each year and submit it to Protection of Human Subjects, Mail Station ER-70, office of health and Environmental Research, U. S. Department of Energy, Washington, DC 20585.

Project Title:

Principal Investigator :	Project Number[1:]

Mailing Address:

Telephone Numbers:

Performing Institution:

Institutional Assurance Number[2]	Estimated Annual Funding[3:]

Funding Sources (Name DOE Program Office (see list in attachment), if applicable, and the largest non-DOE source of funding (up to two):

This project has been reviewed and Approved by the IRB as required under 10 CFR Part 745.

A. Type of Review B. Approval Date:

☐ Full Board ☐ Expedited ☐ Exempt

DOE Program Office:

None-DOE Source:

This project involves the following collaborating institutions

Vulnerable Populations

A. ☐ This project does not involve vulnerable populations.

B. ☐ This project involves the following vulnerable populations:

☐ Minors ☐ Fetuses, Pregnant Women

☐ In vitro Fertilization ☐ Economically or Educationally Disadvantaged

☐ Prisoners ☐ Mentally Disabled

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for assuring required future reviews, approvals, and submissions of certification.

Signature of Institutional Official	Date:
Print or Type Name:	

For DOE Use Only

Date received by ER-70:	Approval Date:	Date Returned to Originating Office:

Reason for Nonapproval:

DOE Reviewers:

[1]Each project must have a unique identification number assigned by the institution – for example, INL-98-001.

[2]Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[3]Approximate total for current federal fiscal year, requested or obtained. Includes both direct and indirect costs.