IRB Institutional Review Board

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Research Eligible for Exempt Review

Some research involving human subjects, their bodily materials, or personal data does not require IRB review and approval, but does require administrative review by the IRB Office. In order to fulfill federal requirements for the proper review of these activities, Lawrence Livermore National Laboratory (LLNL) has assured the Department of Health and Human Services (DHHS) that all research activities involving human subjects or their identifiable, private information, whether funded or not, will be reviewed by the IRB Office to determine whether or not further review by the IRB is appropriate. If the IRB Office determines that the research is exempt from federal requirements governing human subjects research, they will issue a Notice of Exempt Determination. If the activity does not qualify for a Notice of Exempt Determination, the investigator will be notified by the IRB Office.

Research Exempt from 45 CFR 46

45 CFR 46 identifies several categories of human subjects research activities that may not require review by the IRB. These exempt categories do not apply to research involving (1) deception of subjects where the investigator does not disclose the true purpose of the research and/or the results of the subjects' participation in the study; (2) sensitive behavioral research, or (3) protected classes, i.e., fetuses, pregnant women, and invitro fertilization; prisoners; or children shall be conducted in accordance with 45 CFR Part 46 Subparts B, C, and D. Care should also be taken to ensure the proper protections are in place for DOE or DOE site Federal and/or contractor employees who become human subjects of research.

Existing Data, Documents, Records, or Specimens

Research in which the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens is considered "existing" 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. **Note:** Research involving human ova (fertilized or not) is not exempt. (Please see Additional Considerations for further clarification regarding anonymous or existing data, documents, etc.)

Tests, Surveys, Interviews, or Observation of Public Behavior

There are three types of research that fall into this category:

- Research involving the use of educational tests (e.g., cognitive, diagnostic, aptitude, and achievement), surveys, interviews or observation of public behavior, unless: (1) information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects; and (2) 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. The IRB Office is required to review copies of the informed consent form and proposed questionnaires or survey instrument(s) prior to approval and implementation. Survey or interview procedures involving children do not qualify for this exemption. (Please see Additional Considerations for further information regarding research involving surveys or questionnaires.)

- Research involving the use of educational tests (e.g., cognitive, diagnostic, aptitude, and achievement), surveys, interviews or observation of public behavior that is not exempt under Existing Data if (1) the human subjects are elected or appointed public officials or candidates for public office or (2) federal statute(s) require(s), without exception, that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter. (Please see Additional Considerations for further information regarding research involving surveys or questionnaires.)
- Research conducted in established or commonly accepted educational settings that involve normal educational practices, such as (1) research on regular and special education instructional strategies or (2) research on the effectiveness of or the comparison among instructional techniques, curricula or classroom management methods.

Public Service or Benefit Programs

This category includes research and demonstration projects that are conducted by or are subject to the approval of department or agency heads, and that are designed to study, evaluate, or otherwise examine (1) public benefit or service programs, (2) procedures for obtaining benefits or services under those programs, (3) possible changes in or alternatives to those programs or procedures, or (4) possible changes in methods or levels of payment for benefits or services under those programs.

Taste and Food Quality Evaluations

This category includes taste and food quality evaluation and consumer acceptance studies if (1) wholesome foods without additives are consumed or (2) a food is consumed that contains either (a) a food ingredient at or below the level and for a use found to be safe or (b) an agricultural chemical or environmental contaminant at or below the level found to be safe by the U.S. Food and Drug Administration (FDA) or one approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department of Agriculture (USDA).

Fee-for-Service Activities Performed in Support of Research

Based on federal guidance from the Office of Human Research Protections (OHRP), the LLNL IRB has determined that LLNL employees or contractors are considered not to be "engaged" in human subjects research if:

1. Their involvement is limited to performing commercial services for outside organizations or institutions (or performing other genuinely non-collaborative services meriting neither professional recognition nor publication privileges), and

2. They adhere to commonly recognized professional standards for maintaining privacy and confidentiality (e.g., an appropriately qualified laboratory performs analyses of blood samples for investigators solely on a commercial basis).

Fee-for-service activities are not reviewed by the convened IRB. However, the IRB Office does review the requests to verify that the human subjects research activity has received appropriate IRB review and approval at the initiating institution(s). Accordingly, the IRB Office may require the following information from the initiating institution(s) IRB Chair:

- Title of study.
- Date of the last IRB approval.
- If applicable, information regarding vulnerable populations (i.e., pregnant women, fetuses, children, prisoners, or the decision-impaired). Specifically, the vulnerable population should be identified.
- Acknowledgement that samples will be analyzed at LLNL as a fee-for-service activity.
- Review of the initiating institution(s) IRB's Federalwide assurance number.

Investigators should note that due to ethical and legal concerns regarding human subjects research in foreign countries, the LLNL IRB does not currently allow fee-for-service determinations if human subjects are recruited or if samples or subject data are obtained from outside the United States.

If an investigator believes that s/he may be involved in a fee-for-service activity, the investigator must complete Form LL6650, Request for Exemption, and return it, along with supporting documentation, to the IRB Office.

Additional Considerations

Although research in the above-mentioned categories may not require review by the LLNL IRB, there are additional concerns that the IRB Office will consider during the administrative review which may impact the final determination. Receiving a Notice of Exempt Determination does not mean that the investigator is exempted from addressing these concerns.

Anonymous Data

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

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

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

Existing Data

The term "existing" refers to the time period that the data or material was obtained. Federal guidance clearly states that the term "existing" refers to material or tissue that was "archived" or "on the shelf" prior to IRB review of the research. If the data/specimens are collected after the submission of the IRB application, then the data are not preexisting or "archived," the protocol will require IRB review, and the investigator may be required to obtain written informed consent.

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

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

Research Involving Surveys or Questionnaires

Sensitive survey research

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

Breaches of confidentiality

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

Use of Consent Forms

A Notice of Exempt Determination does not necessarily exempt investigators from the requirement of obtaining written informed consent from subjects. Some research involving surveys, questionnaires, or otherwise interacting with subjects may require the use of a consent form. For studies where there are no subject identifiers (i.e., when anonymous data is collected), an information sheet or cover sheet is usually required. Additional information regarding consent forms is available in The Consent Process.

Submitting a Request for Exemption (LL6650)

> ***Note:*** *Investigators are strongly urged to consult with the IRB Office before submitting activities for administrative review.*

If an investigator believes his/her research qualifies for an exempt/administrative review, the investigator must submit Form LL6650, Request for Exemption to the IRB Office, along with the following documents, as applicable:

- A brief abstract of the research activity that includes the purpose and objectives of the study.
- Approval from other participating institutions.
- Recruitment materials (e.g., advertisements, flyers, phone scripts, e-mails, etc.). A sample consent form or information sheet, if applicable.
- Copies of surveys, educational tests, or interview scripts.

When submitting a fee-for-service activity to the IRB Office for an administrative review, the investigator must submit Form LL6712, Request for Fee-for-Service Determination. Please review Fee-for-Service Activities Performed in Support of Research for additional information.