IRB Institutional Review Board

#11
Ongoing Responsibilities After Initial Protocol Approval

After a protocol has been approved by the IRB, the investigator has several ongoing reporting responsibilities to the IRB. Those responsibilities are listed below.

Reporting Adverse Events

Injuries, Illnesses, or Other Unanticipated Complications Possibly Resulting from the Research

Any potentially serious, unanticipated complications affecting a subject require immediate reaction by the investigator to help mitigate the harm suffered and prevent further harm. In addition, investigators are responsible for reporting to the IRB Chair any injuries, illnesses, or other unanticipated complications possibly related to the research. This reporting must take place within 10 calendar days of the occurrence.

Unanticipated Problems or Noncompliance with the Requirements of the Protocol

Investigators are responsible for reporting to the IRB Chair any unanticipated problems or noncompliance with the requirements of the approved protocol within 10 calendar days. The Chair may choose to discuss these matters at a meeting of the full Board.

Making Modifications to Currently Approved Research

All modifications to currently approved research must have IRB review and approval prior to implementation. Investigators should submit "Request for Amendment or Modification," Form LL6657 and, as appropriate, the revised protocol, consent form, recruitment materials, etc. Investigators should highlight or use bold font to indicate where changes or additions have occurred on the revised documents.

Minor Modifications to Currently Approved Research

A minor modification is defined as a change that (1) would not materially affect an assessment of the risks and benefits of the study or (2) does not substantially change the specific aims or design of the study. Minor changes that do not increase the risk to research subjects may receive an expedited review.

Examples of minor modifications include:

- An increase or decrease in proposed human research subject enrollment.
- Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant.
- A decrease in the number or volume of biological sample collections, provided that such changes do not affect the collection of information related to safety evaluations.
- Changes to improve the clarity of statements or to correct typographical errors, provided that such changes do not alter the content or intent of the statement.
- A change in principal investigator or the addition or deletion of qualified investigators and research personnel.
- The addition or the deletion of study sites.

Major Modifications to Currently Approved Research

A major modification is defined as a change that materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study. Major modifications to approved protocols that may increase the risk to subjects require a full board review.

Approval Period for Modifications

The IRB may only approve modifications submitted during a current approval year to the end of that period. For example, if the new or annual review takes place on January 1, 2019, the protocol will have an expiration date of January 1, 2020. If a modification is approved during this time, the expiration date remains January 1, 2020. All modifications, amendments, and, when applicable, informed consent forms should be incorporated into the renewal application for IRB consideration during the annual review.

Continuing Review After Initial Application Approval

The IRB must conduct continuing review of protocols at intervals appropriate to the degree of risk, but not less than once per year. It is the investigator's responsibility to ensure that the research is reviewed on or before expiration of the current approval period, even if the research activity did not begin until sometime after the IRB gave its initial approval. As a courtesy, investigators will be notified by the IRB Office six to eight (6–8) weeks prior to expiration of their IRB approval. An application for continuing review, Form LL6652 must be received by the IRB Office in time for review and approval in advance of the expiration date (3–4 weeks recommended).

Continuing review and approval is also necessary if recruitment of subjects stops, but previously enrolled subjects continue to participate in the research or the study is in data analysis at LLNL.

Submitting a Renewal Application

In the renewal application, Form LL6658, investigators should incorporate all the addenda and modifications submitted to and approved by the IRB during the previous approval period. In addition to describing changes in the research design, number of subjects, or changes in Consent Form, the following information should also be included in the renewal request:

- An updated abstract of the study.
- The number of subjects seen since the last renewal, the total number to date, and the number of additional subjects yet to be recruited.
- The study status, if subject enrollment is complete.
- Any adverse events during the past year.
- A determination of whether or not the risk/benefit assessment remains the same.
- A summary of results and publications.
- Plans for the coming year.

Consent Forms and other supporting documentation must also be reviewed by the IRB each time the protocol is updated. If the research activity involves a collaborating institution, a copy of the other institution's current IRB approval letter is also required.

> ***Note:*** *There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted. If the IRB does not re-approve the research by the specified expiration date, subject accrual and research activities must be suspended pending re-approval of the research by the IRB.*

Enrollment of new subjects cannot ordinarily occur after the expiration of IRB approval. If the investigator is actively pursuing renewal with the IRB and the IRB finds that it may be in the best interests of already-enrolled subjects' safety to continue with study treatments and procedures, the IRB may allow continuation of treatment for already-enrolled subjects during the time required to complete the review process.

Termination for Failure to Obtain Continuing Approval

The IRB has the authority to terminate or suspend approval of research that is not being conducted in accordance with regulatory and LLNL requirements regarding continuing review. When study approval is terminated by the Board due to lack of compliance with continuing review requirements, in addition to stopping all research activities, any subjects currently participating should be notified that the study has been terminated.

Maintenance and Retention of Records and Consent Forms

During the study, all documents, electronic files, videotapes, etc. that contain the subjects' personal identifiers must be kept in locked storage with access restricted to the investigator and/or designee(s). Access restrictions must continue even after the study is completed.

At a minimum, investigators must maintain research records for at least three (3) years after completion of the research. All records must be accessible for inspection and copying by authorized representatives of the IRB, the federal department or agency supporting the research, and sponsor, if any. Beyond three (3) years, requirements for record retention vary with the type of research conducted, the provisions of the investigator's funding source, and LLNL requirements. It is the investigator's responsibility to clearly understand the retention requirements of LLNL (Retention Code: LLNL-RRS-01-00-005, Retention Period: Permanent) and/or their sponsor.

> ***Note:*** *Retention of records produced by human subjects projects is the responsibility of project leadership. Records should be retained in accordance with the Laboratory Records Retention Schedules. Contact the Laboratory Institutional Records Center for assistance.*
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> *Retention of records produced by the LLNL IRB responsible for oversight of the protection of human subjects in research projects is the responsibility of the IRB. IRB record types include, but are not limited to:*
> *Charter*
> *Records of Membership*
> *Policies and Procedures*
> *Decisions and Research Protocol Documentation*
> *Administrative records such as correspondence, email, meeting notes, and agendas*

Based on current DOE direction, research records (including consent forms) involving ionizing radiation experiments on human subjects, or epidemiological studies of LLNL or any other DOE facility workers, must be retained until further notice.

Research records involving ingested, inhaled, or injected materials (other than ionizing radiation) that could represent even a small increase in risk to subjects (or are commonly but erroneously thought to increase such risks) are to be retained until the youngest exposed subject could reach 100 years of age.

Other human subjects' records are to be retained in accordance with LLNL's record retention schedule for Medical Research and Development, Schedule Code 12-03-017, 12-03-018, and 12-03-019.

When human subjects records are sent to LLNL records storage, they should be clearly identified according to the categories identified above. For example, if the records involve ionizing radiation, the records transmittal form should indicate: "These are human subjects research records involving ionizing radiation; these records are under a DOE moratorium on destruction." There should also be an accompanying memo identifying those individuals who have authorized access to the records. If the records reveal the identity of the individual subjects, the access should be limited to the experimental investigators and, if none of the investigators are still employed at LLNL, access should only be with the approval of the Chair of the LLNL IRB.

For further information on records retention or preparing records for shipment to storage, contact LLNL Records Management.

Completion/Termination of Study

To formally complete a study file, the IRB requests that investigators officially notify the IRB Office when a study is terminated or completed or after data analysis is complete. As part of the close-out process, investigators are also asked to submit a 1–2 paragraph summary of the study's results and a completed Request for Closure of a Project Involving Human Subjects, LL6713 form.