Policy & Procedure Review of Non-Exempt Human Subjects Research	Effective Date	02/01/2026
	Revision Date	01/2026
	Revision No.	3.0

I. PURPOSE & SCOPE

The purpose of this document is to establish the policies and procedures for conducting initial and continuing review of non-exempt human subjects research (HSR) protocols under the oversight of the Human Subjects Committee (HSC) at Berkeley Lab, and for reporting its findings and actions to the investigator and the institution. The HSC ensures that all HSR conducted adheres to the ethical principles of the Belmont Report and complies with all applicable Federal, DOE-specific, sponsor-specific, and other applicable requirements, including relevant international requirements. This document applies to all HSR subject to the oversight of the HSC as the cognizant Institutional Review Board (IRB).

II. REVISION HISTORY

Date	Revision No.	Change	Reference Section(s)
1/15/10	1.0	New Procedure Drafted	Not Applicable
9/5/2012	1.1	Reformatted, standardized terminology	All
12/2018	2.0	Updated for consistency with the Revised Common Rule	All
01/2026	3.0	Combined with Criteria for approval, updated throughout.	All

III. POLICY

When the HSC serves as the cognizant IRB, submission, review, and approval of human subjects research protocols are required to adhere to the following standards.

A. The HSC must follow written procedures for conducting initial and continuing review of research and for reporting IRB findings and actions to the investigator and the institution [45 CFR 46.103(b)(4)(i), 21 CFR 56.108(a)(1)]

B. In conducting the initial review of proposed research, the HSC will obtain information in sufficient detail to make the determinations required under 45 CFR 46.111 (or 21 CFR 56.111 for FDA-regulated research).

C. Before the HSC approves any human subjects research, it will determine that all of the applicable requirements for approval are satisfied. This includes, but is not limited to the following:

1. 45 CFR 46.111(a)(1-7) and (b)
2. 21 CFR 56.111 for FDA-regulated research
3. DOE Order 443.1C.chg1 (or current version)
4. The Belmont Principles: Respect for Persons, Justice, and Beneficence.
5. UCOP Policy for Protection of Human Subjects in Research
6. Additional requirements, as applicable (i.e. state laws, sponsor requirements, etc)

D. The HSC must follow written procedures for determining which projects require review more often than annually and determining which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review [45 CFR 46.103(b)(4)(ii), 21 CFR 56.108(a)(2)]

IV. ROLES & RESPONSIBILITIES

Role	Responsibility
All Berkeley Lab Personnel	Berkeley Lab personnel who plan to conduct research involving human subjects are required to submit an application describing their proposed research to the cognizant IRB prior to the initiation of any HSR activity. No intervention or interaction with human subjects in research, including recruitment, and no collection of data about or samples from human subjects, may begin until an investigator's application to conduct human subjects research has received IRB approval.
Protocol Lead Investigators (PLI) & Co-PLIs	Responsible for submitting complete protocols for review by the HSC, and for completing all necessary communication to facilitate the review. PLIs retain responsibility for ensuring that the protocol methods and accompanying materials submitted are accurate and will be followed by the study team as approved.
HSC Chair or Designee	Responsible for designating experienced members qualified to conduct Expedited review.
Berkeley Lab HARC Office	HARC are responsible for completing pre-review and designating reviewers in consultation with the HSC Chair, as well as facilitating all required communications, documentation, and administrative support for the protocol review process
Human Subjects Committee (HSC)	Responsible for reviewing the protocols and applying the criteria for approval as detailed in this policy.

Role	Responsibility
Assigned HSC Reviewers	Members designated as **reviewers** are responsible for reviewing the entirety of the application in order to make the required determinations. Reviewers may contact the PLI or others for more information as needed, and in the case of a Full Board protocol will present the protocol in the convened meeting. Review checklists applicable to the study should be used to guide the review. Assigned reviewers unable to complete their reviews or who have a conflict of interest must contact the HARC office promptly to request that the protocol be reassigned.

V. PROCEDURES

A. Submission Requirements

1. Protocol Lead Investigators (PLIs) must submit a complete application through the Human/Animal Research Protocol (HARP) system for all non-Exempt HSR. A complete initial submission includes:

a) **HARP Protocol Smartform:** Fully detailed project description and methodology. This narrative must be consistent and complete.

b) **Responsible Personnel:** Names and evidence of training completion for all study personnel engaged in the HSR as representatives of Berkeley Lab. In the case of external collaborators, a single responsible investigator from each relying location is also required.

c) **Financial Disclosures:** A statement on potential conflicts of interest related to the research.

d) **Informed Consent Documents:** Including proposed forms and any requests for waivers.

e) **Recruitment Materials:** Advertisements, flyers, notices, and communication scripts, as applicable.

f) **Supportive Documentation:** Required documentation may vary based on the research activities being performed. At a minimum, all research data collection tools (e.g., surveys, interview guides, etc) and other participant-facing materials must be included.

(1) For FDA-regulated studies, additional documentation may include Investigator's Brochure, Copies of the Company Protocol (if sponsored by a for-profit entity), FDA correspondence regarding IND/IDE submissions, dosimetry calculations, or other drug/device documentation as determined necessary to determine safety and integrity of the study design.

(2) For studies involving minors in school settings, an approval letter from the School Principal or School District Office.

2. Protocol Lead Investigators (PLIs) must also submit a complete application to the HSC for HSR that qualifies as Common Rule Exempt under 45 CFR 46.104(d), however the protocol submission requirements are variable based on the category. In all cases, the submission will

be required to meet initial and annual reporting requirements of DOE Order 443.1C.chg1 (or current version). See Policy & Procedures for Exempt Research Review for more information.

3. Continuing Review (CR) of previously approved protocols require submission of a CR form in the HARP System. Should there be changes at the time of CR, an amendment should also be submitted in parallel, see HSC policy for Submission and Review of Changes to an Approved Research Protocol for more information.
   - **a)** A complete CR requires sufficient information to determine whether the proposed research continues to meet the criteria for approval. The entire form must therefore be complete, with particular attention paid to the following elements
     - (1) A status report on the progress of the research, including a summary of enrollment and withdrawal of participants from the research since the last HSC review, including the reasons for withdrawal.
     - (2) A summary of any reportable events or other unanticipated occurrences during the previous reporting period
     - (3) Any other relevant information, especially information about risks associated with the research, or interim findings.
     - (4) The HARC Office and HSC may request additional materials over the course of their review.
   - **b)** The HSC must also determine whether the proposed research requires verification from sources other than the investigator, such as the sponsor, or other third party, that no material changes have occurred since the last HSC review. Key elements to consider include, but are not limited to
     - (1) verification from line leadership or ancillary committees that no additional concerns or compliance issues have been identified since the previous review.
     - (2) when applicable, updates or reports from collaborating institutional investigators or the relying IRB verifying no material changes.
     - (3) additional testimony from subject matter experts regarding developments within the field.

B. Administrative Review & Assignment

1. **Pre-review:** Upon submission of a new protocol or continuing review, HARC Office staff perform an administrative pre-review to identify all applicable requirements and verify that the application is complete. Staff may request additional information as deemed necessary to ensure sufficient detail to make the determinations required.
   - **a.** The PLI must respond to staff comments and questions before the protocol application will be distributed and reviewed by the HSC.
   - **b.** Initial determination of whether the protocol meets the criteria for Expedited review or if it should be elevated to Full Board Review is completed at this stage by HARC staff, with HSC Chair consultation as needed. See the Policy on Expedited Research Review for more information on qualifications.

c. HARC staff and the HSC Chair always retain discretion to require full board review for protocols that otherwise meet the criteria for an expedited or exempt category review, similarly reviewers may also request Full Board Review at any time.

2. **Review Assignment:** Once pre-review is complete, the protocol may be assigned to the agenda of the next available HSC meeting or to an Expedited Reviewer. Reviewers will receive notification and protocol access via an e-mail link sent from the HARP system. Reviewers are responsible for notifying the HARC Office promptly if they are unable to complete their assigned review.

   a. Expedited Reviewers must be designated by the HSC Chair as sufficiently experienced to conduct reviews under expedited procedures. See the Policy on Expedited Research Review for more information on review procedures.

   b. For Full Board Review, both a primary and a secondary reviewer will be designated ahead of the meeting to be responsible for presenting the protocol in the convened meeting, as described in the HSC Membership Policy.

3. **Conflict of Interest:** Assigned reviewers must notify the HARC office promptly if they have a conflict of interest that prevents them from conducting an objective review.

C. HSC Full Board Initial & Continuing Review

1. All HSC members will receive access through the HARP system to all the materials filed for a given protocol. The agenda will be distributed by HARC staff as far in advance of the meeting as practicable.
2. Convened meetings will take place via video conference, and follow the procedures established in the HSC Charter.

   a) HARC staff or the HSC Chair, as available, are responsible for ensuring that quorum is maintained, and must pause or adjourn the meeting should quorum be lost, with no voting to occur until the quorum can be reconvened. Any loss of quorum must be clearly recorded in the meeting minutes.

   b) No HSC member may participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the HSC.

3. **Voting Specifications**

   a) Prior to voting, all members attending a meeting are expected to familiarize themselves with all applications in sufficient detail to make the determinations outlined in D, below.

   b) Members unable to attend a meeting may not vote in absentia, but may submit comments for consideration at the meeting through the HARP Reviewer Note system or via email to HARC staff.

   c) The HSC has authority to approve, require modifications in (to secure approval), or disapprove all research activities submitted as HSR. When requiring modifications, the HSC may vote for either of the following:

      (1) Conditional Approval - Used when the HSC determines that, given the scope and nature of the conditions, and based on the assumption that the conditions are satisfied,

that they are able to make all of the determinations required for approval under the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. Once the investigator makes these specified changes, the HSC Chair or other appropriate reviewer can verify them without a second full-board review.

(2) Deferred/Tabled - Used when the HSC requires extensive changes that require subsequent review by the full committee. Investigators should be mindful of the standing meeting schedule to ensure resubmission in time for review.

D. Criteria for HSC Approval

The HSC shall determine that all of the following criteria have been satisfied in order to secure initial and continuing approval for non-exempt HSR. Checklists are provided to guide reviewers through evaluation of each criterion.

Criterion	Applicable Regulatory Citation	Summary of Requirement
Minimize Risks	45 CFR 46.111(a)(1) 21 CFR 56.111(a)(1)	Risks to subjects are minimized by using procedures that are consistent with sound scientific design and that do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already performed on the subjects for diagnostic or treatment purposes. A human research study should be designed according to proper scientific principles. Medical treatment or device studies should be preceded by adequate laboratory and/or animal studies. A study that will not yield valid data is unacceptable.
Risk/Benefit Ratio	45 CFR 46.111(a)(2) 21 CFR 56.111(a)(2)	Risks to subjects are reasonable in relation to anticipated benefits and the importance of the knowledge that is expected to result. In evaluating risks, the HSC will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSC shall not consider possible long-range effects of applying knowledge gained in the research (for example, possible future effects of the research on public policy). The HSC shall carefully assess each risk and anticipated benefit of the study to determine if the benefits outweigh the risks and therefore justify the use of human subjects.
Equitable Selection	45 CFR 46.111(a)(3) 21 CFR 56.111(a)(3)	Selection of subjects is equitable. In making this assessment the HSC should take into account the purposes of the research and the setting in which the research will be conducted. The HSC should be particularly cognizant of the special problems of research involving a category of subjects in a protected class.

Informed Consent	45 CFR 46.111(a)(4) 21 CFR 56.111(a)(4)	Legally effective informed consent will be sought from each prospective subject or their legally authorized representative (LAR) in accordance with, and to the extent required by, § 46.116 (56.116)
Documentation of Informed Consent	45 CFR 46.111(a)(5) 21 CFR 56.111(a)(5)	Informed consent will be appropriately documented in accordance with relevant regulations (45 CFR 46.117 or 21 CFR 50.27).
Data Monitoring	45 CFR 46.111(a)(6) 21 CFR 56.111(a)(6)	When appropriate, the research plan must make adequate provision for monitoring data to ensure subject safety.
Privacy & Confidentiality	45 CFR 46.111(a)(7) 21 CFR 56.111(a)(7) DOE Order 443.1C.chg1	When appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of the data. Personally Identifiable Information (PII) collected and/or used during HSR projects should be limited to information reasonably necessary for the conduct of the research, and must be protected in accordance with the requirements of DOE Order 206.1.
Protected Classes & Vulnerable Subjects	45 CFR 46.111(b) 21 CFR 56.111(b) DOE Order 443.1C.chg1	Research involving the vulnerable populations identified in Subparts B, C, and D of 45 CFR Part 46 must be conducted in accordance with those Subpart(s). Appropriate protections should be afforded to subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. Care must also be taken to ensure the proper protections are in place for DOE/NNSA Federal and/or contractor employees who become human subjects of research and may be subject to coercion or undue influence. An employee cannot be recruited or consented by a direct supervisor who is the PI and/or a member of the research team, except in unusual circumstances approved by the IRB.

E. Continuing Review Frequency

As part of the initial approval of a study, the HSC or designated reviewer shall determine and document the reason(s) for the frequency of continuing review. The following should be taken into consideration when making these determinations.

1. To meet federal regulations, formal Continuing Review (CR) is required at intervals appropriate to the degree of risk, but not less than once per year for protocols falling under Full Board review or FDA regulations.

a) The effective date of IRB approval will be the date the convened quorum (or Expedited reviewer when applicable) voted to approve the protocol, or the date that conditions for approval have been verified as met.

b) Should the effective approval date be after the Full Board review of the protocol, the ongoing expiration date for the CR requirement shall be set as 365 days from the date of initially convened HSC review.

2. Protocols not requiring formal Continuing Review include protocols that fall under Expedited and Exempt categories, and protocols which have progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

b) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

3. The HSC has the authority in all cases to require CR more often than the regulatory minimum, and should consider factors including but not limited to the following:

a) Risks to subjects

b) Involvement of vulnerable populations

c) Research for which participants would be exposed to additional risks, e.g., phase I studies, breach of confidentiality, disproportionate number or severity of adverse events

d) Research conducted internationally

e) Involvement of recombinant DNA or other types of gene transfer studies

f) Use of waiver of informed consent

g) Classified research

h) Recommendations from other ancillary committees

i) Previous suspensions or administrative holds of the research due to compliance, record-keeping, or other concerns.

4. Annual check-ins remain mandatory to meet Department of Energy reporting requirements for both Expedited and Exempt category HSR, and for all Lab-conducted HSR in which an external IRB is responsible for review of the study. Submissions can be made through the HARP system's CR form or through submission of an HSC-approved annual check-in form.

5. In the HARP system, expiration dates are used to facilitate submission of both CR and annual checkins. Consequences for expiration are dependent on the HSC's determination of CR frequency.

a) Full board protocols and protocols determined by the HSC to require formal CR must adhere to the expiration dates in the HARP system. There shall be no grace period extending the conduct of the research beyond the expiration date imposed by the HSC. A final notice shall be issued to the PLI and all study staff shortly before and immediately after the expiration of the protocol. If the HSC does not re-approve the research prior to the expiration date,

(1) <u>All study activities must cease</u>, pending re-approval of the research.

(2) The investigator must immediately submit the renewal documents to the HSC and address 1) why the PLI did not adhere to renewal procedures; and 2) address whether any subjects were enrolled or completed study activities after expiration.

(3) Should stopping the study place currently enrolled subjects at any increased level of risk, the PLI shall immediately contact the HSC Chair and HARC staff to discuss continuation of necessary activities. The HSC addresses these situations on a case-by-case basis. Enrollment of new subjects shall not occur on or after the expiration date.

b) Protocols not subject to CR (e.g. Expedited and Exempt category HSR), may have this expiration date pass in the system without consequences, however in all cases an annual check-in must be received in time to complete required annual reporting to the DOE HSPP. Any investigators who do not meet this requirement will be considered noncompliant with the DOE Order requirements, a reportable event.

F. Communication of HSC findings and actions

1. All full board decisions are communicated to the investigator in writing through the HARP system, which is received via email.
2. Clarifications that are being requested will be entered into the protocol using the comment function in HARP, and/or as a direct request within email notifications requesting clarification. Investigators are encouraged to discuss any questions or concerns regarding the requests with HARC Office staff prior to resubmission.
3. Should the HSC vote to disapprove a protocol, a clear rationale for the decision and the process for following up will be provided within the Disapproval letter provided through the HARP system.
4. Approval notifications will include the IRB's determinations regarding the approval period/continuing review interval. These approval letters also serve as IRB records documenting the approval period/continuing review intervals.

G. Additional Considerations

1. **Berkeley Lab Institutional Review:** HSR that has been approved by the HSC may be subject to further appropriate review and approval or disapproval by officials within the institution. However, those officials may not approve initiation of the research if it has not been approved by the HSC.
2. **Suspension or termination of IRB approval of research.** The HSC has authority to suspend or terminate approval of research that is not being conducted in accordance with the HSC's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.
3. **Cooperative research.** HSR covered under this policy that involves more than one institution will adhere to single IRB requirements, when applicable. HSR involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) is reviewed and approved by one of the Central DOE IRBs, unless authorized by the DOE and/or NNSA HSP Program Manager to be reviewed by another appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or

Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.

VI. AUTHORITIES AND REFERENCES

Title	Web Link (as of 01/2026)	Description	Type
10 CFR Part 745	https://www.ecfr.gov/current/title-10/chapter-III/part-745	The Common Rule regulations - Dept of Energy version	Regulatory Authori…
DOE Order 443.1C.chg.1 - Protection of Human Research Subjects (or current version)	https://www.directives.doe.gov/directives-documents/400-series/0443.1-border-c-chg1-ltdchg	Dept of Energy Order applicable to research performed by or through LBNL. Contractor Requirements Document is incorporated into Contract 31.	Regulatory Authori…
45 CFR 46	https://www.ecfr.gov/current/title-45/part-46	The Common Rule regulations - HHS	Regulatory Auth…
21 CFR Parts 50 & 56	https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50 https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56	Food & Drug Administration (FDA) regulations governing human subjects research and IRB requirements for FDA-regulated products.	Regulatory Authori…
The Belmont Report	https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html	Foundational document outlining core ethical principles and guidelines for research involving human subjects.	Source Requireme…
UC-DOE Prime Contract	https://www.ucop.edu/laboratory-management/contracts/lbnl/index.html	UC-DOE Prime Contract for the management and operation of Lawrence Berkeley National Laboratory (LBNL).	Source Requireme…
UCOP Policy for Protection of Human Subjects in Research	https://policy.ucop.edu/doc/2500499/ProtectHumanSubject	Governing policy for the University of California system, applicable to research performed by LBNL.	Source Requireme…
Berkeley Lab's Federalwide Assurance for Protection of Human Subjects	https://commons.lbl.gov/download/attachments/93095490/FWA%208-16-2021.pdf?version=1&modificationDate=1629153435063&api=v2	Current version of FWA on file with the Office for Human Research Protections (OHRP)	Source Requireme…
PUB-3000 Chapter 22 03.02.002.001	https://ehs.lbl.gov/resource/esh-manual-pub-3000/ch22/	Overview of standards for Research with Human and Animal Subjects	Source Requireme…
Human Subjects Committee Charter	https://commons.lbl.gov/download/attachments/93095490/LBNL%20HSC%20Charter%202021%20FIN	Charter establishing HSC composition and high level processes.	Implementing Doc…

	AL.pdf?version=1&modificationDate=1633976726304&api=v2		
HSC Website	https://commons.lbl.gov/display/harc/Human+Subjects+Committee	Website for the Human Subjects Committee that holds extensive resources.	Reference Material
California Protection of Human Subjects in Medical Experimentation Act	https://leginfo.legislature.ca.gov/faces/codes_displayText.xhtml?lawCode=HSC&division=20.&title=&part=&chapter=1.3.&article	California Health and Safety Code Section 24170-24179.5	Driving Requirem…
Reliance MOU for IRB Review of Multi-Campus Human Subject Research	https://www.ucop.edu/research-policy-analysis-coordination/policies-guidance/human-subjects/multi-campus-human-subject-research-MOU.html	MOU governing collaborative HSR between the University of California campuses	Implementing Do…
22 CFR Part 62	https://www.ecfr.gov/current/title-22/chapter-I/subchapter-G/part-62	Exchange Visitor Program and U.S. Department of State Guidance Directive 2024-01 - includes a restriction on HSR performance.	Driving Requirem…