CALIFORNIA INSTITUTE OF TECHNOLOGY

Institutional Biosafety Committee (IBC)

Policy & Procedure Manual

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The Administrative Committee on Biosafety

Caltech administrative committees are established by the President for the purpose of advising the administration on policy and procedural matters in a given area. When an administrative committee is established, the President designates a member of the administration to oversee the committee. Administrative committees are established (and may be disbanded) according to the needs of the President and the administrator through whom the committee reports.

- The President appoints committee members, based on the recommendation of the administrator through whom the committee reports.
- A charter approved by the President delineates the duties and responsibilities of each administrative committee. Amendments or revisions to a committee's charter will be recommended to the President by the administrator through whom the committee reports.

Each administrative committee is authorized to adopt its own rules of procedures, as long as such rules do not conflict with the provisions of the charter approved by the President.

The Administrative Committee on Biosafety serves as the Institutional Biosafety Committee (IBC) and the Institutional Review Entity (IRE) for Caltech and its Jet Propulsion Laboratory (the "Institute").

Definitions

- Biosafety Officer (BSO)

  A biosafety professional, sometimes referred to as a Biological Safety Officer or BSO, who develops and participates in programs to promote safe microbiological practices, procedures, and proper use of containment equipment and facilities; stimulates responsible activities among workers; and provides advice on laboratory design. Certain activities as described in this Policy may be delegated by the Biosafety Officer to a qualified staff member as approved by the IBC.

- Institutional Animal Care and Use Committee (IACUC)

  The primary role of Caltech's IACUC is to ensure the ethical and human care and use of animals in research, testing and teaching. All research or teaching activities at Caltech or at JPL involving use of live vertebrate animals or tissues collected from such animals must be reviewed and approved by the IACUC.

- Institutional Review Board (IRB)

  Caltech's IRB approves, monitors, and provides advice on research involving human subjects to ensure the research is guided by ethical principles that protect the rights and safety of human subjects.

- Laboratory Contact

  The Principal Investigator (PI), or a laboratory member designated by the PI to facilitate communications with the IBC regarding protocol submissions.

- NIH Guidelines

  The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) detail safety practices and containment procedures for basic and clinical research involving recombinant or synthetic nucleic acid molecules, including the creation and use of transgenic organisms and viruses containing recombinant or synthetic nucleic acid molecules.

- Principal Investigator (PI)

  The Principal Investigator (PI) is a single faculty member of professorial rank or senior research faculty as defined in the Faculty Handbook, or a Director of an Institute Research Facility with the approval of the appropriate Division Chair(s), or a JPL project lead who is responsible for the scientific and technical direction of a project. The PI submits and is responsible for IBC protocols.

- Recombinant and synthetic nucleic acids (r/s nucleic acid)

  (i) molecules that (a) are constructed by joining nucleic acid molecules and (b) that can replicate in a living cell, i.e., recombinant nucleic acids;

  (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or

  (iii) molecules that result from the replication of those described in (i) or (ii) above.

- Researcher

  A researcher is anyone, other than the PI, who will conduct research under an approved IBC protocol. All protocols must be under the overall direction of a PI.

- Risk Groups

  Agents are classified into four Risk Groups (RGs) according to their relative pathogenicity for healthy adult humans by the following criteria:

  (i) Risk Group 1 (RG1) agents are not associated with disease in healthy adult humans.

  (ii) Risk Group 2 (RG2) agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available.

  (iii) Risk Group 3 (RG3) agents are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available.

  (iv) Risk Group 4 (RG4) agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available.

Authority and Oversight of the Institutional Biosafety Committee (IBC)

The IBC is responsible for review, biological risk assessment, approval and monitoring of all research and teaching and other activities at the Institute involving the use of biohazards. Biohazards are defined as:

- Recombinant and synthetic nucleic acid (r/s nucleic acid) activities covered under the NIH Guidelines-see Appendix A
- Experiments using the CRISPR/Cas9 technology – see Appendix B
- Recombinant organisms administered to animals (vertebrate or invertebrate)
- All microorganisms, regardless of risk group Human, animal, or plant pathogens
- Review and evaluation of material inactivation procedures prior to receiving or sending infectious material – see SOP05
- Certain biological toxins (determination based upon the LD_{50} of the toxin), see *Caltech Biosafety Manual*

- Experiments involving the use of human or non-human primate blood or other potentially infectious human or non-human primate materials, such as unfixed human tissues, primary and established human cell lines, and certain bodily fluids and other specimens
- Genetically modified animals (including invertebrates) and whole plants as covered by the *NIH Guidelines* - see Appendix C and D
- Experiments involving the use of animal species that can pose serious zoonotic health hazards (e.g., Non-Human Primates)

The IBC serves the Institute as the reviewing entity for the Institute for infectious biological and biohazardous agents and ensures that select agents and toxins (as defined by the federal regulations) are appropriately monitored. The IBC may also oversee, as deemed necessary for safety, the use of less hazardous biologics used in the research and teaching at the Institute.

Investigators wishing to perform research requiring BSL-3 or ABSL-3 containment should consult with the Caltech BSO and the Office of Research Compliance prior to preparing a grant or contract proposal or submitting an IBC protocol. The Institute does not have facilities allowing for BSL-4 or ABSL-4 containment. Therefore, research requiring such containment cannot be performed at the Institute.

The Institute is responsible for ensuring that, irrespective of funding source, all research and teaching laboratories using biohazards or hazardous biological material are fully compliant with regulatory guidelines and policy. Violation of the Institute's biosafety policies and procedures may result in limitation, suspension or termination of research or teaching activities by the IBC. Unanticipated incidents may result in the limitation, suspension or termination of research or teaching activities by the BSO or IBC as well.

Unauthorized personnel should not be in the laboratory. Laboratory personnel should not be around biological hazards if not approved to be on a protocol.[1]

IBC Position on the Use of Laboratory Self-collected Human Primary Specimens.

Research projects in biology or bioengineering often rely on the use of human specimens such as blood, urine, swabs, etc. When practical and appropriate for a research project, the IBC strongly recommends the use of commercial vendors to obtain pooled human specimens. These specimens are often tested for common bloodborne pathogens and other relevant infectious diseases for the sample types; they represent a pooled sample of material rather than an individual specimen and are exempt from oversight by the Institutional Review Board (IRB).
Self-collection or collection of human specimens from laboratory personnel, especially with the intent to culture, propagate or identify microorganisms from the samples, carries increased risk when considering biosafety and human subject protection; and is not permitted at Caltech unless a scientific justification has been approved by both the IBC and the IRB.

IBC Position on Minor Volunteers or Employees in Caltech Laboratories

A minor is any person under the age of 18 years. Under the provisions of state and federal law, as well as Caltech's Minors Personnel Memorandum ("Minors PM"), minors may not be employed, intern or volunteer in any hazardous occupations. In addition, pursuant to the Minors PM, minors working, interning or volunteering in

[1] See the Biosafety in Microbiological and Biomedical Laboratories for standard practices for biosafety levels.

laboratories must be approved by the Division Chair or Division Operation Officer in consultation with the supervising PI. Minors working in areas with restricted access must also be approved by the supervising Director. Minors working with regulated subjects or materials must obtain the permission of the appropriate regulating administrative committee. Consideration for approval should be on a case-by-case basis taking into account potential hazards associated with the specific research, the types of equipment to be used, and any potential hazards associated with the specific research, and any potential risk for chemical and/or biological exposures.

The IBC will oversee, review and approve biology experiments that are under the purview of the IBC that minors can perform in Caltech laboratories handling biological material.

- No person under the age of 14 years is allowed to participate in research activity in laboratories handling any kind of biological material. Entry in the laboratory space is authorized only when participating in a supervised tour.

- No person under the age of 16 years is allowed to handle material requiring Biosafety Level 2 (or above) containment and practices – minors aged 14 to 16 can work in laboratories operating at Biosafety Level 1 with the proper approval and training.

- No person under the age of 18 years is allowed to handle material requiring containment and/or practices above Biosafety Level 2 – This includes work with **lentiviral vectors, HIV-pseudovirus or live HIV**. Minors aged 16 to 18 can work in laboratories operating at Biosafety Level 2 with the proper approval and training.

Table 1 Summary of authorized activities for minors

Age	Under 14	14 to 16	16 to 18
Authorized activities	Supervised tour or escorted walk-thru only	Experiments requiring BSL1 containment and practices: *Examples: E.coli cloning, mouse cell culture, yeast or insect cell culture, protein purification, DNA analysis, PCR*	Experiments requiring BSL2 containment and practices: *Examples: human cells culture, use of viral vectors such as AAV or murine retrovirus, some RG2 virus or bacteria*

The biosafety requirements in this section do not apply to Caltech's enrolled graduate or undergraduate students who are under the age of 18.

Research and Teaching Exempt from IBC Review

The following research and teaching activities are exempt from IBC Registration and Review:

1. Work using biological toxins with an LD_{50} above the limit set by the IBC is exempt from IBC registration; however, such work must be conducted in accordance with Caltech's or JPL's applicable Chemical Hygiene Plan.[2]
2. Work using animal cells (other than human and non-human primate), provided that the cells are not modified or further manipulated with r/s nucleic acids or known to contain pathogens.
3. Caltech has neither the resources nor clinical facilities to support human gene transfer research. Any human gene transfer research conducted under the auspices of Caltech must be performed in collaboration with another institution. Such collaboration would be subject to Caltech's Institutional Review Board (IRB) policy which applies to human clinical trials and that policy should be reviewed prior to proposing or instituting any collaborative human gene transfer research. The PI should contact the Chief Research Policy Officer if he or she has interest in human gene transfer research.

Even if the research or teaching is exempt from IBC registration and review, such research or teaching must be conducted in accordance with all applicable Institute safety policies and procedures. Any questions regarding exempt work should be brought to the BSO or the IBC Chair.

IBC Meetings

The IBC meets as needed, but not less than quarterly. Additional special meetings are called as necessary. Members of the IBC, the IBC administrator, and a representative from the Audit Services and Institute Compliance are invited. The IBC may also invite PIs to present or field questions about their protocols. Members of the public who would like to attend may seek permission from the IBC Chair.

Quorum

Quorum requires the presence of (1) either the Chair or Vice-Chair, (2) the Biosafety Officer, (3) a tenured faculty member[3] other than the Chair, and (4) three other voting members of the IBC, for a total of six (6) voting members. Approval by a majority of the voting members present at the meeting is required to approve or terminate a research protocol.

Minutes Policy

The IBC will prepare minutes according to its SOP01, Procedure for Preparing Minutes of the IBC Meetings. Minutes will be made available to the public, upon request, in accordance with section IV-B-2-a-(7) of the *NIH Guidelines,* which state: "*Upon request, the institution shall make available to the public all Institutional Biosafety Committee meeting minutes and any documents submitted to or received from funding agencies which the latter are required to make available to the public."*

Institutional Biosafety Committee Composition

The IBC shall be composed of at least 11 members and shall include **at least three faculty representatives from at least two of the academic divisions**, as well as six ex officio members from administrative offices. The Committee is constituted in accordance with *NIH Guidelines*. Members of the Committee shall collectively have experience and expertise in recombinant and synthetic nucleic acid technology, the capability to assess the safety of recombinant and synthetic nucleic acid research, and to identify any potential risk to public health or the environment. The membership of the Committee shall include one member with understanding of

[2] See the *Biosafety in Microbiological and Biomedical Laboratories* for list of toxin agents.
[3] As defined by the Faculty Handbook

infectious biological agents and one expert in animal containment principles. The Committee may consult with ad hoc experts when review of specific protocols requires additional expertise.

Chair and Vice-Chair

Two faculty members are appointed as Chair and Vice-Chair of the Committee. When the Chair is unavailable, or at the Chair's request, the Vice-Chair may fulfill the duties of the Chair.

Non-Affiliated Members

At least two members of the Committee shall not be affiliated with the Institute (apart from their membership on the Committee). The non-affiliated members shall represent the interests of the surrounding community with respect to health and protection of the environment.

Ex Officio Members

The Director of Environment, Health and Safety (Institute Safety Officer), the Attending Veterinarian, the Chief Research Policy Officer, the Institute Biosafety Officer (BSO), the Senior Director for Research Administration (or his/her designee) and an attorney from the Office of General Counsel serve as ex officio members of the Committee. Ex officio members serve on the Committee as a result of the office or position that they hold. They stand outside any rotation of committee memberships as long as they hold the office designated in this paragraph. With the exception of the attorney member who provides legal counsel, ex officio members are full voting members of the Committee.

With the exception of ex officio members, members of the Committee shall be appointed for three-year terms and shall typically serve two consecutive terms; however, should circumstances require, the President may appoint an individual to fewer or additional terms should such action be deemed appropriate for the Institute, and agreeable to the appointee.

Alternate Members

Individuals may be appointed to the Committee as alternates for specific Committee members. Alternate members may vote in the absence of the member he/she is assigned to as an alternate. If both the member and his/her designated alternate member are present at a convened meeting of the Committee, the alternate member may not vote.

Conflicts of Interest

At times, members have a perceived or actual conflict of interest in the projects under submission to the IBC, for example, when they are the PI on protocols. When such matters are discussed, the member must recuse him-or-herself for the remaining discussion and the vote, unless the IBC requests that the member with a conflicting interest be present to answer questions from other committee members. This is documented in the minutes. Quorum must be maintained after the PI is recused for a vote of the convened Committee to take place.

Roles and Responsibilities

IBC

The IBC is responsible for:

- Reviewing research and teaching conducted at the Institute involving biohazardous agents or recombinant/synthetic nucleic acids for conformity with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* and the Institute IBC policy
- reviewing research conducted at the Institute involving other biologic materials as listed above
- reviewing the potential risk to the environment and public health and evaluating containment levels and adequacy of the facilities and procedures for the research or teaching activity
- working with laboratories to identify relevant prophylaxis
- coordinating with Caltech Occupational Health Provider as needed
- notifying the Principal Investigator of the results of the IBC's protocol review
- lowering containment levels for certain experiments as specified in Section III-D-2-a (Experiments in which DNA from Risk Group 2, Risk Group 3, or Restricted Agents is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems)
- reviewing and evaluating inactivation methods and procedures for inactivated infectious material sent from or received by Caltech laboratories
- setting containment levels as specified in Section III-D, including Sections III-D-4-b (Experiments Involving Whole Animals) and III-D-5 (Experiments Involving Whole Plants)
- periodically reviewing recombinant/synthetic DNA research conducted at the Institute to ensure compliance with the *NIH Guidelines*
- adopting emergency plans covering spills, contamination, or other accidents
- reporting any significant problems with or violation of the NIH *Guidelines* and any significant research-related accidents or illnesses to the appropriate institutional official and NIH Office of Science Policy (OSP) within 30 days, unless the IBC determines that a report has already been filed by the PI
- withholding authorization of experiments that are not explicitly covered by the *NIH Guidelines* until NIH establishes the containment requirement

Principal Investigator

In accordance with the *Caltech Faculty Handbook* on Principal Investigator Eligibility, only those individuals who are eligible to serve as PIs on proposals for external funding may serve as the PI for an IBC protocol. Division Chairs can grant PI status for holding an IBC protocol to Core Center Directors and Managers.

On behalf of the Institute, the PI is responsible for full compliance with the *NIH Guidelines* in the conduct of recombinant/synthetic nucleic acid research and for adherence to the policies and procedures of the IBC. The PI should take particular note of the following responsibilities:

- The PI should make the initial determination of the required levels of physical and biological containment in accordance with the most recent editions of the *NIH Guidelines* and the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL 6th Edition).
- The PI should submit a protocol application to the IBC for review and approval and obtain IBC approval before initiating research subject to the *NIH Guidelines* or Institute policies. The PI should remain in communication with the IBC throughout the duration of the approved protocol and report any significant problems or accidents or illnesses related to the research to the BSO and IBC in accordance with Institute policies.
- The PI should consult with the BSO or the IBC before proceeding with modifications to an approved IBC protocol. An amendment may need to be filed and approved before the modified research may begin.
- The PI should propose the appropriate microbiological practices and laboratory techniques to be used for the research and provide sufficient details to the IBC for it to conduct a proper risk assessment.
- The PI should ensure that the staff listed on the protocol have sufficient knowledge, are sufficiently trained, and have demonstrated the appropriate competence to safely perform the responsibilities for which they have been assigned.
- The PI should ensure that the protocol participants fully understand the steps necessary following any spills or potential exposures to the agents described in the protocol.

Biosafety Officer

The responsibilities of the Biosafety Officer include, but are not limited to:

- serving as a voting member of Institutional Biosafety Committee
- conducting, or appointing a designee to conduct, laboratory inspections to ensure that appropriate laboratory standards as determined by the IBC are rigorously followed
- reporting to the IBC and the Institute any problems, violations of the *NIH Guidelines,* and any research-related accidents, illnesses, or near misses of which the BSO becomes aware
- developing emergency plans for handling accidental spills and personnel contamination involving biologics
- performing root cause analysis, or appointing a designee to perform root cause analysis of laboratory accidents involving r/s nucleic acids, biohazardous agents or any other biologics
- developing, deploying and overseeing a comprehensive Biosafety Program for the Institute
- together with the IBC, overseeing review of BSL-2 research projects that require the use of additional biosafety measures (e.g., BSL-2 with BSL-3 practices, as described in the Biosafety Manual), and conducting all relevant inspections for these facilities
- conducting, or appointing a designee to conduct, biosafety risk assessments
- training personnel to ensure the Institute is in compliance with all applicable federal biosafety laws and regulations
- collaborating with investigators, staff, and students in all matters related to biosafety
- providing expertise for the design and management of containment facilities
- serving the Institute as a resource and leader in all aspects of education and training in biosafety

Protocol/Amendment Submissions

Submission

IBC protocol submissions (or applications), whether they are new IBC protocol submissions, amendments to revise existing submissions, or de novo submissions of approved protocols, must be submitted to the IBC by the PI.

Research or teaching utilizing biohazardous agents or r/s nucleic acids may not be initiated prior to the review and approval of a protocol by the IBC. Once an IBC protocol is approved by the IBC, it will remain active for a period of three years. During that time period, any changes to the approved protocol (e.g., room changes, addition of new procedures or agents) must be reviewed and approved by the IBC prior to initiation of the proposed work.

Submissions will be reviewed as described in "The IBC Review Process," in this document.

When a submission is approved, the research or teaching activity should only begin after the researcher has completed required training and has satisfied any stipulations provided in the protocol approval. Information regarding the training requirements and courses that are offered can be found in the SOP "IBC Training". Training requirements are determined by the BSO upon review of the protocol and are listed in the stipulations section of the IBC status memo. Stipulations will be specified by the IBC and can be found in the status memo accompanying approval.

De Novo Submissions

All approved IBC protocols are valid for three years. A de novo protocol must be submitted for research or teaching that is anticipated to continue beyond the three-year approval term. All de novo protocols must be approved before the expiration date of the existing protocol in order for work to continue. If no de novo protocol is submitted and approved, the IBC Administrator shall close the protocol upon expiration of the existing protocol. As a courtesy, the IBC Administrator will remind PIs to submit a de novo protocol four months before an active protocol expires.

These de novo submissions are reviewed in the same manner as a new protocol submission, unless they qualify for Chair/Expedited review, described below.

Annual Review

No submission is required for annual review. The BSO or a qualified staff member as approved by the IBC will review protocols during the annual biosafety inspection of the lab. The annual review of protocols will consist of (1) confirming which personnel are performing research under the protocol and ensuring such personnel are properly trained and (2) determining whether any new agents or procedures are being used in the lab. If needed, an amendment may be submitted. The IBC will receive annual review statuses in a quarterly report.

Expiration of Protocols

All approved IBC protocols are typically valid for a three-year time period. At the discretion of the Chair, the IBC may entertain approving limited time extensions or shorter time periods. If a de novo protocol has not been submitted by the PI or has been submitted but not approved by the IBC prior to the three-year expiration date,

that protocol will expire. No research under that protocol may be conducted until the de novo protocol is reviewed and approved by the IBC. Expiration of the IBC protocol may require cessation or termination of related research in approved IACUC or IRB protocols.

Protocol and Amendment Submission Review Process

IBC Review Process

Research projects exempt from IBC review do not require an IBC protocol submission; however, PIs are strongly encouraged to contact the IBC Administrator and/or BSO to help determine if their research is exempt from review and approval.

After receipt by the IBC, all protocol submissions are subject to pre-review by the IBC Administrator and the BSO. In the case of protocol submissions requiring Full Committee Review for approval, an IBC member will be appointed to pre-review the submission. Descriptions of these types of pre-review are found below. After pre-review is complete, one or several reviews for approval are conducted based upon the research proposed in the submission (See IBC Review Table). Protocol submissions may be approved by Administrative, Expedited, or Full Committee Review, described below.

Administrative Pre-Review

Upon receipt, IBC protocol submissions are reviewed by the IBC Administrator to ensure that they are complete and contain sufficient description and detail to determine which type of review for approval is required (i.e., Administrative Review, Expedited Review or Full Committee Review).

If the IBC submission involves the use of animals, the IBC Administrator determines whether there is an associated approved Institutional Animal Care and Use Committee (IACUC) protocol that contains a description of biohazardous agent use consistent with what is described in the IBC submission.

If the IBC submission involves the administration of biohazardous or recombinant agents/molecules to humans or the acquisition of tissues directly from humans, the IBC Administrator will confirm with the IRB Administrator that there is an associated approved IRB protocol. It is advisable to have all necessary applications submitted to the appropriate committees with enough time for timely approval.

BSO Pre-Review

Once it is determined that a submission is complete, the submission is reviewed by the BSO, who performs a risk assessment of the proposed work and may meet with the lab to discuss appropriate containment practices and review and refine the protocol.

IBC Member Primary Pre-Review

If a submission is not Exempt, or subject to Administrative or Expedited Review, the submission is pre-reviewed by a voting member of the IBC prior to review by the full committee at a convened meeting.

All submissions requiring Full Committee Review should be adequately pre-reviewed so that the submission presented to the Full Committee is as complete as possible. As such, the PI should expect questions throughout the pre-review process. Any questions or concerns raised during any stage of the pre-review process must be satisfactorily addressed prior to placement of the submission on the agenda of the next convened meeting of the IBC.

Most submissions (new, de novo protocols, and amendments), must be reviewed and approved at a convened meeting. The IBC Review Table lists the various types of review that submissions will undergo based on the submission type, the use of r/s nucleic acids, and the biohazardous agents that may be utilized.

Administrative Review Approval

The following categories of submissions require Administrative Review and may be approved administratively:

- Amendments removing or adding staff for whom training has been completed and properly documented

BSO Review Approval

The following categories of submissions require BSO Review and may be approved administratively, after pre-review and recommendation for approval by the BSO:

- Proposed research or teaching utilizing a well-established cell line of human origin, provided that the cells are not further modified or manipulated with r/s nucleic acids and the material is not being administered to animals
- Amendments adding information or details about variants, strains, cell lines or biologic items for which the risk has already been evaluated and that do not constitute a significant change to the risk assessment
- Amendments adding, changing or removing a room where procedures will be performed. Such amendments requesting the use of new rooms which require research or teaching under BSL-2 conditions must first be reviewed and approved by the BSO prior to approval

The full Committee is informed of BSO and Administrative approvals and ratifies these approvals at its next convened meeting.

Expedited Review and Approval

Upon recommendation of the BSO, after Administrative and BSO pre-review, the following categories of submissions qualify for, and may be approved by Expedited Review:

- Submissions proposing the generation of transgenic animals under BSL-1 containment
- Submissions proposing work falling within Section III-F of the *NIH Guidelines*
- Submissions proposing work with Human or Non-Human Primate harvested material, provided that the material is not further modified or manipulated with r/s nucleic acids, or the manipulation falls under section III-F of the Guidelines, and the material is not being administered to animals
- Amendment submissions indicating a minor change that has no impact on risk (no change in Risk Group) or change in biosafety level
- De Novo resubmissions where the PI is unchanged, and the research proposed is exempt from *NIH Guidelines*, does not use any Risk Group 2 or 3 agents, and does not propose work utilizing animals
- Addition of material that has been reviewed and permitted by a federal or local agency (USDA, CDC) providing that the risk assessment and containment requirement for the protocol does not change significantly

All submissions subject to Expedited Review will be reviewed for approval by the BSO and the IBC Chair. These reviewers may request additional information or clarification from the PI, or designate the submission for Full Committee Review, should they determine that such review is warranted.

Following satisfactory resolution of any issues raised during this review, the IBC Chair and BSO may approve the submission and the PI may proceed with the research or teaching activity. These Expedited approvals are presented to the IBC at the next regularly scheduled meeting of the committee for ratification.

Full Committee Review and Approval

Following Administrative, BSO and IBC Member pre-review, as indicated above, the protocol submission is provided to the Full Committee for review.

The IBC review includes:

(i) independent assessment of the containment levels required by the *NIH Guidelines*, *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), and Institute policies for the proposed research;

(ii) assessment of the facilities, procedures, practices, and training and expertise of personnel involved in recombinant or synthetic nucleic acid molecule research;

(iii) ensured compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the *NIH Guidelines* and Institute policies; and

(iv) determination of whether or not the submission should be referred to the NIH Office of Science Policy (OSP).

Protocol and Amendment Submissions: Approvals and Dispositions

At any time during the submission review process, a protocol may be withdrawn by the PI.

After review, a determination will be made regarding each submission. Protocols may be approved, deferred, or not approved. The determination will be communicated to the PI through a status memo.

Approved protocols can be subject to temporary suspension of work, suspension of the protocol, termination or expiration.

IBC Submission Determinations/Approvals

Approved: The protocol submission satisfactorily addresses all issues and the submission is fully approved subject to standard stipulations (e.g., animal work may not begin until IACUC has approved the corresponding animal protocol. The IBC Administrator and BSO maintain a set of standard stipulations, approved by the IBC, that are issued to the PI in the approval status memo), with no modification by the PI required.

Approved with Stipulations: The protocol submission is approved, but the approval is subject to the satisfaction of specific requirements that are stipulated in the status memo issued to the PI (e.g., specific Personal Protective Equipment is required). No revision of the protocol is necessary, although the PI may need to provide evidence that the stipulations are being addressed.

Approved Pending Modifications: Minor issues remain that must be addressed by the PI prior to approval. The revised protocol submission will be reviewed by the Chair and/or BSO who may have follow-up questions, may

request the response to be evaluated by another member of the Committee, or may require an additional Full Committee Review. After satisfactory review and protocol adjustment, the protocol will either be approved by the IBC Chair, or may be referred back for Full Committee review.

Deferred: The protocol submission is not approved because significant issues remain, requiring the full committee to review the PI's response. Submissions may also be deferred when there is insufficient time to review a protocol during a full committee meeting, or if quorum is lost.

***Not Approved*:** The protocol submission is not approved and withdrawn from further consideration by the Committee.

IBC Action on Approved Protocols

Under circumstances that create an immediate threat to health and safety, the BSO, Chair, or Vice Provost may immediately, and temporarily, suspend the hazardous activity. A temporary suspension of work may also be requested by the Office of the Provost.

***Suspended*:** The approval of the IBC protocol is suspended. None of the activity that is described in the IBC protocol involving IBC-regulated materials may be performed during the period in which the protocol is suspended. The IBC may suspend a protocol during instances of serious or continuing non-compliance with IBC or institutional policies and guidelines or with the *NIH Guidelines.* A protocol, or portion of a protocol, may only be suspended through action in a convened meeting of the IBC. The IBC will provide instruction to a PI with regard to the requirements that must be met in order to lift a suspension.

***Terminated*:** The IBC protocol is no longer approved and will not be reconsidered for approval by the IBC Committee. All activities described in the protocol utilizing IBC-regulated materials must cease upon receipt of the notice of termination. The IBC will not reconsider re-approving the IBC protocol and it may not be re-submitted by the PI for IBC review. The IBC may terminate a protocol during instances of serious or continuing non-compliance with IBC or institutional policies, guidelines or with *NIH Guidelines*. The activity of protocol termination can only be executed in a convened meeting of the IBC.

Expired: Three years have passed since the IBC protocol was approved and no de novo submission was submitted by the PI.

Closed: A protocol may be closed at any time at the PI's request.

IBC Status Memos

As a result of Administrative, Expedited, or Full Committee Review, protocol submissions will be approved, approved with stipulations, approved pending modifications, deferred, or not approved. This determination will be communicated to the PI through a submission status memo sent by the IBC Administrator on behalf of the Committee or the IBC Chair.

Status memos may require additional action on the part of the PI (e.g., in the case of Approved Pending Modifications). Failure to respond to a submission status memo requiring action within 30 days from the date of the memo will result in the issuance of a Final Notice from the IBC Administrator. If the PI fails to respond to the

Final Notice within 30 days from the date of the Final Notice, the original submission shall be considered withdrawn.

Status memos will also be sent to inform the PI about any IBC actions taken on an approved protocol. Should PI action be requested by such a memo, failure to respond to the protocol status memo within the time prescribed may result in termination of the protocol.

The PI should contact the IBC Administrator or the IBC Chair if the PI is unable to respond to any status memo requiring PI action in a timely matter to request an extension.

Table 2. ***IBC Review Table***

Decision Level Review	Research Proposed/Submission	Administrator Review	BSO Review	Chair* Review	Full Committee Review
EXEMPT	If research proposed is: a) Work with **biological toxins**** for which the LD_{50} is above the IBC set threshold, OR b) Acquisition/use of **genomic or fragment DNA/RNA** material and/or **oligonucleotides** or DNA/RNA probes (unable to replicate in microorganisms or cells) c) use of **transgenic rodent**, acquired commercially and or bread for tissue/cell collection.	Exempt. Does not require review and approval by IBC***			
ADMIN	If research proposed is: Amendment adding or removing **trained staff**	**X**	**X**		
BSO	If research proposed is: a) DeNovo Application for work with a **well-established cell line of animal origin**, provided that the cells are not further modified or manipulated with r/s nucleic acids, or falling under III-F and the material is not being administered to animals, b) Amendment to provide extra information or include additional variants, strains, cell line for items already approved, c) Amendment adding or removing **trained staff**, OR d) Amendment adding, changing or removing a **room** where procedures will be performed		**X**		
EXPEDITED	DeNovo Application or Amendment for work transgenic animal production (rodent, flies, worms) or used in conjunction with other biological material (rDNA, etc.) requiring only BSL1 containment		**X**	**X**	
	DeNovo Application or Amendment for project using only RG1 organisms and/or falling within section III-F of the *NIH Guidelines*		**X**	**X**	
	DeNovo Application or Amendment for working with Human or Non-Human Primate harvested material provided that the material is not further modified or manipulated with r/s nucleic acids, and the material is not being administered to animals		**X**	**X**	

	Amendment proposing procedure change with no impact on Safety practices, Biosafety Level – or addition of USDA/CDC permitted material.		X	X	
FCR	**All other submissions**		X	X	X

* The Chair may determine that Full Committee Review is required or request additional review by a committee member.
** Work with biological toxins with LD50 above the IBC set threshold should be performed using administrative and engineering controls as well as PPE described in the Chemical Hygiene Plan.
*** Questions regarding exempt status should be directed to the BSO or the IBC Chair.
# Full Committee Review

Relationships Between IBC Protocols and Other Committees and Offices at Caltech

IACUC

An IBC protocol associated with an IACUC protocol must be approved prior to the IACUC protocol approval. IACUC protocols involving research with biohazards or hazardous biologics in animals cannot begin until the IBC has approved the submission covering this work. IBC submissions that involve the use of animals may receive an "Approved with Stipulation" status and research, described in the IBC submission that can be conducted without the use of vertebrate animals, may proceed without IACUC approval. No research requiring the use of vertebrate animals may proceed until both the IACUC protocol and IBC submission are approved.

IRB

IBC protocol submissions that involve the administration of biohazardous agents, administration of r/s nucleic acids to humans, or direct harvesting of blood, tissues, or specimens from humans, require IRB review prior to initiation.
Reminder: Self-collection or collection of human specimens must receive approval by both the IBC and the IRB.

The IBC Administrator will confirm that exemption or approval from the IRB has been secured for all IBC submissions that require such IRB review. Only after IRB exemption or approval is confirmed will IBC approval be granted for these submissions.

HESC

IBC protocol submissions that involve the use of human embryotic stem cells or human embryos require HESC registration or approval prior to initiation.

The IBC Administrator will confirm that registration or approval from the HESC has been secured for all IBC submissions that require such HESC review. Only after HESC registration or approval is confirmed will IBC approval be granted for these submissions.

Radiation Safety Committee

The IBC Administrator will confirm that exemption or approval from Caltech's Radiation Safety Committee (RSC) if the IBC protocol submission involves the use of radiation subject to review by the RSC.

Office of Sponsored Research

Upon receipt of funding proposals indicating biohazardous work on the Division Approval Form (DAF), the Office of Sponsored Research will provide a copy of the proposal to the Office of Research Compliance (ORC@caltech.edu). The ORC will route the proposal to the IBC Administrator and BSO for review to determine whether an IBC protocol is required to check to assure award congruency when appropriate. If an IBC protocol is required, the IBC Administrator will request that the PI provide a submission and will notify OSR when the submission is approved.

Service Center and Shared Resources

The IBC is responsible for reviewing protocols involving biohazardous material and/or r/s nucleic acid-containing organisms, tissues or microorganisms. Caltech Core and/or Service Centers (https://www.bbe.caltech.edu/research/facilities-and-resources) that provide research services involving the generation and/or manipulations of biohazardous material and/or r/s nucleic acid-containing organisms, tissues or microorganisms may need a dedicated and specific Service Center protocol approved by the IBC.

With the approval of the Division Chair, Core Center Directors or Managers may hold an IBC protocol and assume the role of "Principal Investigator" for all matters related to the submission and approval maintenance for the IBC protocol describing the Core Center operation and risk assessment/management.

The Service Center protocol should describe, in as much detail as possible, the manipulations performed by the Service Center on a routine basis. More detailed information (such as a particular r/s nucleic acid constructs, biohazards used, etc.) that is specific to the work of an individual PI using the Service Center should be listed on the PI-specific IBC protocol and should be provided to the Director of the Service Center at the time the services are requested. Directors should consult with the BSO when using any potentially biohazardous materials with which they are not familiar. The Directors, in consultation with the BSO, will develop appropriate standard operating procedures to ensure that all steps are taken to minimize potential exposures of Service Center staff.

Environment, Health, and Safety (EHS)

Environment, Health, and Safety is responsible for the development and coordination of the Institute's safety and environmental compliance programs on campus. These programs include, but are not limited to, the following:

- industrial hygiene
- fire safety
- biosafety
- radiation safety
- inspections: all buildings and laboratories constituting the Caltech campus are inspected periodically to identify and locate infractions of fire, industrial or general safety concerns
- safety training
- emergency preparedness
- hazardous waste management plan
- ergonomics

JPL

The combined efforts of several JPL organizations provide comprehensive support and oversight of the safety and environmental compliance programs at the JPL campus. Some of the programs include industrial hygiene, laboratory safety, safety training, ergonomics, inspections, environmental compliance, fire/life safety, hazardous waste, and emergency preparedness.

The JPL Occupational Safety Program Office (OSPO) provides onsite biological safety support for JPL related IBC protocols in collaboration and consultation with the IBC and BSO. Support may include: guidance on the submittal of JPL protocols to the IBC; providing appropriate training; performing inspections to ensure the facilities and practices are appropriate for the work being performed; and partnering with other JPL divisions and sections in relation to the implementation of biosafety requirements.

Pre and Post Approval Biosafety Monitoring

Lab Inspections

(i) EHS – General buildings and laboratories comprising the Caltech and JPL campuses are inspected on a periodic basis to identify and locate hazardous conditions and safety concerns.

(ii) Biosafety Officer

a. Protocol Specific Inspections:

i. On the Caltech campus, the BSO will conduct BSL-1, BSL-2, ABSL-1 and ABSL-2 inspections based upon the standards set forth in the most recent edition of the *BMBL*, the *NIH Guidelines*, and Select Agent regulations (when applicable) on a yearly basis. The Annual Protocol Review will also take place during this inspection.

ii. On the JPL campus, Occupational Safety Program Office (OSPO) personnel will conduct BSL-1 and BSL-2 inspections based upon the standards set forth in the most recent edition of the *BMBL*, the *NIH Guidelines*, and Select Agent regulations (when applicable) on a yearly basis. Protocol-specific Inspections will be performed in consultation with the Caltech Institute Biosafety Officer as needed.

b. Ad hoc Inspections: The BSO may conduct inspections on the Caltech campus as necessary.

Annual Review

The BSO will review protocols annually during the annual biosafety inspection of the lab. The Annual Protocol Review will consist of (1) confirming which personnel are performing research under the protocol and ensuring such personnel are properly trained, and (2) determining whether any new agents or procedures are being used or will be used in the lab that may require an amendment. The IBC will receive a status report of Annual Protocol Reviews.

JPL OSPO personnel may review the IBC protocols performed at JPL during the annual biosafety laboratory inspection or at any time prior to the anniversary date of the protocol approval. During the annual review of an IBC protocol, the JPL OSPO will (1) confirm which personnel are performing research under the protocol and verify that personnel are properly trained, and (2) determine whether any new agents are being used or will be used in the lab that may require an amendment to the protocol.

The JPL OSPO will provide the results of IBC protocol reviews to the BSO and the BSO will provide a status report of the Annual Reviews to the IBC.

Training

Research Personnel

The Institute requires that all investigators, technicians and students involved with research activities described on a given IBC protocol be appropriately trained to mitigate research-associated risks as well as to ensure compliance with applicable local, state and federal regulations and guidelines. This training will include IBC-mandated training elements, developed and provided by the BSO at Caltech or OSPO personnel at JPL, as well as lab-specific training, provided by the PI for each of his/her IBC research protocols. Specific training requirements for Caltech are discussed in IBC SOP03, IBC Training.