University of Hawaii Institutional Biosafety Committee

Operating Policies and Procedures

August 2022

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General Definitions and Abbreviations

Adverse Event – An event "associated with the use of a gene transfer product" when there is a reasonable possibility that the event may have been caused by the use of the product.
APHIS - Animal and Plant Health Inspection Service, an agency of the USDA.
AWBP – Animal Welfare and Biosafety Program
Bloodborne Pathogens (BBP) – Pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to hepatitis B virus (HBV) and human immunodeficiency virus (HIV).
BMBL - Biosafety in Microbiological and Biomedical Laboratories, currently in its 6th Edition, published by the CDC. June 2020.
Biological Safety Officer (BSO) professional 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.
CDC – Centers for Disease Control and Prevention
Deliberate Release – A planned introduction of recombinant or synthetic nucleic acid molecule-containing microorganisms, plants, or animals into the environment.
DIO- Designated Institutional Official is the individual who has authority and responsibility for the oversight and administration of the program.
DORC – Director, Office of Research Compliance
DOT – Department of Transportation
DURC – Dual Use Research of Concern is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agriculturalcrops and other plants, animals, the environment, materiel, or national security.
Enrollment – The process of obtaining informed consent from a potential research participant, or a designated legal guardian of the participant, to undergo a test or procedure associated with the gene transfer experiment.
HDOA – Hawaii Department of Agriculture
IATA – International Air Transport Association
Infectious Material – Materials known to contain, or reasonably expected to contain, pathogens or cause disease.
Institution – Any public or private entity (including Federal, state, and local government agencies).
IBC - Institutional Biosafety Committee
Institutional Biosafety Committee – A committee that: 1) meets the requirements for membership specified in Section IV-B-2 of the NIH Guidelines, and 2) reviews, approves, and oversees projects in accordance with the responsibilities defined inSection IV-B-2 of the NIH Guidelines.

LAI – Laboratory Associated Infection

NIH – National Institutes of Health

NIH Guidelines – NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

OBA – Office of Biotechnology Activities

Office of Biotechnology Activities – The office within the NIH that is responsible for: 1) reviewing and coordinating all activities relating to the NIH Guidelines, and 2) performing other duties as defined in Section IV-C-3 of the NIH Guidelines.

Office of Research Compliance (ORC) assures the public that research at UH is performed responsibly.

Pathogens - Micro-organisms (including bacteria, viruses, rickettsia, parasites, fungi) and other agents such as prions which can cause disease in humans, plants or animals.

PI – Principal Investigator- The person who signs the IBC registration form and is responsible for the research activities.

RAC – Recombinant DNA Advisory Committee Recombinant DNA Advisory Committee – The public advisory committee that advises the Department of Healthand Human Services (DHHS) Secretary, the DHHS Assistant Secretary for Health, and the NIH Director concerning recombinant or synthetic nucleic acid molecule research.

Recombinant/Synthetic Nucleic Acid Molecules –

1) Molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids;
2) 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
3) Molecules that result from the replication of those described in (1) or (2) above. **SA** – Select Agent

Select Agent - Select agents and toxins are a subset of biological agents and toxins that the Departments of Health and Human Services (HHS) and Agriculture (USDA) have determined to have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products. A current list of select agents and toxins can also be found at: https://www.selectagents.gov/sat/list.htm

Serious Adverse Event – Any event occurring at any dose that results in any of the following outcomes: death, a life-threatening event, in-patient hospitalization or prolonged existing hospitalization, a persistent or significant disability/incapacity,or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization also may be considered a seriousadverse event when, upon the basis of appropriate medical judgment, they may jeopardize the human gene transfer research subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Standard Laboratory Procedures (SOP) - set of step-by-step instructions compiled by an organization to help workers carry out complex routine operations.

Standard Precautions: Universal Precautions

Toxin - Select agents and toxins are a subset of biological agents and toxins that the

Departments of Health and Human Services (HHS) and Agriculture (USDA) have determined to have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products. A current list of select agents and toxins can also be found at: https://www.selectagents.gov/sat/list.htm

Transgenic Animal - Animal in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line.

Unexpected Serious Adverse Event – Any serious adverse event for which the specificity or severity is not consistent with the risk information available in the current investigator's brochure.

Universal Precautions – Standard Precaution. An approach to infection control. According to the concept of Universal Precautions, all human blood and certain human body fluids are treated as if known to be infectious for HIV, HBV and other bloodborne pathogens.

University Laboratory Inventory Declaration (UHLID) biological materials inventory of researchers and instructional faculty.

USDA – United States Department of Agriculture

SECTION I. SCOPE OF THE INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)

Section I-A. Purpose

The University of Hawaii (UH) Institutional Biosafety Committee (IBC) was created in accordance with the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) to ensure compliance with government regulation and institutional policies. Additional areas of oversight include federal requirements regulated by the NIH Office of Science Policy, and the Hawaii State requirements including Hawaii Department of Agriculture importation regulations and Hawaii Department of Health Infectious Wastes Management.

The IBC is responsible for reviewing all research, clinical and instructional-use activities involving recombinant or synthetic nucleic acid molecules, biological materials, biological derived toxins (toxins), dual use research of concern (DURC), select agents, other biological materials and human gene transfer projects, as well as developing institutional policies to ensure proper biosafety and biosecurity throughout the UH System. This review shall include, but is not limited to, the assessment of (i) containment levels required by the NIH Guidelines for the proposed research; (ii) facilities, procedures, practices, and training and expertise of personnel involved in the proposed research; and (iii) compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the NIH Guidelines.

Section I-B. Applicability and Compliance with the NIH Guidelines

The NIH Guidelines are applicable to all recombinant or synthetic nucleic acid research that is conducted at or sponsored by an institution that receives any NIH funds or support.

The NIH Guidelines is also applicable to all research that involves testing in humans or animals of materials containing recombinant or synthetic nucleic acids developed with NIH funds, if the institution that developed those materials sponsors or participates in those projects. Participation includes research collaboration or contractual agreement, not mere provision of research materials.

As a condition for NIH funding of recombinant or synthetic nucleic acid molecule research, institutions shall ensure that such research conducted at or sponsored by the institution, irrespective of the source of funding, shall comply with the NIH Guidelines. Noncompliance may result in (i) suspension, limitation, or termination of financial assistance for the noncompliant NIH-funded research project and of NIH funds for other recombinant or synthetic nucleic acid molecule research at the institution, or (ii) a requirement for prior NIH approval of any or all recombinant or synthetic nucleic acid molecule projects at the institution.

Section I-C. Program Review

The IBC shall conduct a biennial review of the operating policies and procedures to ensure accuracy and completeness, as well as account for any modifications and/or additions resulting from regulatory expectations or institutional policies.

SECTION II. MEMBERSHIP AND PROCEDURES

Section II-A. IBC Membership (NIH Guidelines IV-B-2-a)

The IBC must be comprised of no fewer than five (5) members who collectively have experience and expertise in recombinant or synthetic nucleic acid molecule technology and the capability to assess the safety of recombinant or synthetic nucleic acid molecule research and to identify any potential risk to public health or the environment.

At least two (2) members shall not be affiliated with the institution (apart from their membership on the IBC) and who represent the interest of the surrounding community with respect to health and protection of the environment.

The IBC shall include at least one (1) individual with expertise in plant, plant pathogen, or plant pest containment principles when experiments utilizing Appendix P of the NIH Guidelines (Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Plants) require prior approval by the IBC.

The IBC shall include at least one (1) individual with expertise in animal containment principles when experiments utilizing Appendix Q of the NIH Guidelines (Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals) require prior approval by the IBC.

The IBC shall include at least one (1) individual with expertise in human gene transfer when experiments utilizing Appendix M of the NIH Guidelines (Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Subjects).

The IBC shall also include at least one (1) individual with expertise in infectious diseases and/or molecular biology.

A Biological Safety Officer is mandatory and shall be a member of the IBC if the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research at BSL3, BSL4, or Large Scale (greater than 10 liters).

When the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human subjects, the institution must ensure that: (i) the IBC has adequate expertise and training (using ad hoc consultants as deemed necessary) and;

(ii) all aspects of Appendix M of the NIH Guidelines have been appropriately address by the PI; (iii) no research participant shall be enrolled in a human gene transfer experiment until the RAC review process has been completed; (iv) final IBC approval is granted only after the RAC review process has been completed.

Finally, the IBC includes representatives of all campuses from the University, as permitted.

No member of an IBC may be involved (except to provide information requested by the IBC) in the review or approval of a project in which he/she has been, currently is, or expects to be engaged or has a direct financial interest. **All IBC participants are required to sign a Conflict of Interest and Confidentiality contract annually.**

DUTIES

Duties

i. Review all protocols involving biological commodities, including assessment of the containment level required for the proposed use (Biosafety Level -- BSL) and assessment of the facilities, procedures, practices, training, and expertise of personnel involved in the research or instruction.
ii. Determine containment levels for certain experiments, as stipulated for experiments in which DNA from Human and Animal Pathogens (Risk Group 2, 3, 4 or Restricted Agents) is cloned into nonpathogenic archaea, prokaryotic or lower eukaryotic host-vector systems.
iii. Setting containment levels for experiments involving whole animals and/or plants.
iv. Periodically review biological commodities usage conducted at the institution to ensure compliance with the NIH, USDA and/or CDC guidelines.
v. Adopt emergency plans covering accidental spills and personnel contamination involving biological materials.
vi. Report any significant problems with or violations of the CDC-NIH guidelines and any significant accidents or illnesses to the Director of Research Compliance and NIH/ Office for Recombinant DNA Activities (ORDA) for r-DNA and PHS, CDC and USDA for other biological commodities.
vii. May authorize initiation of experiments that are not explicitly covered by the NIH, CDC or USDA Guidelines, until NIH, CDC, USDA or PHS, establishes the containment requirements.
viii. Identify members of the IBC to the OBA annually.
ix. Ensure appropriate training for the IBC Chair and members, the BSO, Principal Investigators (PI), and laboratory staff regarding this Policy, its implementation, and laboratory safety. Responsibility for training IBC members is carried out through the IBC Chair. Responsibility for training laboratory staff is carried out through the PI. The University of Hawaii is responsible for seeing that the PI has sufficient training.
x. Establish the level of medical surveillance for each project, if appropriate.
xi. Protocols receiving IBC approval may be subject to further administrative review by the DIO or by another officer of the University appointed to that purpose by the

President. This review may result in limitations and restrictions on the use of recombinant DNA, infectious agents, or other biological commodities beyond that required by the IBC. In extreme cases, the use of recombinant DNA, infectious agents or other biological commodities may be denied. Under no circumstances can the administration approve a project not approved by the IBC or ease any restrictions imposed by the IBC.

xii. Report at once to the DIO (Designated Institutional Official) suspensions of research activity, significant problems with or violations of this Policy, and any significant research-related accidents or illnesses.

xiii. Review suspensions of research activity ordered by the BSO and determine whether the activity shall: (a) proceeds without changes; (b) proceeds only with changes; or (c) terminate.

xiv. Perform additional functions as may be assigned to the IBC.

Section II-B. Terms and Officers

Full Voting Member - Full voting members are appointed by the Manager of the Animal Welfare and Biosafety Program and serve a three (3) year, renewable term.

Members must attend and vote in a minimum of seven (7) meetings in a calendar year, serve as subcommittee reviewers, and participate in a minimum of one (1) IBC inspection per calendar year. Hosting one's own lab inspection does not meet the requirement of participating in an inspection for the IBC. Members must notify the IBC Coordinator no later than seven (7) days prior to the scheduled meeting that they are unable to attend.
Members who are unable to meet the above requirements may be ineligible for renewal of their term of service or may be removed from the IBC prior to the end of their term of service.

Non-voting Members – Non-voting members are appointed by the Manager of the Animal Welfare and Biosafety Program for the Office of Research Compliance. They serve the IBC in an advisory capacity and count towards quorum.

Special Members – Special members are appointed by the Manager of the Animal Welfare and Biosafety Program for the Office of Research Compliance. Due to their specialization or expertise, they may serve the IBC in an advisory capacity, review applications, vote and count towards quorum, but are not adhered to the above requirements.

***Ad Hoc* Consultant** – *Ad Hoc* Consultants are appointed by the Manager of the Animal Welfare and Biosafety Program for the Office of Research Compliance for a three (3) year renewable term. *Ad Hoc* Consultants are not members. They will be called on to assist and vote only on specific issues for which they are consulted based on their area of expertise.

Chairperson – The IBC Chair is a full voting member and appointed by the Manager of the Animal Welfare and Biosafety Program for the Office of Research Compliance for a three (3) year, renewable term. During a meeting the IBC Chair is responsible for ensuring fairness and order. The duties and authority of the IBC Chair include, (i) preside over meetings, (ii) liaison between the PI and the IBC, and (iii) review and monitor IBC procedures.

Vice Chairperson – The Vice Chair is a full voting member and appointed by the Manager of the Animal Welfare and Biosafety Office for the Office of Research Compliance for a three (3) year renewable term and oversees the committee activities in the absence of the Chair.

IBC Coordinator – The IBC Coordinator is appointed by the Animal Welfare and Biosafety Program. Manager The duties include, (i) advising PIs on registration application preparation, (ii) coordinating and assigning registration application reviews to committee members, (iii) notifying PIs of the committee's comments and decisions regarding application review, (iv) coordinating facility/program/project inspections, (v) communicate with appropriate agencies and UH Designated Institutional Official regarding IBC matters, and (vi) coordinate the committee's monthly business meetings.

Director of Office of Research Compliance – The Director serves as a non-voting consultant of the IBC and oversees the committee activities in the absence of the Chair and Vice Chair.

Manager of Animal Welfare and Biosafety Program - Oversees, develops, and monitors the biological safety program covering all research projects involving human, animal, or plant tissues and pathogens.

Designated Institutional Official – The individual who has authority and responsibility for oversight and administration of the program.

Biological Safety Officer (BSO) – The Biological Safety Officer is voting member that serves the IBC in an advisory capacity and counts toward quorum.

Ex Officio – An *Ex Officio* is appointed by the Director for the Office of Research Compliance and is a nonvoting consultant that serves the IBC in an advisory capacity. The Director of EHSO is an *Ex Officio.*

Members may resign from their appointments by submitting a resignation letter to the IBC Chair. The notification should provide at least 3 months notice of their effective resignation and the letter should include names for their suggested replacement.
**It is understood that some unforeseen circumstances may not allow for a member to provide 3 months notice of their effective resignation.*

SECTION III. IBC MEETINGS AND MINUTES

Section III-A. IBC Meetings

The IBC convenes on the last Wednesday of every month unless otherwise indicated. Agenda topics include, but are not limited to:

- Approval of previous month's meeting minutes
- Old business related to the IBC
- New business related to the IBC
- Protocol review
- IBC related announcements
- Announcements for the next meeting

Submission deadline is typically on the 1st of each month.

Emergency Meetings – The IBC may conduct emergency meetings as needed and when a quorum can be attained.

Quorum – Quorum consists of more than 50% (50+1) of the combined total of full voting members and non-voting members, at least one of which must be a Non-Institutional (community) member.

Voting – Only full-voting members may vote on IBC related matters. For reasons other than conflict of interest, abstentions from voting will not alter the quorum number or the number of votes required. The results for the voting will be recorded in the meeting minutes with any comments and recommendations and will be communicated to the PI within five (5) business days of the meeting.

- A majority vote is more than 50% of the quorum votes.
- Abstention – A member has the right to abstain from voting.
- A member is obligated to abstain from voting if a Conflict of Interest, perceived or real, exists.

Conflict of Interest - No member of an IBC may be involved (except to provide information requested by the IBC) in the review or approval of a project in which he/she (i) has been, currently is, or expects to be engaged or (ii) has a direct financial interest. **All IBC participants are required to sign a Conflict of Interest and Confidentiality form annually.**

Any reviewer can choose to opt out of an assigned protocol review if he/she does not feel comfortable with the subject matter or feels there is a conflict of interest.

Non-IBC members and Visitors interested in attending an IBC meeting must obtain prior approval from the Director of ORC. Please submit requests with the following information to uhibc@hawaii.edu.

- Full Name

- Phone Number
- Email address
- Reason for attending

Comments or Questions from the general public will be reviewed by the IBC chair, Manager of the Animal Welfare and Biosafety Program, DORC, and IBC Coordinator before being presented to the full IBC. If public comments are made on IBC actions, the institution shall forward both the public comments and the IBC's response to:

Office of Biotechnology Activities
National Institutes of Health
6705 Rockledge Drive, Suite 750
MSC 7985
Bethesda, MD 20892-7985 (20817 for non-USPS mail)
Phone: (301) 496-9838
Fax: (301) 946-9839

Section III-B. IBC Meeting Minutes

Upon written request, the institution shall make available to the public all IBC meeting minutes and any documents submitted to or received from funding agencies, which the latter are required to make available to the public. If public comments are made on IBC actions, the institution shall forward both the public comments and the IBC's response to the Office of Biotechnology Activities, National Institutes of Health, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892-7985 (20817 for non-USPS mail), Phone: (301) 496-9838, Fax: (301) 946-9839.

Prior to public release, any proprietary and federally regulated information shall be redacted.

The cost of copies and the hours to process the request shall be charged back to the persons requesting the documents.

SECTION IV. PROJECT REGISTRATION AND REVIEW

Section IV-A. Project Registration

All protocol registration applications are due by the 1st of every month to uhibc@hawaii.edu. Incomplete applications will be returned for completion and not reviewed.

Application forms can be found at:

IBC Registration

Supporting documentation to submit with the registration to assist the IBC in providing an adequate review include (cradle to grave statements: acquired, expanded, treated, stored and destroyed):

- Equipment certification records (i.e. Biosafety Cabinet, Autoclave, Centrifuge, etc.). Include make and model no.
- Biosafety Staff Training Documentation (Date of Training, Name of Person being trained, Trainer, Description of training, how was training validated; test, visual, verbal)

  For more information on the biosafety training program and requirements, see Appendix D.
- Standard Lab Procedures (SOP) specific to the research activity of the regulated biological materials and its activities.
- Waste disposal (autoclave parameters: pressure, temperature, time and quality control) and decontamination procedures (type of disinfectant and concentration)
- Emergency Plans/Incident Response Plan (spill plan procedures, exposure control, contamination, sharps injuries, accidental release, etc.)
- Facility validation reports from outside agencies (required for BSL3 labs, insectary, GMP)

Applications received after the deadline of the 1st of the month will be held over until the next regularly scheduled meeting.

Only Principal Investigators may sign the registration application. Post-doctoral students and Junior Researchers may also sign the registration as long as there is a PI co-signing. Graduate students and staff are not authorized to sign the forms. Emeriti faculty may serve as Principal Investigators. (Only board appointees may serve as principal investigator for an externally funded contract or grant. In the context of this policy, adjunct faculty, research affiliates, and emeriti faculty in non-compensated University appointments may serve as PI).

Oversight of individuals engaged in research PIs and/or supervisors are responsible for the oversight of all students and/or individuals engaged in research under their direction, whether or not the University compensates the students and/or individuals. This responsibility extends to visiting scientists, trainees, postdoctoral appointees, graduate students, undergraduate student assistants, staff employees, pre-collegiate students, or participants in life-long learning or other special programs. The PI and/or supervisor must ensure requirements are met (See Board of Regent Policy, RP 12.202).

Responsibilities for researchers - Any such person engaged in research at UH understands and adheres to all applicable regulations, follows all University policies, and adheres to high ethical standards of honesty and integrity in research.

Absence is defined as a reasonable period wherein the PI does not fulfill the "physically present at the university at least 75% of the time" requirement of existing

IBC Policy.

Designation of PI herein is for the purposes of IBC and Biosafety Office purposes and does not imply other changes to authorities and responsibilities of the original signing PI.

TEMPORARY PRINCIPAL INVESTIGATOR

In the event of an absence of less than three months by the PI of an IBC registration (e.g. a 6-week medical leave where a complete return to duties is expected), a qualified faculty member should assume PI responsibilities relating to biosafety for the interim, without a formal change of PI noted on the existing IBC registration.

The Temporary PI should be designated by memo from the original signing PI, counter-signed by the new, Temporary PI and the division or department chair, and confirmed by a BSO as meeting the biosafety requirements of the signing PI. This Designation of the Temporary PI memo shall be attached to the prior-approved registration. The Designation of Temporary PI need not be reviewed by the IBC, unless requested by the BSO. Other modifications to the original registration (e.g.room changes, additional changes to personnel, modification of protocols, etc.) require IBC review following existing registration amendment procedures.

ACTING PRINCIPAL INVESTIGATOR

In the event of a leave of absence for 3 months or longer by the PI of an IBC registration (e.g. a year- long sabbatical in another country or to take another full-time position elsewhere "on leave"), a qualified on-campus Acting PI must be formally appointed by amendment to the prior-approved registration.

The Acting PI will assume all PI responsibilities relating to biosafety and biosecurity. Designation of an Acting PI requires submission of an amendment to the existing IBC registration, following existing policies and procedures. Both the original signing PI and proposed Acting PI should sign the application to amend the original IBC registration. A division or department chair should provide a memo supporting this transfer of responsibility. The amendment should include an expected return date of the original signing PI, where upon the role of PI reverts to the original signing PI. Confirmation of resumption of duty by the original signing PI should be made to the BSO.

Protocols expire three (3) years after the initial approval date. Expired registration can be extended for no-cost extension for 30 days (use of IBC Extension Form).

Approvals letters may only be signed by the Chair of the IBC or the Vice-Chair upon absence of the Chair.

Amendments - Any major or minor changes to the initial registration must be submitted to the IBC for review and approval. Examples include, but not limited to the following:

> **Major Changes -** Major changes require full IBC review. Examples include, but are not limited to, change of PI or changes in scope of research and/or procedures. Please submit a completed registration application, updated emergency/incident response plans, project specific procedures and updated training records and facility inspection reports. PI changes require submission of a current CV with emphasis with use of biological materials.
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> **Minor Changes -** Minor changes do not require full IBC review. Examples include, but are not limited to, staff changes, location changes, addition of transgenic mice strains (providing the project is already approved for transgenic animal work), addition of cell lines or other biological materials and/or title changes, which does not change the biosafety level or risk group. PIs submit an amended registration, updated training records, and facility inspection reports. The amendment can be approved by the IBC Chair.

Renewals - All active protocols are required to be renewed every three (3) years. Renewals require full IBC review. Submit a completed registration application, updated emergency/incident response plans, project specific procedures, staff addition and deletion, and updated training records and facility inspection reports.

Exempt- Protocols that are deemed "exempt" can be submitted using an Exempt IBC Registration form. This form notifies the Biosafety Program of use of biological material and items manipulated are not considered by Federal or State agencies as regulated.

Federal regulation and policy and UH IBC policy requires that active IBC protocols are required to be reviewed every three years. Notification of an upcoming expiration is sent to the PIs from the IBC at least one month prior to expiration as a courtesy. Failure to renew protocols on a triennial basis is considered a serious noncompliance. It is acknowledged that unforeseen circumstances may prevent triennial renewals of protocols to be submitted to the IBC for review prior to the protocol renewal deadline. In such situations, PIs may apply for a 30-day extension in order to complete the necessary electronic filing of a protocol renewal to keep the IBC protocol active. The request must be reasonably justified. The IBC Chairman/or Designee in consultation with a Regulatory Compliance Office official will determine whether the request is eligible for the extension.

Section IV-B. Projects That Require IBC Review

Research and/or storage of biological materials at the University of Hawaii involving any of the following, must be submitted tothe IBC for review and approval prior to initiation of the storage or research activity:

Recombinant and Synthetic Nucleic Acid Molecules – The NIH Guidelines defines it as:

(i) Molecules that (a) are constructed by joining nucleic acid molecules, or 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)

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

Select Agents and/or Toxins - Select agents and toxins are a subset of biological agents and toxins that the Departments of Health and Human Services (HHS) and Agriculture (USDA) have determined to have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products. A current list of select agents and toxins can also be found at: HHS and USDA Select Agents and Toxins 7CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73 (https://www.selectagents.gov/sat/list.htm)

Introduction or insertion of any piece of recombinant DNA/RNA, synthetic nucleic acid, infectious agent or toxin into another organism, plant or laboratory animal model.

Somatic Cell Experiments - Any recombinant DNA modifications to the somatic cells of non-transgenic animals are subject to the NIH Guidelines.

Infectious Agents Risk Group 2, Risk Group 3 and Risk Group 4.

Nanomaterials/Nanoparticles - Research involving materials less than 100 nanometers in diameter or technology in creating nanoparticles will require an IBC registration if used with recombinant DNA, biological materials, or when used with vertebrate animals.

Animal experiments (both invertebrate and vertebrate) - All laboratory animals housed at University of Hawaii animal facilities or use of wild animals. Research is conducted in BSL2 or higher containment regardless of the animal's minimum containment level requirement. Thus, research involving recombinant DNA and laboratory animals require IBC review and approval. Experiments include, but are not limited to:

1. Transgenic Animal Guidelines (See Appendix L)
2. Animals and their by-products that may naturally harbor zoonotic biological agents must follow the guidance provided in the Biosafetyin Microbiological Laboratories, 6th Edition (or latest publication). As a general rule, the biosafety level (facilities, practices and operational requirements) recommended for working with biological agents *in vivo* and *invitro* are comparable.

Note: Notification to Animal and Veterinary Services (AVS) - Animal Handlers must be informed of the risks associated with research involving recombinant DNA modified microorganisms used with animals. The AVS Director will be notified of any protocol registrations involving recombinant DNA and animal use. PIs must contact the AVS Operations Supervisor at least ten (10) business days prior to initiation of the activity.

Note: Purchase or Transfer of Transgenic Animals. Written notification to BSO can be forwarded via email to uhibc@hawaii.edu to determine what type of review is necessary. Include the information of the transgenic animals, the purpose of the project and the following information: 1) animal species and specific strain (Tg, KO, KI) 2), transgene sequence, 3) transgene function, 4) transgene source, 5) vector(s) used, 6) method of animal transformation, and 7) physical location of the laboratories and research animals at the University. **A minor amendment to the IBC must be submitted to include the changes. Pending BSO review and approval, the IBC Chair can approve the amendment in lieu of full IBC review.**

The PI should clearly indicate if the gene encodes a toxin or other hazardous agent.

Animal Waste Policy and Procedure. Appendix G-II-B-2-i and Appendix G-II-C-2-n require all wastes (including transgenic animal carcasses) from laboratories and animal rooms be appropriately decontaminated before disposal. Means of appropriate decontamination include autoclaving (waste) and tissue digestion (carcasses).

Human Gene Transfer Projects - The deliberate transfer into human research participants of either:

(1) Recombinant nucleic acid molecules, or DNA, or RNA derived from recombinant nucleic acid molecules, or
(2) Synthetic nucleic acid molecules or DNA, or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:
    (a) Contain more than 100 nucleotides; or
    (b) Possess biological properties that enable integration into the genome (e.g., *cis* elements involved in integration); or
    (c) Have the potential to replicate in a cell; or
    (d) Can be translated or transcribed.

Dual Use Research of Concern - - Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, material, or national security.

Research that involves one or more of the agents or toxins listed in the Agents and Toxins list below or is reasonably anticipated to produce one or more of the effects listed in the Categories of Experiments below:

1. <u>Agents and Toxins:</u>
    a. Avian influenza virus (highly pathogenic)
    b. *Bacillus anthracis*
    c. Botulinum neurotoxin

d. *Burkholderia mallei*
e. *Burkholderia pseudomallei*
f. Ebola virus
g. Foot-and-mouth disease virus
h. *Francisella tularensis*
i. Marburg virus
j. Reconstructed 1918 Influenza virus
k. Rinderpest virus
l. Toxin-producing strains of *Clostridium botulinum*
m. Variola major virus
n. Variola minor virus
o. *Yersinia pestis*

2. Categories of experiments:
   a. Enhances the harmful consequences of the agent or toxin;
   b. Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification;
   c. Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies;
   d. Increases the stability, transmissibility, or the ability to disseminate the agent or toxin;
   e. Alters the host range to tropism if the agent or toxin;
   f. Enhances the susceptibility of a host population to the agent or toxin; or
   g. Generates or reconstitutes an eradicated or extinct agent or toxin listed in the Agents and Toxins list above.

HUMAN EMBRYONIC STEM CELL (hESC) RESEARCH All research that involves the use of human stem cells, human embryos, or their derivatives, must be reviewed and approved by the appropriate oversight committee (e.g. IRB, IBC, and/or IACUC) and the Embryonic Stem Cell Research Oversight Committee (ESCRO) as appropriate. Review and approval must be prior to the commencement of the activity. Prior to the use of NIH funds, funding recipients should provide assurances when endorsing applications and progress reports submitted to NIH. Ensure that the hESCs are listed on the NIH registry.

Imported biological materials as defined under HDOA Plant and Non-Domestic Animal, Microorganisms Rules Hawaii Revised Statutes (HRS Section 70, 71, 71a and 72). Imported in to US as per CDC, USDA, and NWFS.

Section IV-C. Projects to be considered for exemption (Section III-F of the NIH

Guidelines)

The following experiments and/or storage of biological materials are considered exempt from the NIH Guidelines; however, otherfederal and state standards of biosafety may still apply to such research. If a project falls into one of the categories listed below, or does not meet the criteria described in Section IV-B above, that project may be considered for exemption. **Exempted under NIH does not mean does not require registration**. Contact Biosafety Program for help determining the classification of your usage/storage.

EXEMPT DOES NOT MEAN EXEMPT FROM REVIEW. Exempted projects are still required to adhere to the BMBL 6th Edition and all other UH, federal and state policies and requirements.

- Those synthetic nucleic acids that: 1) can neither replicate nor generate nucleic acids that can replicate in any living cell, and 2) are not designed to integrate into DNA, and 3) do not produce a toxin that is lethal for vertebrates at an LD50 of lessthan 100 nanograms per kilogram body weight.

- Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes.

- Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.

- Those that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means

- Those that consist entirely of nucleic acids from a eukaryotic host including its chloroplast, mitochondria, or plasmids (but excluding viruses) when propagated onlyin that host (or closely related strain of the same species).

- Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments maybe a synthetic equivalent.

- Those genomic DNA molecules that have acquired a transposable element provided the transposable element does not contain any recombinant and/or synthetic DNA.

- Those experiments that utilize preserved tissues, such as cadavers.

Section IV-D. Project Review Criteria

All protocols will be reviewed by 3 to 5 IBC members with expertise in the subject matter and the IBC Coordinator and presented to the full IBC at the next regularly convened meeting with recommendations based on, but not limited to, the following criteria:

- Assessment of the biosafety containment levels required by the NIH Guidelines for the proposed research.
- Assessment of the laboratory environment including adequacy of facilities, procedures, practices, training and expertise of personnel involved in the research activity.
- Assessment of biosafety risk assessment.
- Review of emergency plans relating to accidental spills and personnel contamination.
- Review to determine if a health surveillance program is necessary.
- Routes of exposure.
- Safety concerns due to the attributes of the materials (e.g., nanomaterials/nanoparticles).

Note: Protocols NIH r-DNA Classified as III-A, III-B and III-C must be submitted to Office of Biotechnology Activities (OBA) Recombinant DNA Advisory Committee (RAC) for review and cannot be approved by the IBC until RAC review is completed.

Transfer of recombinant DNA/RNA into human subjects (Human Gene Transfer)

Deliberate transfer of recombinant DNA, or DNA, RNA derived from recombinant DNA or synthetic nucleic acid into human subjects must be reviewed by OBA and the RAC. The IBC cannot approve the protocol until the RAC review is completed (Appendix M of the NIH Guidelines).

Protocols must be submitted to Office of Biotechnology Activities Recombinant DNA Advisory Committee for review and receive approval before the UH IBC can approve the protocol. PI requesting approval must submit an IBC registration, all laboratory procedures involved in the gene transfer activity, and a memo requesting OBA and RAC review to the IBC Executive Secretary via the UH IBC.

Chemical, Physical and Radiation Hazards

University of Hawaii's Environmental Health and Safety Offices (EHSO) (at the UH Cancer Center, College of Tropical Agriculture and Human Resources, UH Community Colleges, UH Hilo,John A. Burns School of Medicine, UH Mānoa, UH West Oahu) have oversight on hazardous chemicals and radioactive materials. Contact the respective campus EHSO for more information.

Section IV-E. Project Review Status

All protocols will be presented at the regularly convened meeting and the IBC full committee will vote on the outcome based on the criteria listed in UH IBC Working Policy Section IV-C Exemption Section. Possible outcomes include:

Approved - Research activities on the protocol may commence immediately. Protocol adequately meets all federal, state and local regulations and IBC policies. The protocol will expire three (3) years from the date of approval.

Not Approved - Research activities on the protocol cannot begin until additional information or clarification required by the committee has been reviewed and approved by the IBC Chair, Vice Chair or Designated Institutional Official. Information must be submitted within ten (10) days of notice or the protocol will be placed in disapprove status and the PI must re-submit for consideration.

Deferred - Research activity on the protocol cannot begin as the protocol has serious defects that require significant justification and review by the full committee. The protocol will be deferred until the information is provided. The protocol will require a full review once adequate information is provided.

Disapproved - Research activity on the protocol cannot begin and has been terminated because the IBC has determined the research activity cannot be conducted safely at the institution or for other reasons supplied. The protocol does not adequately address all requirements of the NIH Guidelines, BMBL and any federal or state regulations.

Withdrawn - Protocol has been withdrawn from consideration by the IBC, the PI or IBC Coordinator because modifications to the protocol are required.

Exempt - Research activities have been reviewed and categorized as being exempt through Section III-F of the NIH Guidelines. Exemptions are valid for three (3) years from the date of approval. Completed Exemption Forms can be approved by the Chair.

Appeal - An appeal must be in writing and addressed to the IBC. The appeal must be specific for the concerns addressed in the "not approved" or “deferred” memorandum. Appeals will be reviewed and a final decision will be rendered at the next scheduled IBC meeting.

Administrative Approval by BSO

The IBC has delegated authority to the BSO to approve minor administrative matters with notification to the full committee during the next regularly scheduled meeting. Minor matters include but are not limited to:

- IBC Registrations that are exempted from NIH Guidelines, that are classified

under III-F of the *NIH Guidelines*
- Minor amendments that do not affect the originally assigned biosafety level(s), risk group, or NIH classification(s)
- Addition of grant titles utilizing the same host/vector systems
- Non rsNA registrations
- Non-regulated biological material use

Section IV F. Violations of the Biosafety Guidelines

Existing Protocols

University policies, state and federal regulations require that all research involving biological materials have oversight by University of Hawaii's Institutional Biosafety Committee (IBC) and/or Biosafety Program. IBC oversight includes research, teaching and diagnostic activities that involve biological materials. The IBC defines biomaterials as

> "Biomaterials" include but are not limited to plants, animals, arthropods, invertebrates, insects, bacteria, viruses, parasites, fungi, oomycetes, mycoplasmas, RNA, recombinant DNA, prions, proteins, GMOs, cell lines [specify if transformed, immortalized], tissues (e.g., blood, lung), human specimens (sputum, urine, feces, tissue, swabs), non-human animal specimens, fetal calf serum, algae, protoclones and nematodes, weeds, biological control agents (including those not presently discovered or known to exist in Hawai'i) and "new" microorganisms identified as those "combining genetic material from organisms in different genera.".

Research activities involving biological materials must be reviewed and approved by the BSP or IBC prior to initiating the project.

Reporting Suspected Noncompliance

UH is committed to operating with integrity and in full compliance with all university policies, county, state laws, and federal regulations. Suspected compliance violations may be reported by Principal Investigators (PI), laboratory staff, support staff or the general public. UH provides a number of avenues to individuals reporting a suspected compliance violation involving biological related activities including to his or her supervisor, Human Resources, IBC Chair, Biosafety Officer, Director of Research Compliance, or the Vice President for Research and Integrity. Additional anonymous call can be reported to 285-7619 (whistleblower hotline).

Examples of Noncompliance

Noncompliance with university policies or federal regulations can be classified as serious, moderate, or minor. Serious violations are the result of willful and malicious violations of safety practices, federal regulations, or violations that pose a real or potential threat to individuals, the university, or the environment. Moderate violations include violations where

university policies were unclear and do not pose a threat to individuals, the university, or the environment. Minor is mostly administrative.
Examples of violations include:

- Failure to acquire the appropriate export, import or collection permits for applicable research activities (major).
- Failure to obtain IBC approval prior to initiating research that utilizes biohazard materials or to deviate from methods and procedures of an approved IBC protocol prior to approval (e.g., addition of biohazard materials or procedures that increase the risks of the research) (major).
- Failure to report any significant problems and/or violations of the NIH Guidelines, Select Agent Regulations, Federal and State regulations, or UH policies (major).
- Failure to report work related accidents/exposures and illnesses to the Biosafety Officer and IBC (major).
- Failure to comply with International Air Transport Association (IATA) and/or Department of Transportation (DOT) shipping or transport requirements for biohazard materials. (minor).
- Failure to instruct, train, and document training of personnel in the procedures and techniques consistent with safety practices and procedures for dealing with reporting accidents (moderate)
- Instances demonstrating that biohazard material was not appropriately contained, inactivated, or disposed of properly (major).
- Failure to demonstrate and document the correction of work errors and conditions that may have resulted in the release of biohazard materials (moderate).

The committee has authority to withdraw or suspend protocol approval in response to violations of the NIH Guidelines or UH biosafety policies and procedures:

In general, the PI is expected to implement corrective actions in a timely manner (upon notice of a deficiency). The OVPRI may also administer additional consequences, up to and including suspension of access to research funds, restrict entry into labs, etc.

Reinstatement of Suspended Protocols

A suspended protocol can be reinstated when the following occurs:

The IBC will discuss reinstatement at the next meeting following completion of the items above and a decision will be made about reinstating full approval of the protocol. The PI will receive a letter notifying as to the IBC's decision.

Unapproved Work Activities

If it is discovered that a PI is conducting work activities for which he/she is not approved, the IBC or BSO on behalf of the committee will notify the PI and require immediate submittal of a IBC registration for review by the IBC and suspension of work activities if the activities are subject to review by the committee prior to initiation. ORC

may also administer additional consequences, up to and including suspension of access to research funds, restrict access to laboratories, etc.

PROTOCOL FOR REMEDIATING NON-COMPLIANCE WITH BIOSAFETY GUIDELINES

In case of non-compliance with UH Biosafety Guidelines, the following actions will be taken:

a. Upon notification of a non-compliance incident, the BSO or delegate will:

   i. Contact the Principal Investigator (PI) by email, telephone and memo. This notification will outline the PI's responsibilities, instruct the PI of actions needed to remedy the non-compliance, advise the PI to take immediate action, and outline the risks associated with continued non-compliance. The PI will be given 7-10 working days to remedy the situation and will also be directed to suspend the work in question until compliance is achieved.

   ii. Contact and inform the IBC Chairperson, Manager of Animal Welfare and Biosafety Program, and the Director of Office of Research Compliance of the incident.

b. If 7-10 days pass and non-compliance persists, the BSO or delegate will:

   i. Send a second email to the PI, with copies going to the IBC Chairperson, the Department Chair or the Program Director, and the Director of ORC. This email will reiterate the PI's responsibilities and the risks associated with continued non-compliance, and outline the actions needed to remedy the non- compliance. At this point, the PI will be given an additional 7-10 days to comply or face immediate suspension.

   ii. Call the Department Chair or Program Director directly to solicit assistance in obtaining compliance.

c. On the 11th day following the previous notification of the incident, the following will occur if theissues of non-compliance have not been resolved:

   i. The BSO or delegate will inform the Director of ORC that the PI is still not in compliance.

   ii. The Director of ORC will send a final email notice of non-compliance to the PI, with copies going to the Department Chair/Program Director, the IBC Chairperson and the entire IBC committee, of immediate cease and desist.

d. If non-compliance is still not addressed at the end of this period, the following will

happen:

i. If the PI has a currently approved protocol, the IBC will take immediate action to cease all work under the protocol until compliance is achieved. A special meeting of the IBC will be called if necessary to execute this action.
ii. The ORC will take additional steps to ensure compliance from the PI or impose appropriate consequences, including suspension of funding.

SECTION V. INSPECTIONS/AUDITS AND VIOLATIONS

Section V-A. Why are we getting inspected?

Biosafety inspections and audits are conducted to meet federal, state, county government rules, regulations, statutes and university policy requirements.

These inspections and audits serve as an educational mechanism which allows institutional biosafety representatives and Institutional Biosafety Committee (IBC) members to provide person-to-person on-site training, to assist colleagues with government and granting agency expectations, and to meet industry standards (CDC, NIH, and OSHA) associated with laboratory biosafety principles and best practices.

Inspections and audits are intended to evaluate laboratory compliance with biosafety principles and to identify concerns or departures from best practices. The inspections also provide an opportunity for laboratory personnel to ask questions regarding issues related to biosafety matters related to research and teaching criteria.

All research, teaching, and clinical (diagnostic) laboratories using biologic materials in their programs will be inspected annually. The interval of the laboratory visits will be determined by risk assessment category and biosafety containment, the nature of the biological materials used, and whether external agency expectations (e.g., permits) require frequent monitoring.

This Policy affects the use of all relevant biological materials used by research, teaching, and clinical personnel associated with this university. Programs which are not clearly defined to be research, teaching and clinical may not be covered by this policy. This policy's application to institutional activities not defined as research, teaching or clinical will be determined by the biosafety program representatives in consultation with unit representatives and administration officials (e.g., DNA sequencing service).

Biosafety inspection criteria and standard operating procedures are further detailed in the Biosafety Program Description and Guidelines. (See Appendix B and Appendix C)

Security and Inventory of Biological Agents-Each PI must develop site-specific criteria that safeguard all biological materials, regardless of their risk group, from unauthorized

removal. It is the PI's responsibility to ensure that his or her laboratory and storage areas implements sufficient security measures and procedures to prevent unauthorized access to biological agents. A contingency emergency written plan must be generated.

The PI is responsible also to have an up-to-date biological materials inventory (UHLID B). A copy is required at the time of annual inspection.

Section V-B. Violations

Any purported or observed non-compliance will be investigated and documented in an inspection report. Each violation will be evaluated on a case-by-case basis and classified as either major or minor and subject to the following IBC action.

Major Violations

The PI will be notified to immediately cease and desist all research activities and a full investigation will be conducted. During such time, grant funding may be withheld or access to laboratory may be restricted. The PI's Department Chair and Dean will also receive copies of the notification. The IBC will inform all parties when research activates may recommence.

Situation details, investigation findings and corrective actions will be reported to all appropriate agencies no later than 30 days from the initial inspection report.

Minor Violations

First infraction/notice – The PI will receive a copy of the report which serves as the first notification of the violation. The report will contain the recommended corrective action and a deadline for completion. The lab will be required to undergo a follow-up inspection to verify that the violations were corrected. The PI and any lab personnel involved in the non-compliance will also have to complete a re-training session with the Animal Welfare and Biosafety Program (AWBP) Training Specialist.

Second infraction/notice – If the PI fails to complete the corrective actions within the given time frame, or is found to be non-compliant a second time, the IBC will issue the PI a second notice. The PI's supervisor will also receive a copy of the notification.

Third infraction/notice – If the PI still fails to complete the corrective actions, or is found to be non-compliant a third time, the IBC will issue a notification to cease and desist all research activities, access to laboratory will be restricted, etc. The situation may be reported to the appropriate agencies and grant funds may be withheld.

SECTION VI. MEDICAL SURVEILLANCE PLAN

Medical or Health Surveillance program may be required for some research activities and will be determined by the IBC with review of the OSHA, BMBL, USDA and CDC regulations. The purpose of a medical surveillance program is to assess the employee's/student's health to determine if any medical conditions associated with the biological agents exists and to potentially implement precautionary measures such as immunizations or specialized personal protective equipment, such as a respiratory.

The institution shall determine the necessity for health surveillance of personnel involved in connection with recombinant or synthetic nucleic acid molecule projects and infectious agents; and if appropriate, conduct a health surveillance program for such projects. The institution must establish and maintain a health surveillance program for personnel engaged in large-scale research or production activities involving viable organisms containing recombinant or synthetic nucleic acid molecules, which require BL3 containment.(NIH Guidelines Section IV-B-1-i)

The specific laboratory must establish and maintain a health surveillance program for personnel engaged in animal research involving viable recombinant or synthetic nucleic acid molecule-containing microorganisms and infectious agents that require BL3 or higher laboratory containment. (NIH Guidelines Section IV-B-1-i) Contact Animal and Veterinary Services.

The institution shall determine the necessity for a health surveillance program for research activities involving recombinant or synthetic nucleic acid molecules and/or infectious agents at a BSL2 or ABSL2 level.

The medical surveillance program shall include, but is not limited to, the following:

- A pre-screen physical or health screen described
- Description of each infectious agent the research activity will involve
- The signs and symptoms of an infection
- Description of the risks involved
- Description of the potential risks involved. (i.e. centrifuge tube breakage, PPE failure, spills)
- Mitigation efforts to minimize the risks (i.e. PPE, BSC, detailed procedures)
- Procedures in the event of a suspected laboratory acquired infection
- Emergency Contact Information for Physicians and Hospital
- Declination Statement if a staff/student elects to not enroll in the surveillance program.

Section VI A. MEDICAL SURVEILLANCE FOR WORKING WITH BIOLOGICAL MATERIALS

All employees in biological laboratories working with, or who may be exposed to, biological materials, including infectious agents, recombinant viral vectors, sensitizing agents must be aware of signs or symptoms consistent with diseases caused by these materials. In some cases, medical evaluations, vaccinations and/or other medical surveillance are required.

General Awareness. All employees in biological research laboratories must be aware of signs or symptoms consistent with diseases caused by the agents and materials present in their lab. For example, personnel working with recombinant lentiviral vectors should be aware of the signs and symptoms of human immunodeficiency virus (HIV) infection. Personnel exposed to these agents may or may not become sick; however, they may have the potential to transmit them to others outside the laboratory if proper biosafety practices have not been followed. Laboratory-specific training must include:

1. Hazard communication related to the risks of these agents

2. Anticipated signs/symptoms associated with these agents to facilitate recognition of potential occupational illnesses

3. Procedures to follow if a potential exposure has occurred

Medical surveillance must be undertaken prior to working with biological materials as designated by the Institutional Biosafety Committee (IBC). Examples include laboratories working with human pathogens, such as Hepatitis B virus, or with agents for which vaccination may offer protection, such as for *Salmonella typhi* (TS;Ty21a and Vi Capsular Polysaccharide). In addition, all personnel must be made aware by their supervisors that certain medical conditions increase their risk of potential health problems when working with pathogenic microorganisms, animals, and certain plants. These conditions include pregnancy (both male and female), immunosuppressant, animal related allergies, toxins, and chronic skin conditions. All personnel should discuss their work with their personal physician/health care professional if any of these conditions apply.

Certain types of work may require the use of a respirator to protect against aerosol exposures. In such cases, personnel must get medical clearance, fit-testing and training. Fit testing and training must be repeated on an annual basis or when there are physical changes or change in type of respirator.

Vaccinations. Personnel may be required by the IBC to be offered vaccinations to protect them from workplace hazards. Examples include the Hepatitis B vaccine for all workers with reasonable expectation of exposure to human blood or other potentially infectious materials (OPIM), which includes human and non-human primate cell lines, including those

acquired from commercial sources. Tdap vaccination, which is highly effective for the prevention of diphtheria, tetanus and pertussis, should be offered to personnel working with PT or handling animals dosed with PT. Protective vaccines, if available and appropriate based on workplace hazards, will be provided by employer at no cost to the employee. In most cases, if there is limited public health concern, employees may choose to decline the recommended vaccinations after understanding their risks. The employer is obligated to document the offer and obtain a signed declination by the employee that they understand the risks, yet chose to decline the vaccination. If the employee changes his/her mind, the vaccination will be made available to them
upon request.

Post Exposure Surveillance Exposures or potential exposures should be reported to the supervisor and the Biosafety Officer. In the event of a life-threatening event call 911 immediately. Exposed individual should self-quarantine and do two time temperature checks (as needed) and report these readings to your supervisor. The duration of reports and other unusual symptoms are determined by the physician. Employees must also follow the Incident Reporting Policy described in their laboratory Exposure Control Plan or Biosafety Manual. The medical professionals will determine the need for post-exposure prophylaxis, treatment, and continued medical surveillance at that time. Employees must notify the medical professionals if the agent involved is modified in any way to allow the medical professionals to treat the agent appropriately. The Principal Investigator (PI) or Biosafety Officer may be required to provide additional information about agent modifications and their potential effects on treatment. PI's should make available to all personnel post- exposure procedures for all agents used in the laboratory. IBC requires plans to address how a biological exposure incident to be developed by the PI: details must be incorporated into the laboratory IBC registration and should be part of the laboratory-specific exposure control plan and/or Biosafety Manual. This should include identification of any post- exposure prophylaxis options and/or medical monitoring plans for those who may have been exposed to the agents, documentation of important aspects of the experimental design and procedures, such as changes in drug sensitivity and/or genetic modifications, which may modify the risks of exposure of these agents. In the event of an exposure, it is recommended that laboratory personnel bring completed post exposure SOPs with them to the health care provider to ensure proper communication to those who may be providing care, particularly for agents that are genetically modified agents.

SECTION VII. EMERGENCY/INCIDENT RESPONSE PLAN (SECTION IV-B-2-b-(6) AND B-7-a-(6))

The IBC will adopt emergency plans and policies for research activities involving recombinant or synthetic nucleic acid molecule research for the following situations:

- Incident Report Form (Personnel contamination, Research related illnesses, Loss of containment, etc.…) (https://research.hawaii.edu/orc/wp-content/uploads/sites/6/2019/07/Biolab_Incident_Report_Form.pdf)

- Accidental spills (https://research.hawaii.edu/orc/wp-content/uploads/sites/6/2019/07/UH_SPILL_PLAN.pdf)
- Biohazardous waste disposal (https://research.hawaii.edu/orc/wp-content/uploads/sites/6/2019/07/UH_Bio_Waste_Guidelines.pdf)

These plans are made available to researchers conducting recombinant or synthetic nucleic acid molecule research at the University of Hawaii. PIs must have a current emergency response plan (spills and natural disaster) that is reviewed and understood by all research staff prior to beginning any approved research activity.

SECTION VIII. PROJECT/LABORATORY CLOSE OUT (Decommissioning)

Upon completion of a project, the PI must notify the IBC and include any decontamination and disposal procedures. The IBC lab decommissioning form can be found at http://manoa.hawaii.edu/policies/pdfs/M2.400-Laboratory-Decommissioning.pdf

The UH IBC adopts the UH Manoa EHSO procedures for decommissioning. Complete and proper laboratory decommissioning procedures can be found at http://manoa.hawaii.edu/policies/pdfs/ApprovedDecom031811.pdf

Note: If the project included any microbiological organisms, please contact the Biosafety Officer for further close out procedures. An approved BSP2 form is required for any movement, transfers and/or destruction of biological commodities.

SECTION IX. PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The Principal Investigator (PI) is responsible for full compliance with the NIH Guidelines, the University of Hawaii IBC Policy, other applicable University of Hawaii policies, and all Federal and State regulations pertaining to biological materials.

This policy applies to all research and teaching/training laboratories and facilities on all of the University of Hawaii campuses, including community college campuses, and Animal and Veterinary Services.

The IBC has the authority to investigate and to stop any previously approved ongoing research activity that does not comply with the requirements described in this policy.

The Principal Investigator shall:

- Submit all initial research protocol applications and any subsequent changes to the IBC for review and approval or disapproval using the current IBC registration form (https://research.hawaii.edu/orc/wp-content/uploads/sites/6/2019/07/IBC_registration_form.pdf). The PI must also remain in communication with the IBC throughout the conduct of the project.

- Make an initial determination of the required levels of physical and biological containment in accordance with the NIH Guidelines and select appropriate microbiological practices and laboratory techniques to be used for the research.

- Ensure that all aspects of Appendix M of the NIH Guidelines have been appropriately addressed prior to submission of a human gene transfer experiment to NIH OBA, and provide a letter signed by the PI(s), on institutional letterhead, acknowledging that the documentation being submitted to NIH OBA complies with the requirements set forth in Appendix M of the NIH Guidelines. No research participant shall be enrolled (see definition of enrollment in the General Definitions section) in a human gene transfer experiment until the RAC review process has been completed (Appendix M-I-B of the NIH Guidelines); IBC approval (from the clinical trial site) has been obtained; Committee for Human Studies (CHS) approval has been obtained; and all applicable regulatory authorization(s) have been obtained.

  For a clinical trial site that is added after the RAC review process, no research participant shall be enrolled at the clinical trial site until the following documentation has been submitted to NIH OBA: (1) IBC approval from the clinical trial site; (2) CHS approval; (3) CHS-approved informed consent document; (4) curriculum vitae of the PI(s) (no more than two pages in biographical sketch format); and (5) NIH grant number(s) if applicable.

- Adhere to IBC approved emergency plans for handling accidental spills and personnel contamination.

- Make available to all laboratory staff the protocols that describe the potential biohazards and the precaution to be taken as well as inform them of the reasonsand provisions for a precautionary medical practice advised or requested (e.g., vaccinations or serum collection).

- Be adequately trained in good microbiological techniques and supervise the safety performance of the laboratory staff to ensure that the required safety practices andtechniques are employed. This includes monitoring PPE compliance.

- Periodically instruct and train laboratory staff in: (i) the practices and techniques required to ensure safety, (ii) the procedures for dealing with accidents and adverseincidents, and (iii) good microbiological techniques.

- Keep written training documentation, which includes, but is not limited to, name of the staff member, date of training, description of the training, who provided the training, and how the training was validated (verbal/written quiz, proficiency demonstration etc.)

- Report any significant problems, violations, or research related accidents and illnesses to the Biological Safety Officer within 24 hours of the event.

- Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the Biological Safety Officer within 24 hours of the event.

- Correct work errors and conditions that may result in the release of recombinant or synthetic nucleic acid molecule materials, and ensure the integrity of the physical containment (e.g., BSCs and autoclaves) and the biological containment (e.g., purity and genotypic and phenotypic characteristics).

- Comply with all biological material transfer policies and requirements set forth by the UH Animal Welfare and Biosafety Program, NIH Guidelines, DOT, IATA, BMBL, HDOA, and USDA/APHIS.

Other Things PIs Should Consider

Securing an IBC approval does not automatically mean that the proposed research activity can begin immediately. There may be other important factors that need to be considered. It is the PI's responsibility to confirm that all applicable federal, state, local and institutional regulations, policies, and expectations have been met prior to commencement of the research activity. If applicable, PIs are also required to ensure that the following independent reviews, permits, approvals, certifications and/or licenses have been obtained before starting research activities:

- The UH Institutional Animal Care & Use Committee (IACUC) is required to review, approve and provide continuing oversight to research involving all live vertebrate animal use activities. The IACUC review is independent of IBC protocol review and approval. https://research.hawaii.edu/orc/programs/animal-welfare/institutional-animal-care-use-committee-iacuc/

- The UH Committee for Human Studies (CHS or IRB) is required to review, approve and provide continuing oversight to research involving human subjects. The CHS review is independent of IBC protocol review and approval. The three areas of CHS oversight are:
  1. Biomedical – projects involving clinical trials that evaluate investigational drugs and devices or medical procedures.
  2. Social and Behavioral Sciences – projects in the fields of psychological, education, sociology, etc., or that involve behavioral interventions.
  3. Cooperative – federally funded research that is performed by two (2) or more member of a cooperative of local institutions. Members of the cooperative include UH, Queen's Medical Center, Hawaii Pacific Health, and Castle Medical

Center.
For more information, visit https://research.hawaii.edu/orc/programs/human-studies/

- UH Animal and Veterinary Services (AVS) - After receiving IBC approval, the AVS Operations Supervisor must be notified at least ten (10) business days prior to initiation of any research activity involving recombinant or synthetic nucleic acid molecules in animals, transgenic animals, knockout animals, infectious agents or biological derived toxins with animals. For more information, visit https://research.hawaii.edu/orc/programs/animal-veterinary-services/.

- Select Agent Program - The College of Tropical Agriculture and Human Resources (CTAHR) provides oversight for the University of Hawaii Plant Select Agent Program. Select Agent Regulations (7 CFR Part 331) and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 require all persons who have access to, possession or use select agents or toxins to be registered with the Select Agent Program (USDA/APHIS or CDC).

- The Hawaii State Department of Agriculture (HDOA) requires importation permits for most biological commodities, including but not limited to, microorganisms and vertebrate/invertebrate animals. The HDOA may also require special permits for certain research procedures (e.g., when biological agents are administered or introduced to vertebrate animal species). Please note that the permit approval process may take several months to over a year due to processing, HDOA board review, scientific advisory reviews and in some cases environmental assessment. For more information, visit https://research.hawaii.edu/orc/programs/biological-safety/transport-authorizations/.

- The Hawaii State Department of Land and Natural Resources (DLNR), Division of Aquatic Resources (DAR) and Division of Forestry and Wildlife (DOFAW) may require special research, collection and/or access permits if work is to take place on state lands. See website for more information.
http://hawaii.gov/dlnr/dofaw/permit_info or
https://dlnr.hawaii.gov/dar/fishing/licenses-and-permits/.

- The Centers for Disease Control (CDC) may require an import permit for any infectious agent known or suspected to cause disease in humans. Visit the Centers for Disease Control Etiologic Agent Import Permit Program for more information.
http://www.cdc.gov/od/eaipp/

- A United States Department of Agriculture (USDA/APHIS) permit may be required for:
  1. Importation, interstate movement, or release of a genetically-engineered organism

2. Imported veterinary biological products
3. Plant and plant products imported into the United States
4. Transit through and interstate movement within the United States of plant pests and Biological control organisms of plant pets and weeds, parasitic plants, and federally-listed noxious weeds under regulatory authorities

Visit the USDA website for more information.
http://www.aphis.usda.gov/permits/index.shtml

SECTION X. UH IBC POLICIES

POLICY 1.0: Research Involving Recombinant or Synthetic Nucleic Acid Molecules
Effective Date: December 18, 2013

POLICY

All research at the University of Hawaii (UH) potentially involving recombinant or synthetic nucleic acid molecules and/or other infectious agents is subject to review by the IBC in accordance with the review standards contained in the NIH Guidelines.
Principal Investigators are responsible for:

- Submitting all documents and information required to apply for project approval and any subsequent changes;
- Complying with the NIH Guidelines and all applicable UH policies and procedures.

APPLICABILITY

This applies to all research conducted at UH potentially involving recombinant or synthetic nucleic acid molecules and/or other infectious agents.

PURPOSE

As a condition for NIH funding or recombinant or synthetic nucleic acid molecule research, UH is required to ensure that such research conducted or sponsored by UH, irrespective of the source of funding, shall comply with the NIH Guidelines.
Non-compliance may result in suspension, limitation, or termination of financial assistance for the noncompliant NIH-funded research project and of NIH funds for other recombinant or synthetic nucleic acid molecule research at UH.

DEFINITION

Recombinant/Synthetic Nucleic Acid Molecules:

1) Molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids;
2) 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
3) Molecules that result from the replication of those described in (1) or (2) above.

Infectious biological agent: A microorganism (including, but not limited to, bacteria (including rickettsia), viruses, fungi, or protozoa) or prion, whether naturally occurring, bioengineered, or artificial, or a component of such microorganism or prion that is capable of causing communicable disease in a human.

REFERENCES

Department of Health and Human Services, National Institute of Health, Office of Biotechnology Activities, *NIH*
Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

POLICY 2.0: Conflict of Interest
Effective Date: December 18, 2013

POLICY

No member of an IBC may be involved (except to provide information requested by the IBC) in the review or approval of a project in which he/she has been, currently is, or expects to be engaged or has a direct financial interest.

All IBC participants are required to sign a Conflict of Interest and Confidentiality form annually.

APPLICABILITY

This applies to all IBC Members, Ad-Hoc Consultants, Ex Officio Consultants, Biological Safety Officers, UH Biosafety Program Staff and the Assistant Vice Chancellor for Research Compliance.

PURPOSE

The purpose of this policy is to ensure compliance the membership and procedures requirements outlined in the *NIH Guidelines* and to ensure that every protocol reviewed by the IBC is done so through fair and unbiased proceedings.

REFERENCES

Department of Health and Human Services, National Institute of Health, Office of Biotechnology Activities, *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*, Section IV-B2-a-(4).

POLICY 3.0: Research Involving Human Clinical Samples
Effective Date: December 18, 2013

POLICY

Human clinical samples that fall under the OSHA Bloodborne Pathogens Universal Precautions Standard will be designated as Risk Group 2 unless it has been irradiated or chemically inactivated. In those cases, they can be designated as Risk Group 1.

The IBC reserves the right to raise or lower Risk Group classifications as deemed appropriate.

APPLICABILITY

This policy applies to all projects reviewed by the UH Institutional Biosafety Committee (IBC) that involve human clinical samples.

PURPOSE

To standardize the review and classification of projects involving human clinical samples.

DEFINITIONS

Bloodborne Pathogens: Pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to, hepatitis B virus (HBV) and human immunodeficiency virus (HIV).

Universal Precautions: An approach to infection control. According to the concept of Universal Precautions, all human blood and certain human body fluids are treated as if known to be infectious for HIV, HBV and other bloodborne pathogens.

Risk Group 1 (RG1): Agents that are not associated with disease in healthy adult humans.

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

Risk Group 3 (RG3): Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available.

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

REFERENCES

United States Department of Labor, Occupational Safety and Health Administration Standard 29 CFR Part 1910.1030.

Department of Health and Human Services, National Institute of Health, Office of Biotechnology Activities, *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*.

POLICY 4.0: Dual Use Research of Concern (DURC) Effective Date: December 18, 2013

POLICY

If a project is determined to be DURC, a risk mitigation plan will be required. The plan includes mitigation measures and procedures to implement them with the aim of minimizing the risk of misuse of the knowledge, information, products or technologies generated by the research.

If during the course of research, the research becomes DURC, the grantee is required to inform the NIH immediately of the change in DURC status and develop a risk mitigation plan as outlined above. Risk mitigation plans must be submitted to the appropriate NIH Grants Management Officer for administrative review and approval.

Projects suspected to have DURC potential may be periodically reviewed to monitor DURC status.

APPLICABILITY

This policy applies to research that involves one or more of 15 listed pathogens and toxins that are being used in projects with specified experimental aims that may result in research products, technology or information that could be misused to pose particular risks.

See Appendix A, "*United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern"*

PURPOSE

To implement the *United States (US) Government Policy for Oversight of Life Sciences Dual Use Research of Concern* which establishes federal review of US government funded or conducted research with certain high consequence pathogens and toxins for it potential to be DURC in order to mitigate risks where appropriate and collecting information needed to inform the development of an updated policy, as needed, for the oversight of DURC.

DEFINITIONS

Dual Use Research of Concern (DURC): DURC is defined as a life science research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

Life Science: pertains to living organisms (e.g. microbes, human beings, animals, and plants) and their products, including all disciplines and methodologies of biology such as aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, synthetic biology, environmental science, public health, modeling, engineering of living systems, and all applications of the biological sciences. The term is meant to encompass the diverse approaches for understanding life at the level of ecosystems, organisms, organs, tissues, cells, and molecules.

REFERENCES

United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern. *(Issued 3/29/2012)*

National Institute of Health Policy on Mitigating Risks of Life Sciences Dual Use Research of Concern. *(Notice Number NOT-OD-13-107, Released 8/28/2013)*

Notice of Clarification to NIH Policy on Mitigating Risks of Life Sciences Dual Use Research of Concern. *(Notice Number NOT-OD-13-110, Released 8/30/2013)*

APPENDIX A: United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (Issued March 29, 2012)

Section I: Purpose and Principles

1) The purpose of this Policy is to establish regular review of United States Government funded or conducted research with certain high-consequence pathogens and toxins for its potential to be dual use research of concern (DURC) in order to: (a) mitigate risks where appropriate; and (b) collect information needed to inform the development of an updated policy, as needed, for the oversight of DURC. The fundamental aim of this oversight is to preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.

2) This Policy complements existing United States Government regulations and policies governing the possession and handling of pathogens and toxins. Currently, the Select Agent Regulations ensure appropriate oversight of biosafety and biosecurity of the possession and handling of pathogens and toxins that have the potential to pose a severe threat to human, animal, or plant health, or to animal and plant products. In addition, recommendations from Federal advisory bodies, such as the National Science Advisory Board for Biosecurity (NSABB), have helped inform United States Government policies for identifying and managing DURC. This Policy will be updated, as needed, following domestic dialogue, engagement with our international partners, and input frominterested communities including scientists, national security officials, and global health specialists.

3) The following principles guide implementation of this Policy:
    a) Life sciences research is essential to the scientific advances that underpin improvements in the health and safety of the public, agricultural crops and other plants, animals, the environment, materiel, and national security. Despite its value and benefits, some research may provide knowledge, information, products, or technologies that could be misused for harmful purposes.
    b) Accordingly, some degree of Federal and institutional oversight of DURC is critical to reducing the risks to public health and safety, agricultural crops and other plants, animals, the environment, materiel, and national security.
    c) Measures that mitigate the risks of DURC should be applied, where appropriate, in a manner that minimizes, to the extent possible, adverse impact on legitimate research, is commensurate with the risk, includes flexible approaches that leverage existing processes, and endeavors to preserve and foster the benefits of research.
    d) The United States Government will facilitate the sharing of the results and products of life sciences research conducted or funded by United States Government agencies, and honor United States Government obligations within relevant international frameworks and agreements, while taking into account United States' national security interests.
    e) In executing this Policy, the United States Government will abide by and enforce all relevant Presidential Directives and Executive Orders, all applicable laws and

regulations, and support the implementation of legally binding treaties, commitments, and United Nations Security Council resolutions prohibiting the development and use of biological agents as weapons.

Section II: Definitions

1) For the purpose of this Policy, DURC is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security[1].

2) "Life sciences" pertains to living organisms (e.g., microbes, human beings, animals, and plants) and their products, including all disciplines and methodologies of biology such as aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, synthetic biology, environmental science, public health, modeling, engineering of living systems, and all applications of the biological sciences. The term is meant to encompass the diverse approaches for understanding life at the level of ecosystems, organisms, organs, tissues, cells, and molecules.

3) Extramural research is that which is funded by a department or agency under a grant, contract, cooperative agreement, or other agreement and not conducted directly by the department or agency.

4) Intramural research is research which is directly conducted by a department or agency.

Section III: Scope

Under this Policy, review will focus on research that involves one or more of the agents or toxins listed in Section (III.1) below, which pose the greatest risk of deliberate misuse with most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence, and produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in Section (III.2) below:

1) Agents and toxins[2]:
   a) Avian influenza virus (highly pathogenic)
   b) *Bacillus anthracis*
   c) Botulinum neurotoxin
   d) *Burkholderia mallei*
   e) *Burkholderia pseudomallei*
   f) Ebola virus
   g) Foot-and-mouth disease virus
   h) *Francisella tularensis*
   i) Marburg virus
   j) Reconstructed 1918 Influenza virus
   k) Rinderpest virus
   l) Toxin-producing strains of *Clostridium botulinum*

m) Variola major virus
n) Variola minor virus
o) *Yersinia pestis*

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[1]This definition of DURC is derived from the NSABB definition, but is modified for purposes of this Policy.
[2]These agents and toxins are regulated by the Select Agent Program under Federal Law (7 C.F.R. part 331, 9 C.F.R. part 121, and 42 C.F.R. part 73), and have the potential to pose a threat to human, animal, or plant health, or to animal and plant products.

2) Categories of experiments:
   a) Enhances the harmful consequences of the agent or toxin;
   b) Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification;
   c) Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies; d) Increases the stability, transmissibility, or the ability to disseminate the agent or toxin;
   e) Alters the host range or tropism of the agent or toxin;
   f) Enhances the susceptibility of a host population to the agent or toxin; or
   g) Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section (III.1) above.

Section IV: Department and Agency Responsibilities

Federal departments and agencies that conduct or fund life sciences research should implement the following actions:

a) Conduct a review to identify all current or proposed, unclassified intramural or extramural, life sciences research projects that fall within the scope of Section III. This review will include, at a minimum, initial proposals and any progress reports.
b) Determine which, if any, of the projects identified in Section (IV.l.a) meet the definition of DURC in Section (11.1) of this document.
c) Assess the risks and benefits of such projects, including how research methodologies may generate risks and/or whether open access to the knowledge, information, products, or technologies generates risk.
d) Based on the risk assessment, in collaboration with the institution or researcher, develop a risk mitigation plan to apply any necessary and appropriate risk mitigation measures. In addition:
   i) For DURC that is proposed and not yet funded, departments and agencies will assess whether to incorporate risk mitigation measures in the grant, contract, or agreement.
   ii) For currently funded DURC, funding departments and agencies will consider modifying the grant, contract, or agreement to incorporate risk mitigation measures. If such modifications are not possible or desirable, departments and agencies will seek voluntary implementation of mitigation measures by the institution.

e) A risk mitigation plan may include, but not be limited to, the following risk mitigation measures:
   i) Modifying the design or conduct of the research.
   ii) Applying specific or enhanced biosecurity or biosafety measures.
   iii) Evaluating existing evidence of medical counter measures (MCM) efficacy, or conducting experiments to determine MCM efficacy against agents or toxins resulting from DURC, and where effective MCM exist, including that information in publications. iv) Referring the institution to available DURC educational tools such as: http://oba.od.nih.gov/biosecurity/biosecuritv.html
   v) Regularly reviewing, at the institutional level, emerging research findings for additional DURC.
   vi) Requesting that institutions notify funding departments or agencies if additional DURC is identified, and propose modifications to the risk mitigation plan, as needed.
   vii) Determining the venue and mode of communication (addressing content, timing, and possibly the extent of distribution of the information) to communicate the research responsibly.
   viii) Reviewing annual progress reports from Principal Investigators to determine if DURC results have been generated, and if so, flagging them for institutional attention and applying potential mitigation measures as described above, as necessary.
   ix) If the risks posed by the research cannot be adequately mitigated with the measures above, Federal departments and agencies will determine whether it is appropriate to:

   (a) Request voluntary redaction of the research publications or communications [3]; (b) Classify the research:
      (i) In accordance with National Security Decision Directive/NSDD-189, departments and agencies will make classification determinations within the scope of their classification authorities and appropriate classification guidelines or may consult with other departments and agencies to make these determinations.
      (ii) Departments and agencies may consider whether to refer classified research to another department or agency for funding.

   (c) Not provide or terminate research funding.

2) Federal departments and agencies are requested to report the following to the Assistant to the President for Homeland Security and Counter terrorism:
   a) Within 60 days of issuance of this Policy, the following results of the review conducted in response to Section (IV.I.a):
      i) Aggregate number of current and proposed unclassified, intramural, and extramural research projects identified that include work with one or more of the agents and toxins in Section (III.1).
      ii) Aggregate number of current and proposed unclassified, intramural, and extramural research projects that include work with one or more of the agents and toxins in Section (III.1) and produces, aims to produce, or are reasonably anticipated to produce one or more of the effects listed in Section (III.2).

b) Within 90 days of issuance of this Policy, the following results of the review conducted in response to Sections (IV.l.b. c. and d):
   i) Number of unclassified current and proposed DURC projects.
   ii) Number of current projects identified as DURC through initial proposals versusprogress reports.
   iii) Summary of risks, mitigation measures already in place that address those risks, any additional mitigation measures that have been proposed or implemented, and number of projects to which each mitigation measure would be applied.

3) Following completion of the reporting requirements in Section (IV.2), Federal departments and agencies are requested to submit periodic reports on items in Section (IV.2.a. and b) biannually.
4) Federal departments and agencies should implement Section IV in accordance with their relevant and applicable authorities, regulations, and statutes.
5) For additional guidance on how to conduct the risk assessment identified in Section (IV.l.c), departments and agencies may refer to the "Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information," which identifies useful assessment tools and is available at: http://oba.od.nih.gov/biosecurity/biosecuritv documents.html

Actions taken to restrict the publication of technology may have implications under export control laws and regulations (e.g., 15 CFR parts 730-774 and 22 CFR parts 120-130). Report the number of projects by agent and/or toxin, plus the category of experiment.

Section V: Consultation

As necessary and appropriate, the United States Government will continue to consult with the NSABB (in compliance with provisions of the Federal Advisory Committee Act) or convene the Countering Biological Threats Interagency Policy Committee for guidance on matters relating to the review and conduct of DURC and the mitigation of DURC risks.

NIH Policy on Mitigating Risks of Life Sciences Dual Use Research of Concern

Notice Number: NOT-OD-13-107

Update: The following update relating to this announcement has been issued:
August 30, 2013 - See Notice NOT-OD-13-110. Notice of Clarification to NIH Policyon Mitigating Risks of Life Sciences Dual Use Research of Concern.

Release Date: August 28, 2013

Purpose

On March 29, 2012, the Federal government issued a policy for the oversight of life sciences "Dual Use Research of Concern" (DURC). The purpose of this Guide Notice is to implement the March 2012 policy establishing federal review of United States government funded or conducted research with certain high-consequence pathogens and toxins for its potential to be DURC in order to mitigate risks where appropriate and collecting information needed to inform the development of an updated policy, as needed, for the oversight of DURC.

Background

DURC is defined as life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security. Despite its value and benefits, some research may be misused for harmful purposes. The fundamental aim of this oversight policy is to preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.
The policy applies to research that involves one or more of 15 listed pathogens and toxins that are being used in projects with specified experimental aims that may result in research products, technology or information that could be misused to pose particular risks. The policy requires that Federal agencies continually monitor funded research for dual use research potential. When DURC is identified, Federal agencies are to work with the institutions and investigators conducting the research to develop an appropriate risk mitigation plan.

NIH Policy

If a project is determined to be DURC a risk mitigation plan will be required. In these instances, institutions, Project Directors, and Principal Investigators will develop a plan that includes mitigation measures and procedures to implement them with the aim of minimizing the risk of misuse of the knowledge, information, products, or technologies generated by the research. If during the course of the research, the research becomes DURC, the

grantee is required to inform the NIH immediately of the change in DURC status and develop a risk mitigation plan as outlined above. Risk mitigation plans must be submitted to the appropriate NIH Grants Management Officer for administrative review and approval. A copy of the full policy and other related information may be found at: http://oba.od.nih.gov/biosecurity/bio_usg_activities.html.

Implementation

NIH will conduct an administrative review of all current and future awards to determine if they involve research that could be considered DURC. If they do, a term of award will be added requiring the institution to submit a letter from the Institutional Biosafety Committee, or another appropriate review body, indicating its assessment of the DURC status of the research proposed, including the reason for its determination, and cosigned by the institutional official. If the institution determines that the research is DURC, an assessment of the risks and benefits of the research must also be included. If an institution determines that the research is not DURC, the IC will conduct a subsequent analysis and make a final determination.

If a final determination is made that research is DURC (either during the initial institutional review or during subsequent IC review), the institution must provide a proposed Risk Mitigation Plan within a time frame to be negotiated with the IC. The US Government Policy for Oversight of Life Sciences Dual Use Research of Concern
The following NIH and National Science Advisory Board for Biosecurity (NSABB) educational materials are available from the NIH Office of Biotechnology.

Website to assist in the development of these plans (http://oba.od.nih.gov/biosecurity/biosecurity_educational.html).

The institutional determination that research is DURC must be reassessed at least annually and the outcome included in the annual progress report. If the planned research is determined to be DURC, consistent with the U.S. Government policy and responsibility, NIH requests that grantees share with the Program Official for review any resulting manuscripts within at least 10 business days prior to planned journal submission. NIH also requests that grantees share with the Program Official any meeting Abstracts summarizing research activities supported by this grant that are intended for presentation at scientific conferences at least 10 business days prior to anticipated submission. The scope of the research and the level of support may be adjusted upon completion of all DURC assessments and the approved Risk Mitigation Plan. Failure to comply with the DURC policy and special award term and condition may result in an enforcement action as outlined in the NIH Grants Policy Statement Section
8.5, Special Award Conditions and Enforcement Actions" available at http://grants.nih.gov/grants/policy/nihgps_2012/nihgps_ch8.htm#_Toc271264977.

Inquiries

General inquiries about this Guide Notice should be directed to:

Office of Biotechnology Activities
Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892
Telephone: 301-496-9838
Fax: 301-496-9839
Email: oba@od.nih.gov

Inquiries regarding specific grant applications or projects should be directed to the assigned Program Official of the relevant
NIH Institute or Center.

Notice of Clarification to NIH Policy on Mitigating Risks of Life Sciences Dual Use Research of Concern

Notice Number: NOT-OD-13-110

Release Date: August 30, 2013

Related Announcements: NOT-OD-13-107

Purpose

The purpose of this notice is to clarify the NIH Policy on Mitigating Risks of Life Sciences Dual Use Research of Concern. The original Notice included language requiring the participation of "…the Institutional Biosafety Committee (IBC), or another appropriate review body…" in the institution's assessment of the DURC status of the research proposed. This incorrectly implied that institutions must now begin establishing institutional DURC review entities and conducting DURC reviews.

Instead, NIH is clarifying the Implementation section to read as follows:
“NIH will conduct an administrative review of all current and future awards to determine if they involve research that could be considered DURC. If NIH identifies a project that may be considered DURC, it will work collaboratively with the institution and grantee to develop a risk mitigation plan, which may be implemented through a term of award. NIH may request that institutions periodically review a project for its DURC potential and share any resulting manuscripts with their Program Official prior to submitting the manuscript to a journal.”

Inquiries

General inquiries about this Guide Notice should be directed to:

Office of Biotechnology Activities
Office of Science Policy
National Institutes of Health
Telephone: 301-496-9838
Fax: 301-496-9839
Email: oba@od.nih.gov

Inquiries regarding specific grant applications or projects should be directed to the assigned Program Official of the relevant NIH Institute or Center.

APPENDIX B: Institutional Biosafety Program Policy Statement- General Inspection and Audit Policy

I. Purpose

Biosafety inspections and audits are conducted to meet federal, state, county, government rules, regulations, statutes and university policy requirements.

These inspections and audits serve as an educational mechanism which allows institutional biosafety representatives and Institutional Biosafety Committee (IBC) members to provide person-to-person on-site training, to assist colleagues with government and granting agency expectations, and to meet industry standards (CDC, NIH, OSHA, and USDA) associated with laboratory biosafety principles and best practices.

Inspections and audits are intended to evaluate laboratory compliance with biosafety principles and to identify concerns or departures from best practices. The inspections also provide an opportunity for laboratory personnel to ask questions regarding issues related to biosafety matters related to research, teaching and clinical criteria.

II. Scope

All research, teaching, diagnostic laboratories using biological materials in their programs will be at minimum inspected annually. The interval of the laboratory visits will be determined by risk assessment category and biosafety containment, the nature of the biological materials used, and whether external agency expectations (e.g., permits) require frequent monitoring.

This guideline affects the use of all relevant biological materials used by research, teaching, and clinical personnel associated with this university's campuses, college, schools, educational centers and community colleges. Programs which are not clearly defined to be research, teaching and clinical may not be covered by this policy. Applicability of this policy to institutional activities not defined as research, teaching or clinical willbe determined by the biosafety program representatives in consultation with unit representatives and administration officials.

Biosafety inspection criteria and standard operating procedures are further detailed in the Biosafety Program Description and Guidelines.

The predominant criteria or industry standard, used in the inspections are referenced in the CDC-NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition, June 2020. Other guidelines may be referenced due to the specific nature of the laboratory activities. Laboratories (Table 1) or other facilities with multiple projects at different containment levels will be assessed at the higher risk assessment and containment level.

The Biosafety program inspection (Biosafety Program (BSP) of the Office of Research Compliance (ORC) is independent from Environmental Health and Safety office (EHSO) laboratory visits conducted by chemical safety, general laboratory safety, and radiation safety program representatives.

III. Description - Basic Elements

- Laboratories will be inspected by a representative of the Biosafety Program at least once annually.

- Inspection criteria will be based on the laboratory activities performed as related to risk assessment and biological containment as defined in Table 1 and described in the IBC registration.

  Members of the IBC will attend at least one-inspection per year. The BSO is encouraged to have at least one IBC voting member present at each lab inspection.

- Inspection reports, once approved by the IBC, will be forwarded to the Principal Investigator (PI). If IBC identifies concerns or departures from best practices; the PI is required to respond in writing within 5-7 days from the receipt of the inspection report explaining the timeline in which the infractions will be corrected.

- Re-inspections will occur within 30 days from the period when the correction of the infraction was corrected. If progress to correct the matter is unsatisfactory, a subsequent inspection report will be sent to the PI and the departmental level with an explanation that satisfactory corrective action is required. Outside agency (HDOA, HDOH, USDA, CDC) may require a shorter timeframe.

- IBC may impose additional corrective actions that could include additional or repeated training, more frequent follow-up, or other proactive measures.

- Principal Investigators documented with repeated infractions may be required to appear before the Institutional Biosafety Committee (IBC) to explain their departure from expectations and best practices. If the situation is not resolved, the IBC will refer the matter to the Office of Vice President for Research and Innovation for administrative action. Laboratories that fail to resolve the concerns of noncompliance may find their laboratory activities suspended indefinitely until the concerns are confirmed to be corrected.

- All Principal Investigators are responsible for maintaining safe laboratory working conditions by implementing internal safety self-inspections and follow-ups.

- Conduct self-risk assessments for activities that involve the use of biological materials (e.g., identify agent hazards, procedure hazards, routes of transmission, etc.). Self-assess whether containment facilities are appropriate for the designated experiments.

- Promote and implement the appropriate biosafety administrative policies, best practices, facility design, and safety equipment.

- Prevent the transmission of biological agents to personnel and the immediate laboratory environment

- Always comply with applicable federal, state, and local government rules regulations, and statutes, and institutional guidelines and policies.

Table 1 - Biosafety Regulations, Standards, and Guidelines

- U.S Federal Agencies (CDC, USDA, OSHA, EPA, DOI, DOJ, FBI, FDA, Commerce, Customs)
- Funding Agencies (NIH, NSF, or other external funding agencies),
- State of Hawaii (HDOA, HiOSH, DLNR, DOH, OHA)
- University or Institutional Requirements,
- Codes of Best Practice (Good Laboratory Practices)

Inspection Subject	Compliance Requirements	Reference
Use of biological materials	BMBL (CDC-NIH)	Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th EditionHS Publication No. (CDC) 21-1112. Revised June 2020. Code of Practice
Use of biological materials	OSHA General Duty Clause	15 USC § ; Duties of employers and employees
Use of biological derived toxins	BMBL (CDC-NIH)	Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th EditionHS Publication No. (CDC) 21-1112. Revised June 2020.
Blood borne (blood, tissues)	HiOSH/OSHA	Blood borne Pathogens and Needle stick Prevention 29 CFR 1910.1030
Importation of biologic	HDOA, CDC, USDA	Title 4, Hawaii Administrative Rules §70, 71, 71A HHS/CDC Foreign Quarantine Regulations; 42 CFR § 71.54
Recombinant and Synthetic Nucleic Acid	NIH	Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. Amendment Effective April 15, 2016, Federal Register, April 15, 2016 (81 FR 22286)
Select agents and toxins	CDC, USDA, DOJ	CDC Select Agents Regulations (42 CFR Part 73), APHIS Select Agents Regulations (7 CFR Part 331 and 9 CFR Part 121), Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act Of 2001 (USA PATRIOT Act)
Arthropods	ACG ASTMH	American Society of Tropical Medicine and Hygiene, Arthropod Containment Level, 3.2 Vector Borne Zoonotic Dis. 2019 Mar;19(3):152-173. doi: 10.1089/vbz.2018.2431. Epub 2019 Jan 29.
Large scale usage (>10 Liters)	BMBL (CDC-NIH)	American Society of Microbiology, Chapter 32 April 2017
Generation of biological wastes	DOH	Hawaii Administrative Rules, Title 11, Department of Health, Chapter 104.1, Management and Disposal of Infectious Wastes).
Plant pests, noxious weeds, CITES	USDA	Plant Protection Act 7 U.S.C. 7701 et seq.
Laboratory animals	BMBL (CDC-NIH)	Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th EditionHS Publication No. (CDC) 21-1112. Revised June 2020.
Greenhouse	Information System for Biotechnology	Practical Guide to Containment Plant Biosafety in Research Greenhouses Information System for Biotechnology 2008 Virginia Tech
Biological Safety Cabinet	NSF CDC, NIH	NSF International, /ANSI Standard 49, 2019 Primary Containment for Biohazards: Selection, Installation and Use of Biological safety Cabinets
Biosafety Competence	CDC	Guidelines for Biosafety Laboratory Competence MMWR 2011; 60(Supplement)
Laboratory Biorisk Standard	European Committee for Standardization (CEN)	**CWA 15793** Laboratory Biosafety and Biosecurity, CEN Workshop Agreementon Biorisks - CEN Workshop 31 Feb 2018
Biosafety Teaching Guidelines, Appendix and Home of DIY Microbiology Lab Kits.	American Society of Microbiology	Journal of Microbiology and Biology Education, 2019

Appendix C: Biosafety Inspection and Auditing Program Description and Guidelines

Purpose

The purpose of the biosafety inspection is to evaluate laboratories and facilities that conduct research, teaching, and clinical activities using biological materials, recombinant or synthetic nucleic acid molecules and other potentially hazardous biological materials. The inspections are required at minimum, annually. Risk assessment may dictate increase inspection from annually to semi-annual or quarterly. These inspections also provide a mechanism to improve biological safety awareness by keeping laboratory personnel apprised of regulatory changes. The site visits are required by federal, state, county requirements or university policies (Table 1).

Routine inspections are scheduled in advance and are conducted in the presence of the Principle Investigator (PI) or a lab designate to minimize the disruption of on-going laboratory activities. Unannounced inspections may occur as a result of filed complaints or an outside agency request.

The lab designee is usually appointed or assigned by the PI, and is someone who is knowledgeable of the activities being conducted in the laboratory (i.e., Laboratory Manager) and has the authority to represent the laboratory on the behalf of the PI.

At the conclusion of each inspection, an inspection report will be forwarded to the PI.

Scope

I. Authority and Responsibility

A. Biosafety Program is responsible for:

- Conducting periodic inspections and audits of all biological facilities: laboratory and support of research and non-research areas.
- Conducting follow-up evaluations of laboratory and support areas identified for re-inspections.
- Ceasing activities in which the current practices significantly deviate from good laboratory practices, industry standards and regulatory expectations and pose an immediate safety concern to faculty, staff, students and visitors.
- Contacting faculty, staff, students and visitors in the work area in circumstances where there is a significant biosafety concern.
- Organizing and leading an exit interview with the PI or designated safety contact following the evaluation of the inspected laboratory or facility.
- Providing laboratory and facility evaluations to the:

- o Principal investigator and IBC
- o Safety contact, upon request; and to the Facility manager in summary format

- Ensuring corrective action is implemented in a reasonable manner and timeframe for all documented concerns.

B. Laboratory Directors or Principal Investigators are responsible for:

- Complying with all aspects of a biosafety inspection and audit.

- Providing access to all areas and rooms which biological materials have been designated areas of their responsibility.

- Correcting work practices which deviate from acceptable biosafety good laboratory practices, industry standards and conflict with government regulations.

II. Types of Inspections

A. Start-Up/Preliminary

This is the consultation phase, which refers to moving into a new location. Reference is made to the general laboratory layout, which includes but is not limited to laboratory design, mechanical ventilation, location of biosafety cabinet and other containment equipment, security, and storage.

B. Initial

Upon initiating work on a Biosafety Level 2 (BSL2) or higher risk categories, the initial inspections will confirm the implementation of biosafety measures described in the project's Institutional Biosafety Committee (IBC) registration, the project proposal or the objective of the facility. The PI must correct all items that are determined to be of concern with the approved IBC registration.

A follow-up inspection is required with the Biosafety Program representative to confirm the concerns have been corrected, satisfactorily implemented and only then will the protocol be permitted to proceed.

The PI is required to work closely with biosafety program to ensure that adequate training has been provided to employees and students, containment equipment is working as designed and meets certification criterion as engineered, and the daily work practices are appropriate for the study described in the protocol.

Protocol amendments and initial inspections are required for additional new locations, agents, or methods are proposed.

C. Periodic (Annual, Semi-Annual, Triannual or Quarterly) Inspections and

Audits

Depending on the biosafety risk factors, biosafety inspections are usually conducted annually; however, some projects may warrant more frequent monitoring as a result of the risk assessment; nature of the study, facilities and biological material(s) used.

Inspections or audits will focus on the effectiveness of risk management systems to determine whether the program in place is satisfactory to government and industry expectations and standards.

Verification of program compliance is largely dependent on documentation of daily events and recording of procedures complimentary to IBC approved protocols.

D. Follow-up

A follow-up inspection is required to determine whether concerns have been satisfactorily resolved and corrected.

E. Closure of Laboratory /Decommissioning

Standard closeout procedures will be conducted by biosafety program representatives to ensure facility decontamination when faculty have retired or relocated to another study site (see UHM M2.400 Laboratory Decommissioning Policy, Attachment 4).

F. Incident (Adverse Event)

Biosafety program will conduct an inspection of the laboratory as part of the investigation in the event an accident or adverse event that involves the use of biological materials.
During the course of the inspection, the biosafety program representative should be educating the affected personnel on "best safety practices" in an effort to prevent recurrences of the reported incident.

G. Outside Agency

Regulatory agencies may inspect any University facility or operation at any time. These agencies include: FEDERAL – Centers for Disease Control and Prevention (CDC), US Department of Agriculture (USDA), National Institutes of Health (NIH), Occupational Safety and Health Administration (OSHA); STATE - Department of Health (DOH), Department of Agriculture (DOA), Department of Labor and Industrial Relations (DLIR), Hawaii Occupational Safety and Health (HIOSH); Department of Land and Natural Resources (DLNR), CITY AND COUNTY - Honolulu Fire Department (HFD), Honolulu Police Department (HPD), Board of Water Supply.
See Section VII.

H. Specialty

Non-laboratory areas (e.g., anterooms, storage, walk-in refrigerators) or use of non-

hazardous biological materials (e.g.; invertebrates) may have periodic or required inspections depending on the risk and nature of the biological material being used.

III. Biological Risk Groups (RG) and Definitions

A. Risk Group 1: Biological commodities in a biosafety level (BSL) 1 containment facility,

Laboratories meeting the basic requirements of a BSL-1 containment facility and usingRG-1 commodities will be inspected periodically, not necessarily annually.

B. Risk Group 1 or 2: Biological commodities in a BSL-2 containment facility

Projects restricted to a laboratory meeting the basic requirements of a BSL-2 containment facility or using RG-2 or RG-1 commodities will be inspected at a minimum annually.

The majority of laboratories at the University of Hawaii are in this risk group category.

Laboratories in this risk group manipulate biological materials of human, animal and plant origin, recombinant material, and imported biological material under permits.

C. Risk Group 3: Biological commodities in a BSL-3 containment facility

Projects utilizing RG-3 biological commodities will be inspected minimum annually. IBC members will be asked and encouraged to participate in annual inspections. The inspections will assess the operating status of biosafety cabinets (BSC) and HVAC HEPA filters to determine whether these units are functioning as engineered and are able to withstand accidents and emergencies. Outside agencies may be asked to join the inspection.

D. Risk Group 4

There is no BSL-4 containment facility at the University. No work with RG-4 commodities can be conducted.

E. BSL-Ag (Agricultural)

Use of plant or animal pest as it relates to agriculture practices and required by USDA.

F. Recombinant and Synthetic Nucleic Acid Activities (BL-N)

Laboratory assessment is required for recombinant or synthetic nucleic acid molecules that are regulated by the NIH guidelines. The Biosafety program will monitorr registered laboratories working at biosafety level 1 (BL1), level 2 and level 3 (BL3) facilities to ensure compliance with recombinant activities at minimum

annually (NIH Guidelines Section IV-B-2-b(1) and IV B-2 b-(5), Appendix G, K. P, and Q).

Recombinant activities experiment at biosafety level 3 (BL3/ABL3) will be inspected by an IBC appointed inspection team comprising of no less than two members of the IBC and a representative from the biosafety program.

BL3 laboratories are inspected, at minimum, annually by the IBC.

IV. Scheduling the Inspection:

An inspection or re-inspection may result from any of the following:

A. An inspection may be pre-arranged between the PI/lab staff and the BSO/IBC Coordinator/designate/IBC Member (initial, annual, periodic)

B. A PI may request an inspection

C. An inspection may be required as a submittal of a biosafety protocol registration

D. An inspection is required after a reported incident. (e.g., an accident/injury investigation, improper procedures).

E. Response to a complaint or issue

F. As a request by outside agency

Inspection criteria will be made available to the Principal Investigator or lab staff prior to the inspection.

V. Procedures

A. All biosafety facilities which manipulates regulated biological materials, including but not limited to, laboratories, vivarium procedure rooms, growth chamber, bioreactors/fermenters, greenhouses, instructional, clinical, and diagnostic spaces, animal housing, and field sites shall be reviewed in accordance with the procedures described below:

- Verify the use of personal protective equipment (PPE).
- Ensure the proper containment, safety equipment, and controls are present, utilized, tested, certified when appropriate, maintained, clean and decontaminated.
- Verify the availability of safety documentation, Pathogen Safety Data Sheets and Risk Assessment, laboratory specific biosafety standard operating

procedures (e.g., emergency, wastes, and occupational exposure) and all staff training records

- Verify records, including but not limited to training records, non-confidential,medical records, IBC registrations, biosafety manual, standard operating procedures.

- Verify the proper storage and biosecurity of biological materials.

- Verity the proper decontamination and disposal of biological materials and contaminated equipment and instruments. Including quality controls.

B Inspection process

- Pre-Inspection

  A review of the IBC registration or other pertinent documentation on the types of project or protocol is being conducted in the laboratory. Staff training records of the active users are reviewed.

- Notification

  PI is notified on date and time of inspection. IBC member(s) and/or ORC staff are invited to attend.

- Introduction or Opening Meeting:

  The purpose of the meeting is for the inspecting team (biosafety program representative and IBC members) to meet with key personnel from the facility to discuss the details of the inspection. The biosafety program representative will confirm the purpose and scope of the inspection. The PI or representative will explain the projects being conducted in the laboratory.

- Site Inspection:

  The purpose of the site inspection is to determine the degree to which operations are conducted in reference to the biosafety rules and regulations, industry standards, good laboratory practices and institutional policies. The biosafety program representative and accompanying IBC members will review documentation and records (SOP, training, equipment certification), and will visit laboratory facilities and areas that fall within the domain of the biosafety program oversight.

  During these activities the biosafety program representative may interview the personnel responsible for the activity or facility being inspected. Proficiency demonstration by lab staff of knowledge of contingency plans may take place. Any observations or concerns noted during the inspection will be discussed with the PI or laboratory representatives in person at the time.

- Summary or Closing Meeting:

  The purpose of the meeting is for the biosafety program representative to present a verbal summary of the inspection findings, and to allow the PI or laboratory representatives the opportunity to resolve misunderstandings, and to explain the conditions that may have led to presumed concerns or departures from standard laboratory practice. The inspector would use this meeting to describe the post inspection activities that may follow.

  Correction of concerns may be rectified at this time. Correction will be noted on the biosafety lab report as corrected.

- IBC and/or the Director of the ORC Animal Welfare and Biosafety Program will approve the biosafety laboratory report.

- A written report will be submitted to the PI within 30 business days post-inspection.

C. Definition of Concerns:

- Inspection findings are classified as critical, major or concern:

  - Critical Concern: A concern that indicates a significant risk

  - Major Concern: A concern that if not addressed immediately may lead to a facility, system or study being out of compliance.

  - Concern: A departure from the principles of best practices

D. Inspection Report

A preliminary inspection report will be sent to the PI within 30 business days regardless of whether matters of concern were identified or the laboratory was determined to be operating in full compliance. The report will provide written confirmation of any concerns reported verbally at the closing meeting. The PI is required to respond to matters raised during the inspection by providing details that include timelines of any corrective and remedial actions which have been implemented or are proposed, within 5-7 days. Reports are marked as, “Meets Expectations” or “Does Not Meet Expectations.” Reports as labeled as “not meet expectations is summarized as to what is not meeting expectations: training, administration, facilities, etc.

If a laboratory does not resolve matters of concern, the inspection results will be forwarded to the IBC for review. The committee will engage in communication with the PI until such time as the committee decides that a second (follow-up) inspection or alternate action (such as protocol suspension) is appropriate.

If the protocol is suspended, the committee will notify the Vice Chancellor for Office

of Research Compliance. The Office of Research Services will be notified for the purpose of informing any granting agencies that are providing support for the studies conducted in the laboratory.

VI. Corrections

- The usual timeline for correcting concerns and departures from best practices is 30 days, unless a time limit is agreed upon between the laboratory and the inspecting biosafety program representative who conducted the inspection. Outside agency may require a shorter corrective timeframe. A written report of correction must be forwarded within the established timeline to IBC.

- If the concerns are not corrected, the matter will be brought to the attention of the IBC, which may result in administrative action that leads to the possible suspension of the project or the cessation of all activities conducted in a laboratory.

- Experiments may continue only after the concerns have been corrected. A written report is required to be submitted to the IBC, and a follow-up inspection of the facility is required to determine whether the correction of the concerns or departures have been resolved satisfactorily, complies with the appropriate rules and regulations, and best practices or expected industry standards.

- Failure to comply with a "protocol suspension" from the IBC will be reported to the PI's departmental chair and the Office of Research Compliance for possible administrative action.

- The University is obligated to report institutional failures to correct concerns to city and county, state, federal and granting agencies whose jurisdiction is impacted.

VII. Appeals

Appeals must be in writing and addressed to the IBC Chair. The appeal must be specific for the concerns addressed in the Biosafety Inspection Report.

Appeals will be reviewed and a decision will be rendered at the next scheduled IBC meeting.

No work can be conducted under the protocol suspension until a full committee decision is rendered.

VIII. External Regulatory Agencies

- External regulatory agencies may conduct announced or unannounced inspections on University properties and/or to review components of the biosafety program in order to determine institutional compliance with government regulations pertaining to study personnel safety, health, and

environmental issues which fall within the jurisdiction of the biosafety program.

- It is important that a representative from Biosafety program accompany agents from external agencies on all inspections conducted on the University premises and to facilitate their site visits.

Recommended Procedures to Facilitate an External Agency Inspection:

- If you do not know the agency representative, you should ask the person for credentials. Acceptable identification is an agency badge and identification card with photograph.

- (Optional) Ask whether the agency representative has a warrant for the inspection or whether it is a routine scheduled agency visit. Do not demand a warrant; simply inquiry whether or not one exists.

- Before an inspection, the agency representative usually will conduct an opening conference, during which the agent will explain the nature of their assignment. Ask the agent to wait while you assemble the appropriate people for the opening conference.

- Ensure that all access requirements are followed, e.g., areas labeled for “Authorized Personnel Only” must not be entered unless everyone meets the entry requirements, i.e. Training, medical, PPE.

- Contact the Biosafety Program to inform them about the arrival of the agent. Do not begin the opening conference without a representative from biosafety program.

- After the opening conference, the agent will conduct a walk-around inspection. Biosafety program and department representatives are required to accompany the agent during the inspection.

- Be courteous. Do not argue or be rude to the agent.

- Answer any questions truthfully. Never articulate false statements or intentionally mislead an agent. If you do not know the answer to a question, explain that you are not certain and that you will look into the matter further, if necessary.

- Do not offer information unless asked for it. Do not talk about accidents or incidents that have occurred in the past unless specifically asked.

- Departmental and biosafety program representatives will discuss the findings and observations with the agent. Initial plans to resolve concerns and/or departures from best practices will be discussed. Politely ask for a written report.

- If the inspector(s) request pictures, approval must be obtained from an institutional official of the Office of Research Compliance. If the request is approved, and before the inspector's departure, make a written request for copies of all photographs and for an opportunity to make appropriate business confidentiality claims. Compile a list of all pictures taken.

- Notices of violation are required to be posted in the work area where the infraction was observed for a minimum of 5-7 business days.

- Monetary penalties incurred as a result of inspection infractions are the responsibility of the principal investigator/department for payment to the agency issuing the charges. It is advisable before paying money penalties to consult with a representative of the UH Legal Affairs and General Counsel.

IX. Liability for Noncompliance

- All NIH-funded and non-NIH-funded projects involving recombinant or synthetic nucleic acid molecules must comply with the NIH guidelines. Failure to comply and deviate from federal rules and regulations may result in the suspension, limitation, or termination of financial assistance for NIH-funded research projects. Repeated and/or multiple departures from the federal requirements and expectations may result in institutional forfeiture of receiving NIH funding for other recombinant DNA research conducted at this University.

  Redundancy in enforcement, just as in containment, is needed because individuals may unconsciously develop unsafe practices or fail to recognize unsafe conditions. For this reason, all PIs and other supervising personnel who oversee biohazard activities are expected to closely and prudently monitor the ongoing activities, laboratory work practices and condition of the subordinates. When departures from good laboratory practices are observed to have occurred, it is important to expeditiously correct any unsafe conditions before the matter worsens.

X. Reporting to IBC

The responsible biosafety program representative will present a summary of the inspections that were conducted after the last scheduled business meeting. Biosafety inspection reports will be approved by the IBC at their monthly committee meeting or by the AWBP Director.

XI. Inspection Subject Categories Related to Biological Activity-type

Table 2. Biological Activities Monitoring

Inspection Subject	**Start-Up**	**Initial**	**Periodic**	**Close-Out**	**Post-Monitoring**	**Incident**
Inspector:	**Biosafety**	**Biosafety**	**Biosafety**		**Team (Biosafety/IBC)**	**Team**
biological materials	●	●	●	●	●	
biological derived toxins or drugs	●	●	●	●		
bloodborne (blood, tissues, cell lines)	●	●	●	●		
Recombinant activities Exempt)	●	●	●	●	●	
Recombinant activities (nonexempt)	●			●	●	●
arthropods	●	●	●	●		
Large scale usage (>10 Liters)	●	●	●	●		
biological wastes	●		●	●		
plant pests, noxious weeds, CITES	●	●	●	●		
Vertebrate laboratory animals	●	●	●	●		
Growth chamber, greenhouse	●	●	●	●		
invertebrates	●	●	●			
field trial	●		●	●	●	

Appendix D: Biosafety Training Program Policy and Guidelines

Purpose

The University of Hawai‘i (UH) is committed to providing a safe and healthy work environment for those who work in research and academic laboratory settings. The use of Biological materials in these settings has increased greatly withthe advent of newer technologies, more sophisticated techniques and increased fundingopportunities. With these newer innovations comes the need to better train and prepare these researchers and laboratory staff to be able to have the tools and understanding soas to provide a safe working environment in which to conduct biological research at the UH. This policy is to set forth a series of guidelines on the training requirements for any UH laboratory conducting research utilizing biological materials.

It covers a wide range of specialized trainings, which might be required for conducting research in the biomedical and biological laboratories some based on Federal, State and other oversight guidelines. These have specific requirements for training individuals who plan on working and conducting research with specific biological commodities.

Authority and Responsibilities

A. Biosafety Program is responsible for:

1. Providing the appropriate level of basic training through the Biosafety program (BP) to ensure that all personnel are provided basic safety training in the use of Biologicals when working within any of the University of Hawai‘i’s (UH) laboratories. Basic training provided include but are not limited to:

   General Biosafety training
   Bloodborne Pathogens and Safe Sharps
   Shipping & Receiving Biological Materials
   Select Agent training
   Biological Safety Cabinet Use
   Biological Awareness
   Bloodborne Pathogens Awareness
   Institutional Biosafety Committee training
   AVS staff basic biosafety trainings
   BSL3 or high containment lab trainings

   Both Initial and Refresher trainings are conducted and available through the Biosafety training programs.
   *Bloodborne Pathogens Training for non-research individuals is administered through EHSO.

   At minimum an individual must receive *General Biosafety training* within 10 working days upon commencement of work in ANY UH laboratory that uses biological materials.

2. The Biosafety compliance program will monitor laboratories using Biological materials to ensure that there is an active and current training program in place for lab personnel with regard to the specific activities being conducted

in the lab. The magnitude and variety of research activities being conducted in UH biological laboratories make it difficult for the Biosafety program to monitor each lab and their research specific types of lab training needed. Verification that an active training program is in place which focuses on a lab's specific training needs will be in done in conjunction with the Biosafety program regular laboratory audits through documentation provided by each lab. Principal investigators are responsible for their staff and students and visitors with regards to this laboratory specific training and documentation.

3. Non-compliance of training requirements will be evaluated by Biosafety and the IBC. The IBC will prescribe administrative actions appropriate for the level of non-compliance and the AWBP will conduct follow up evaluations of remedial actions to ensure compliance.

B. Principal Investigator (PI) Responsibilities

1. The Principal Investor (PI) shall be responsible for ensuring that all staff, students and visitors working in their lab have the appropriate level of training in order to provide a safe working environment and to stay in compliance with Federal and State regulatory and institutional policy guidelines. Basic Biosafety training shall be completed and documented within 10 working days of commencement of any active work in the laboratory.

2. A PI and/or Director of any UH laboratory that is not actively working in the lab but is listed on any research protocol (IBC, IACUC, IRB) is still required to have Biosafety and/or Bloodborne Pathogens training and to keep that training current with UH guidelines.

3. PIs are responsible for making sure all staff, students and visitors are compliantwith regards to current and updated training needed for the lab to use biological materials.

4. PIs are responsible for ensuring that there is an active "lab specific" training program in place for their lab. This program will address all specific training in relation to the general research direction of the laboratory. These "lab specific" trainings will be documented and maintained in the laboratory Biosafety Manual. Verification of "lab specific" training will be done during normal inspections and audits of the lab by Biosafety program. Lab specific trainings should be reviewed and updated at least annually in order to remain compliant with current programs.

5. If working in an "Open Bay" style laboratory any PI working with Bloodborne pathogens is required to inform and notify those researchers in adjacent bays to the presence of BBPs and determine through a risk assessment based on the PI's research activities the need for these neighboring PI to undergo BBP training.

UH Training Programs - Descriptions

General Biological Safety Training

UH researchers, laboratory staff and students working with biological commodities are required to complete an initial training. Refresher training is then required annually and can be completed on-line.

General training covers UH policies regarding biological safety, principles of safe lab practices, appropriate storage, transport and disposal, and decontamination of biological substances used in research. Using Risk assessment…defined by CDC, BMBL 6TH Ed., "….as the process used to identify the hazardous characteristics of a known infectious or potentially infectious agent or material, the activities that can result in a person's exposure to an agent, the likelihood that such exposure will cause a LAI (Laboratory Acquired Infection), and the probable consequences of such an infection. The information identified by risk assessment will provide a guide for the selection of appropriate biosafety levels and microbiological practices, safety equipment, and facility safeguards that can prevent LAIs."

This training is geared for first time users of biological materials in a UH research laboratory and includes...

- Introduction to the UH Biosafety Program
- Biological Safety Levels (BSL)
- Personal Protective Equipment (PPE)
- Using the Biological Safety Cabinet
- Decontamination and Disinfection
- Dealing with Biological Spills
- Biological Waste Management
- Risk Assessment
- Record Keeping and Documentation
- PI responsibilities
- General overview of a Biological Safety Manual

Refresher trainings are required annually and provide the latestand up to date information on changes in biological safety requirements.

Understanding and comprehension of presented materials is evaluated via a quiz at the end of each training session.

Bloodborne Pathogens Standard and Safe Sharps Use Training

This is a required course designed for all University of Hawai'i research staff that may come into contact with human fluids and other biological materials including cell lines derived from human materials. It is also required of any research staff that use vertebrate animals in the course of their work. Bloodborne Pathogens training is not required of personnel who only work with preserved tissues and do not work in the same lab/open bay area with PIs who do work with bloodborne pathogens.

This training covers:

- Copy of the OSHA Bloodborne Pathogens Standard
- Epidemiology and symptoms of selected BBP
- HIV, HBV and HCV in the research lab
- Modes of transmission
- Hepatitis B vaccination and exposure control methods
- Site-specific exposure control plan
- Use of engineering, work practices and PPE
- Proper sharps handling and containment
- Proper waste management
- Hazard recognition and Risk assessment
- Question and answer session

Bloodborne pathogens training is required when there is an occupational exposure to blood or other potentially infectious materials OSHA 1910.1030(a).

Training is required if you work with or handle:

- Human blood products
- Human body fluids (including but not limited to, blood, semen, synovial fluid, amniotic fluid, CSF, pleural fluid, peritoneal fluid, pericardial fluid)
- Unfixed human tissue and organs
- Human cell lines, even if certified free of bloodborne pathogens
- Human organs or tissues
- Tissues or body fluids
- Hepatitis B virus or other bloodborne pathogens
- Enter or work in areas where other individuals work with any of the above materials where risk of exposure may occur.
- Vertebrate animals, their tissues or blood. This requirement has been added by the UH for researchers who utilize animals or animal products in their research.

NOTE: Non-lab personnel. *For Non-laboratory Faculty, Staff and Students; Bloodborne Pathogens training is provided by UH Environmental Health and Safety Office (EHSO) Occupational Health and Safety Program.*

Initial Bloodborne Pathogens training is required by OSHA to provide an opportunity for interactive questions with the instructor. It is provided online during regular business hours with access to the instructor. Refresher training is required annually and online.

Understanding and comprehension of presented materials is evaluated via a quiz at the end of each training session.

Transportation of Infectious and Biological Substances Training
This is a required course designed for University of Hawai‘i personnel who intend to transport and/or plan on receiving any Biological substances, ***Category A*** infectious substances, including Select Agents and Toxins.

This training has two sections:

1) Transport of Biological and Infectious Substance Transport Awareness.
Personnel who complete “Transport Awareness” training will be able to understand and be able to:

- Prepare biological materials for shipment
- Marking and Labeling of packages
- Prepare shipping documentation
- Accept/receive packages (Importation)
- Supervise the transport of packages

Training includes State of Hawai‘i Department of Agriculture (HDOA) Importation regulations overview, shipper’s responsibilities and provides necessary guidelines and references to ensure compliance with dangerous goods transportation.

Both Initial and refresher “Transport Awareness” training can be completed online. Refresher training is required annually.

2) Category A Infectious Substances Shipper, (includes Select Agents and Toxins)
Transfer of any Infectious Materials classified by the International Civil Aviation Organization (ICAO) and International Air Transport Association (IATA) as a **Category A**, Infectious Substance including select agents and toxins requires, first completion of “Transport Awareness” training **PLUS** an additional **Category A**, Infectious Substance training. Refresher training is required to be completed everytwo (2) years.

After completing these training programs, participants will be able to:

- Differentiate between a Category A, B or exempt substances
- Identify how to properly pack biological or infectious substances for transport
- Identify required markings/labeling on packages submitted for shipment
- List what must be on shipping papers (DGD) and when one is required.
- Explain the requirements for importing biological commodities into the State of Hawai‘i.
- Understand the different requirements and documentations as required by IATA, DOT, DOC, CDC, USDA- APHIS, and CFR regulations.

Understanding and comprehension of presented materials is evaluated via a quiz at the end of each training session.

Select Agent and Toxins

Initial and Annual training on current Select agent regulations, biosafety principles and practices, biosecurity, bio-containment and any other applicable Biosafety Compliance Program trainings are required for all researchers and staff enrolled in a University of Hawai‘i Select Agent Program. All applicable training must be completed prior to being granted access to Select agents and/or toxins. Retraining is mandated and required annually.

After completing this training program, participants will understand:

- ◻ Who should register with the UH Select Agent (SA) program
- ◻ Understanding all applicable Select Agent Regulations
- ◻ What the requirements are to be to participate in the program
- ◻ How to register with the UH Select Agent Program
- ◻ UH Select Agent Training

Understanding and comprehension of presented materials is evaluated via a quiz at the end of each training session.

Note: Access to the UH Select Agent Program Laulima site is restricted to researchers and staff preparing for enrollment and who are currently enrolled in a UH Select Agent Program

Understanding and Using the Biological Safety Cabinet.

This training provides an understanding of the basics of how Biological Safety Cabinets (BSC) works and how they protect the person, the material / product and the environment in a research lab.

After completing this presentation, participants will:

- ◻ Understand the basics of how the Biological Safety Cabinet (BSC) works
- ◻ How the BSC protects the **person**, the **material / product** and the **environment.**
- ◻ Be able to describe the basic differences between the 3 Classes of BSCs
- ◻ How they differ from the Chemical Fume hood and the Laminar Flow Clean Bench.
- ◻ Describe basic procedures for working safely and effectively in a BSC.
- ◻ Maintenance requirements, certification and alarms

- □ Understand the basic procedures for dealing with spills in the BSC

Understanding and comprehension of presented materials is evaluated via a quiz at the end of each training session.

Biological Training Mandates, Regulations and Guidelines

From the "Biosafety in Microbiological and Biomedical Laboratories" (BMBL) (NIH) 6th ed.:

- □ (**All BSLs 1-4**) Laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures.
- □ (**All BSLs 1-4**) The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. Personnel must receive annual updates or additional training when procedural or policy changes occur.

From the **NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.**
(Effective April 2019) (NIH Guidelines)**:**

- **Section IV-B-1-a**. Establish and implement policies that provide forthe safe conduct of recombinant DNA research and that ensure compliance with the NIH Guidelines.
- **Section IV-B-1-h**. Ensure appropriate training for the Institutional Biosafety Committee Chair and members, Biological Safety Officer and other containment experts (when applicable), Principal Investigators, and laboratory staff regarding laboratory safety and implementation of the NIH Guidelines. The Institutional Biosafety Committee Chair is responsible for ensuring that Institutional Biosafety Committee members are appropriately trained. The Principal Investigator is responsible for ensuring that laboratory staff are appropriately trained. The institution is responsible for ensuring that the Principal Investigator has sufficient training; however, this responsibility may be delegated to the Institutional Biosafety Committee.
- **Section IV-B-7-d-(2).** (Principal Investigator) Instruct and train laboratory staff in: (i) the practices and techniques required to ensure safety, and (ii) the procedures for dealing with accidents.

From **Bloodborne Pathogens 29 CFR 1910.1030 Occupational Safety and Health Administration (OSHA):**

- **1910.1030(g)(2)(i)** The employer shall train each employee with occupational exposure in accordance with the requirements of this section. Such training must be provided at no cost to the employee and during working hours. The employer shall institute a training program and ensure employee participation in the program.

- **1910.1030(g)(2)(i)** The employer shall train each employee with occupational exposure to bloodborne pathogens (including human cell lines and tissues) initially upon employment and annually thereafter.

From the **Bloodborne Pathogens §12 205.1 Hawai'i Occupational Safety and Health (HiOSH)**

(2)(i) Employers shall ensure that all employees with occupational exposure participate in a training program that must be provided at no cost to the employee and during working hours.

(2)(ii) Training shall be provided as follows:

(A) At the time of initial assignment to tasks where occupational exposure may take place;
(B) At least annually thereafter

(2)(iv) Annual training for all employees shall be provided within one year of their previous training.

(2)(v) Employers shall provide additional training when changes such as modification of tasks or procedures or institution of new tasks or procedures affect the
employee's occupational exposure. The additional training may be limited to addressing the new exposures created.

From **42 CFR 73 Select Agents and Toxins**:
An entity must provide training at the time of an individual's initial assignment to an area where Select Agents and Toxins are present and annual refresher training thereafter.

From **49 CFR 172.704 Shipping hazardous biological materials**:
Employees must receive general awareness and function specific training initially and every 3 years thereafter. (UH requires refresher training annually)

From **OSHA - 29 USC 654 (General Duty Clause)**

- Each employer – (1) shall furnish to each of his employees' employment and a place of employment which are free from recognized hazards that are causing orare likely to cause death or serious physical harm to his employees; (2) shall comply with occupational safety and health standards promulgatedunder this Act.

- Each employee shall comply with occupational safety and health standardsand all rules, regulations, and orders issued pursuant to this Act, which are applicable to his own actions and conduct.

Training Staff	General Biosafety	Bloodborne Pathogens	Biosafety Awareness	Shipping and Receiving Biologicals	BSC	SAP
Principal Investigator	X	D		D	O	D
Researcher	X	D		D	O	D
Student	X	D	X		O	D
Visitor	D	D	X	D	O	D
Teaching Assistant (TA)	D	D	X	D	O	
Working in SAP	X	X		X	X	X

Training Matrix

X=Required**; D**=Required but dependent on labs type of biological use**; O=**Optional;

SAP=Select Agent Program

APPENDIX E. BIOLOGICAL COMMODITIES: TRANSPORT,USE, AND POSSESSION (BSP2)

Transport of Biological Commodities may be regulated by international, federal, state and/or county regulations. A permit, license, or approval may be required for the transport and/or collection. All requests for the procurement or transport (transport, import, export) of biological commodities must be authorized by the Office of Research Compliance after completion of the Biological Commodities Transport Training. Items that may require authorization: 1) microorganisms or microbial products (products containing micro-organisms including Baker's yeast); 2) serum and like products (bovine, calf, sheep, etc.); 3) quality control kits; 4) reference strains; 5) proficiency testing kits (positive controls); 6) biotechnology kits (competent cells, cloning vectors); 7) recombinant DNA, RNA or other recombinant material; 8) tissue cells (animal, insects, plants, etc.); 9) bacteriophages, plasmids and other DNA/RNA particles; 10) nanoparticles; 11) native, threaten, CITES plant used for propagation and plants and plant parts (cutting, grafts, scion, bud, seed, leaf, root, etc.); 12) soil; 13) animals (invertebrates, amphibians, reptiles, fish, birds, and mammals); and 14) human products. The Authorization for Procurement Form, BSP-2, may be obtained from the Office of Research Compliance at:

https://research.hawaii.edu/orc/wp-content/uploads/sites/6/2019/07/BSP2.pdf

Additional Information can be found here:

https://research.hawaii.edu/orc/programs/biological-safety/transport-authorizations/ (from UH Administrative Policy A8.265)

The purpose of the BSP2 Form:

- **Movement** - The BSP2 form is used to document the movement of biological material (biologicals) within UH (e.g., Building to building). Movement can be the importation, exportation, or relocation of biologicals. Importing biologicals often requires permits from state or federal agencies.

- **Permits** - The BSP2 form is used to initiate the process of obtaining these permits. Whenever commercial or private carriers are used to transport biologicals, whether importing, exporting, or relocating, the carrier will require authorizations from UH.

- **Regulation** - Failure to provide this authorization can lead to severe state and federal penalties. The BSP2 form serves this purpose. A completed and signed BSP2 form must accompany each shipment. Non-authorized transport is not under UH auspices. Fines and penalties are the responsibility of the PI/Shipper.

- **Location** - Even if biologicals are moved from one location on campus to another, a BSP2 form must accompany the biologicals.

- **Accountability** - An important reason for this is so emergency personnel can respond appropriately should the biological be lost, stolen, or spilled or should you be incapacitated and cannot provide any information about the contents of the shipment.

APPENDIX F Laboratory Inventory Declaration (LID) of all biological agents (biological materials, select agents/DURC and biological derived toxins must be completed annually and submitted to ORC

Upon annual biosafety inspection a declaration of select agents and a biological materials inventory is due annually, at the time of annual biosafety inspection.

> "Biomaterials" include but are not limited to plants, animals, arthropods, invertebrates, insects, bacteria, viruses, parasites, fungi, oomycetes, mycoplasmas, RNA, recombinant DNA, prions, proteins, GMOs, cell lines [specify if transformed, immortalized], tissues (e.g., blood, lung), human specimens (sputum, urine, feces, tissue, swabs), non-human animal specimens, fetal calf serum, algae, protoclones and nematodes, weeds, biological control agents (including those not presently discovered or known to exist in Hawai'i) and "new" microorganisms identified as those "combining genetic material from organisms in different genera."

Inventory Form (Part 1 & 2):

- UH Laboratory Inventory Declaration Part A
- UH Laboratory Inventory Declaration Part B

Toxin Checklist Annual Exempt Quantities

The Principal Investigator (PI) must complete this checklist on an annual basis (upon annual biosafety inspection) to ensure your laboratory is meeting all institutional, CDC and USDA-APHIS-VS-Select Agent Programs and Dual Use Research of Concern (DURC) requirements for possession of toxins including exempt levels of Select Agent Biological Toxins. The PI is responsible for all documentation regarding inspections, including findings of deficiencies and corrective actions.

Please forward to Biosafety Safety Program, ORC (original signed copy only, no faxes). If you have further questions or need more information please call 956-3197 or e-mail at biosafe@hawaii.edu.

Principal Investigator Name (PRINT):_____

Department/Unit:_____**Bldg./Room No.**: _____

E-mail Address:_____**Telephone**_____

[ ] I have no biological derived toxin in this laboratory.

The following toxins are not regulated if the amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed, at any time, the amounts indicated in the table below.

HHS Toxins [§73.3(d)(7)]	Amount
Abrin	1000 mg
Botulinum neurotoxins	1 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	10,000 mg
Ricin	1000 mg
Saxitoxin	500 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	100 mg
T-2 toxin	10,000 mg
Tetrodotoxin	500 mg

Y	N	Toxin (circle above)
		Not Listed Above (not a select agent toxin): Complete below: Biological Toxin name:
		General Safety
		Inventory Verification
		1. PI has taken an inventory of each toxin listed below and verifies that the maximum quantity in their possession at this time (as of date recorded) does not exceed the maximum, exempt quantities. If toxin quantity exceeds quantity allowed, then PI is required to immediately contact the Responsible Official at the Biosafety Program Environmental Health and Safety Office at 956-3197 or biosafe@hawaii.edu
		1. Appropriate procedures are in place to ensure safe handling, storage, and disposal of toxins (I.e., written SOP)

		Approved Users/Training
		2. PI has reviewed and verified current list of approved handlers. Current Quantity:_____ Toxin_____ ______Date: _____
		3. All approved handlers have been provided site specific safety training on the biological derived toxin involved process and follow the SOP procedures (LIST STAFF)
		Storage/Physical Security Measures
		5. All biological derived toxins, especially select agent toxin have been properly labeled, with full chemical name.
		6. All Select Agent toxins are stored within a locked facility, within a lock room/cabinet
		7. A chemical hygiene plan is written
		8. A written security plan is in place:
		9. Briefly explain use of toxin:
		10. Use of toxin has been authorized by the IBC. IBC Authorization No. _____ [ ] Not applicable only storage
		11. The toxin is produced by viable agent(s). Please describe procedures
		12. Dilution procedures or other manipulation is done in a [ ] fume hood, [ ]biosafety cabinet or [ ] other: _____ _____
		13. How do you decontaminate and disposal:

Comments:

Declaration:

Signature:_____ _____Date:_____ _

Official Use:
Report No:
BSP-2 Form for import/transfer:
Toxin Completely destroyed: Witnessed by:
IBC Authorization No.: Date:

APPENDIX G: Service Animals in Facilities Overseen by the UH IBC

Version 12/12/18

Position

The following will apply to service animals (animals) as defined (Ref. 1) for facilities overseen by the University of Hawai‘i (UH) Institutional Biosafety Committee (IBC). Pets belonging to colleagues, contingent workers or visitors are discussed under separate policy, UH Mānoa M11.102 Animals on Campus (ref 5).

The IBC recognizes the important roles service animals play. However, there are health and safety concerns that animals may pose in laboratories (labs), as well as the potential risks and liabilities to colleagues that may be associated with these animals. These include, but not limited to, allergies affecting some individuals who may be sensitive to the proteins found in animal dander, skin flakes, saliva, and urine. Unlike people, who can wear appropriate Personal Protective Equipment (PPE), animals may have increased exposure to biological commodities in the lab, and could potentially transfer these commodities outside of the lab on their bodies. They may also inadvertently introduce biological commodities into the lab such as, but not limited to, fleas, ticks, other parasites, bacteria, and viruses. Rights of individuals need to be respected, and the presence of animals may also result in stress to some individuals who may feel threatened or be distracted by them. Though service dogs are usually well behaved in public, there is always the potential for them to attack other people and/or dogs, and/or be disruptive in their surroundings, and/or cause property damage, especially if they have not been appropriately screened for temperament and trained properly. Therefore,

- Service animals are not permitted in any laboratories/classrooms overseen by the IBC requiring BSL2 or ABSL2 or higher practices. This is based on the Center for Disease Control’s Biosafety in Microbiological and Biomedical Laboratories, 6th edition, which states:
    - BSL2 and higher Special Practices, “Animals and plants not associated with work being performed must not be permitted in the laboratory.”
    - ABSL2 and higher Standard Microbiological Practices, “Animals and plants not associated with the work being performed must not be permitted in the areas where infectious materials and/or animals are housed or manipulated.”
- If a student feels they cannot enter without the service animal and they are working in a BSL2 or higher lab, the instructor will provide an alternative learning experience.
- Requests for service animals, are restricted to service dogs entering ABSL1 or BSL1 or lower spaces, and will be handled on a case-by-case basis by the unit to

whom the request is made, if reasonable accommodations can be made. See process below.

- Service animals are not permitted in the biomedical and neuroscience vivarium. The welfare of the resident laboratory animals is of primary concern. This is based on the concerns described above. In addition, a service animal may cause additional stress to the resident animals by creating a predator-prey relationship. These become confounding factors affecting animal research in the vivarium.

Process

- Individuals requesting to use a service dog in an BSL1/ABSL1 Laboratories/classroom overseen by the IBC, complete form *Request to Use Service Dog in Labs/Classrooms Overseen by the IBC* (attached).

- When a request to use a service dog is entertained, only two questions may be asked of the requestor:

  - Is the dog a service animal required because of a disability?
  - What work, or task has the dog been trained to perform?

  We may NOT ask the requestor what their disability is nor to ask the dog to perform the task it is used for.

- Owners of the service dog are required to provide health, vaccination history of the dog, including current flea/tick control information from a veterinarian licenses in the United States of America (USA) by having them complete *Request to Use Service Dog in Labs/Classrooms Overseen by the IBC* form (attached). In some cases, the service dog may be required to undergo a “quarantine” period if they are to enter facilities using similar species present.

- Owners of a service dog are required to follow the guidelines described in University of Hawaiʻi at ā M11.102 Animals on Campus policy (Ref. 5).

- The Dean of the College to whom the individual reports will authorize the use of the service dog, in consultation with the Biosafety Program, is responsible for assisting with the interpretation and application of this policy and coordinating efforts with the Environmental Health and Safety Office, Animal and Veterinary Services Program, Institutional Animal Care and Use Committee, Office for Students with Disabilities (KOKUA), and other University groups.

- An individual requesting to use a service animal must acknowledge in writing that they understand the ADA rules and the State rules regarding service dogs, by reviewing the material found at University of Hawaiʻi at Mānoa, M11.102 Animals on Campus prepared by KOKUA Program.

- A dog that is not well behaved, not under control, destructive to its surroundings, or not potty trained, even if the individual claims it is a service dog, can be removed from the facility.

- In case of an emergency, service dogs may be asked to be removed from the premises for health and safety reasons.

- Individual sends completed form to the Biosafety Compliance Office, uhibc@Hawai'i.edu for review and approval prior to use of service dog in IBC overseen BSL1/ABSL1 laboratories.

Procedures:
Violations of this policy should be directed to the appropriate Dean, Director, or Department Chair.

Definitions and References

- Service Animal – The Americans with Disabilities Act (ADA) defines service animals as "dogs that are individually trained to do work or perform tasks for people with disabilities. Examples of such work or tasks include guiding people who are blind, alerting people who are deaf, pulling a wheelchair, alerting and protecting a person who is having a seizure, reminding a person with mental illness to take prescribed medications, calming a person with Post Traumatic Stress Disorder (PTSD) during an anxiety attack, or performing other duties. Service animals are working animals, not pets. The work or task a dog has been trained to provide must be directly related to the person's disability. Dogs whose sole function is to provide comfort or emotional support do not qualify as service animals under the ADA.

  The definition does not affect or limit the broader definition of "assistance animal" under the Fair Housing Act or the broader definition of "service animal" under the Air Carrier Access Act.

  Some State and local laws also define service animal more broadly than the ADA does. Information about such laws can be obtained from the State attorney general's office."

  See ADA Service Animals revised regulations published September 15, 2010. https://www.ada.gov/service_animals_2010.htm

- Hawai'i Revised Statutes §515-3 Chapter 10 Service Animals further defines http://health.Hawai'i.gov/dcab/ada-coordination/state-of-Hawai'i-ada-resources/programs-and-services-manual/chapter-10-service-animals/

- Hawai‘i Revised Statutes §347-2.5 Service dog, defined https://www.lawserver.com/law/state/Hawai‘i/hi-statutes/Hawai‘i_statutes_347-2-5

- Disability and Communication Access Board (DCAB) Programs and Services Manual, Excerpts from Chapter 2 General Nondiscrimination Requirements based onHawai‘i Revised Statutes, chapter 368. http://health.Hawai‘i.gov/dcab/ada- coordination/state-of-Hawai‘i-ada-resources/programs-and-services- manual/chapter-2-general-nondiscrimination-requirements/

- University of Hawai‘i at Mānoa, M11.102 Animals on Campus prepared by KOKUA Program.

  https://www.Hawai‘i.edu/kokua/access-services/service-or-assistance-animals.php

1. University of Hawai'i at Manoa, M11.102 Animals on Campus prepared byKOKUA Program.

   https://www.hawaii.edu/kokua/access-services/service-or-assistance-animals.php

Request to Use Service Dog in BSL1/ABSL1 Laboratories Overseen by the Institutional Biosafety Committee (IBC)

(revised 4/12/19)

Send completed form to the UH IBC at uhibc@hawaii.edu

Date of Request *(month/day/year)*: Start Date: End Date:

Name of Dog Sex: Male ☐ Female ☐ Neutered/Spayed? Yes ☐ No ☐

Description of Dog: Weight of dog (pounds):

Facility where dog will be used: Campus: Building: Room:

IBC Registration Number under which service dog will be used:

Type of Activity: Teaching Laboratory/Classroom ☐ Research Laboratory ☐

1. Is the dog a service animal required because of a disability as defined by the Americans with Disabilities Act? https://www.ada.gov/service_animals_2010.htm Check the box:

   Yes ☐ No ☐

2. What specialized work, or task has the dog been trained to perform? Provide a short description.

I acknowledge that I have read and will comply with the ADA rules and the Hawaii State rules regarding **service dogs**, based on the information found in Policy M11.102 Animals on Campus http://manoa.hawaii.edu/policies/pdfs/Animals_On_Campus.pdf

_____

Print Individual's Name Signature of Individual Date

Certification by a Veterinarian Licensed in the United States of America (USA):

I certify that the dog described above is current on vaccinations and flea/tick control, and is in good health to perform the tasks described above. Date next vaccinations are due _____

_____

Print Name of Veterinarian Signature of Veterinarian Date

Authorization by Principal Investigator (PI):

_____

Print Name of PI Signature of PI Date

Authorization by Dean of the College:

_____

Print Name of Dean Signature of Dean Date

APPENDIX H Minors in Laboratories

Purpose and Scope

UH provides educational opportunities to minors under the age of 18 and must ensure a safe environment for the students. Labs under the oversight of the UH IBC often come with risks and dangers that students and parents must understand and acknowledge. Restrictions are placed on minors in the labs.

Lab hazards may include chemicals, radioactive materials, biohazards, physical hazards, and hazardous equipment. Minors who are volunteering shall additionally comply with the UH policy A9.041 Utilization of Volunteer Services at UH. All minors performing work in a lab setting must be at least 16 years of age, officially approved, and part of an official sanctioned program. Official sanctioned programs include faculty sponsored, educational outreach tours, summer student internships, high school students working on science fair projects, volunteers seeking educational research experience.

Employees are not permitted to bring their children into a lab unless their children are participating in an officially sanctioned program or activity and meet requirements of this policy. Written consent of the minor's legal guardian is required as part of the approval process.

Under special circumstances, and only with written approval from the campus Dean, may a person under the age of 16 but over the age of 14, be allowed to work in the lab under the oversight of the UH IBC.

Visiting Minors

Visiting minors participating in a group tour shall have written consent of the responsible teacher and legal guardian, and each minor shall submit a completed UH Liability Release form. Visiting minors must be under direct supervision of a UH adult employee who is trained and knowledgeable of all the area's hazards. A visiting minor may be present in a lab solely as an observer, unless the person has met high school or minor laboratory worker requirements as specified in this policy.

During lab visits or tours, activities with potential to expose students to hazards shall be suspended.

Prior to allowing minors to tour or observe in a lab, the supervising employee must conduct a basic safety orientation, including both general safety information, hazards specific to the lab, and basic emergency response and evacuation.

Visiting minors will not be permitted into any animal facility, except with the specific written permission of the lab or animal facility director/designee.

High School or Minor Lab Workers

Before a high school student or minor may perform work in a lab overseen by the UH IBC:

The student must be sponsored by a UH faculty member. The sponsoring UH faculty member must complete the High School Student of Minor Lab Worker Agreement and Consent Form,

describing the work the student will perform and obtaining signatures from the Principal Investigator, Department Chair or Lab Director, and the direct supervisor of the student. The completed form is kept on file with the PI and the Dean of the College/Unit. A separate form is required for each officially, sponsored program a minor participates in.

The student and his/her legal guardian must review and sign the UH Liability Release form, also kept on file with the PI and the Dean.

The completed forms should be submitted at least 2 weeks prior to the start date.
The high school student or minor completes a Lab Personnel/Student Safety Checklist with the direct supervisor before initial assignment to the lab. A copy of the completed checklist is kept on file with the PI.

The high school student or minor receives specific training specific to the tasks and areas that the student will be working in, provided by the direct supervisor. The training shall be documented and filed with the PI.

The student or minor complete the following trainings, at minimum:

Initial Lab Safety Training (site specific)
Initial Biosafety Training
Initial Blood borne Pathogen and Sharps Hazard Prevention Training
Hazardous Waste Generator Training (site specific)

The high school student or minor must be under direct supervision in the lab at all times and trained by a knowledgeable, UH, adult employee. Direct supervision generally means being physically present, or within an immediate distance, and available to respond to the needs of someone immediately.

Minors are restricted from working with specific materials and from working in specific areas. For example, minors may not work with/in:

Labs designated Biosafety level 3 or higher
Labs designated Biosafety level 2 with Biosafety level 3 practices
Non-human primates
Select Agents
Human and non-human primate blood, body fluids, or tissues
Human and non-human primate retroviruses

General rules for minors performing work in the UH lab include:

- Never work in the lab environment without direct supervision from the PU/Mentor or designated supervisor.
- Never work alone handling potentially dangerous materials/ performing hazardous operations.
- Complete all safety trainings
- Always follow and obey rules
- Always use the personal protective equipment (PPE) as trained and dispose of it appropriately (i.e.: eye/face protection, gloves, coats/gowns, closed toe shoes)

- Always keep your hands away from your face and wash them well with soap and water after removing PPE and after exiting the lab.
- Do not touch your cell phone or other personal items with your gloves on.
- Never eat, drink, chew gum, apply lip balm or touch contact lenses while in the lab.
- Do not store food/drink items in the lab.
- Always wear closed toe shoes in the lab.
- Always tie back long hair.
- Always wear clothing that reduces the amount of exposed skin.
- Always report incidents (regardless of severity) immediately to the PI or supervisor.
- If an exposure occurs, wash immediately as trained and then report the incident.

Always ask questions if you do not understand the safety requirements.

Responsibilities

All UH employees have a continuing responsibility to ensure that a safe work environment exists for themselves, their co-workers, visitors and their guests.

Any employee who brings a minor to the lab must have necessary approvals as presented in this policy.

When notified that a minor will be in an area that a PI is responsible for, the PI shall conduct a risk assessment to determine if it is appropriate for the minor to enter. The PI shall inform the Lab Director or Chair of the assessment and if any safety concerns exist. PIs are responsible to ensure that employees who bring minors to the workplace are aware of the requirements of this policy and that proper approvals have been received.

PIs are responsible for adding any minors to IBC and/or IACUC protocols, as appropriate, and the minor's status must be disclosed.

Lab Directors and Department Chairs are responsible for determining if an area is safe for a minor to enter. He/She must provide written approval to the employee(s) requesting admittance of a minor to the lab or otherwise hazardous area. If the Lab Director/Department Chair has any safety concerns, the/she should contact the IBC.

MINOR & HIGH SCHOOL STUDENT LABORATORY WORKER AGREEMENT AND CONSENT FORM

- *This completed form should be turned in to the Department Chair or Laboratory Director at least two weeks prior to the start date or as soon as possible.*
- *A copy of the completed form will be kept on file with the Principal Investigator, HR, and the student.*

Name of the University of Hawaii Sponsored Program: _____

Principal Investigator_____

Email & Phone Number:_____

Faculty or Staff providing direct supervision:_____

Email & Phone Number: _____

Department/Unit:_____

Lab Location: _____

Name of the High School Student and/or Minor: _____

Birth Year:_____: Start Date:_End Date: _____

The student or minor is a:

☐ Student Intern ☐ Volunteer ☐ Other (specify): _____

Project title and description of role of minor (attach a separate sheet if necessary):

Description of work activities, including materials and equipment that will be used (attach a separate sheet if necessary):

**This form is not applicable to UH students registered for a course*

Chemicals – Check all categories to be used.

Category	
Flammable	☐
Reactive	☐
Carcinogenic	☐
Toxic	☐
Corrosive	☐
Oxidizer	☐
Cryogenic	☐
Pharmaceuticals	☐
Gases	☐
Other	☐ Specify:

Biological Material – Check all categories to be used.

Category	☐
Recombinant DNA	☐
Bacteria	☐
Viruses	☐
Fungi	☐
Parasites	☐
Human Source Material	☐
Insects	☐
Plants	☐
Animals	☐

Equipment – Check all equipment or processes to be used or encountered.

Category	☐
Fume Hood	☐
Biosafety Cabinet	☐
Laminar Clean Bench	☐
Autoclave	☐
Centrifuge	☐
Analytical Instruments	☐
Industrial Equipment	☐
Noise Producing Equipment	☐
Microtome or Other Histology Equipment	☐
Other	☐ Specify:

Training Required:

4. Initial Laboratory Safety Training (site specific)
5. Initial Biosafety Training
6. Initial Bloodborne Pathogen Standards and Sharps Hazard Prevention Training
7. Hazardous Waste Generator Training (site specific)
8. Task and Site-Specific Training (provided by the PI and/or Direct Supervisor)
9. Other Trainings (specify):

Potential Hazard Information

Professional Research Laboratories have inherent risks and hazards. When deciding to allow your child to participate in research conducted at a University of Hawaii Laboratory, it is important that you are aware of the potential hazards he or she may encounter. The following information is intended to provide an overview of what may be encountered, <u>but is by no means intended to identify all potential hazards.</u> You are encouraged to discuss any questions or concerns with your child's sponsor.

Your child's research activities may involve one or more of the following potential hazards.

	Definition	Hazards	Examples
Chemicals	Can be in the form of a solid, liquid or gas. These may or may not be hazardous. Some may have numerous hazard classifications (e.g. flammable, corrosive, and carcinogen). Potential injuries include skin and eye burns, respiratory problems, allergic reactions, skin, eye and mucous membrane irritation and illnesses.	Flammable: will burn or explode	Ethanol, Acetone, Xylene, Methanol
		Reactive: unstable and will self-react under certain conditions	Peroxides
		Carcinogenic: may cause some sort of cancer with long-term exposure	10% Formalin
		Toxic: may cause illness or death	Sodium Azide
		Corrosive: will cause tissue damage with contact through direct skin contact, eye contact, ingestion, inhalation	Acids and Bases
		Mutagenic: causes changes to DNA and RNA and can be inherited by offspring	Ethidium Bromide
		Cryogenic: extremely cold and can cause instant severe frostbite/burns	Liquid Nitrogen or Dry Ice
Biological Materials **Biohazards** **Human Sourced Materials (Blood, tissues, cells, etc.)** **Recombinant DNA**	Living organisms or products of living organisms such as viruses, bacterial, fungi, parasites. Hazards from infections with these materials are organism specific and can range from mild and treatable to severe and untreatable. Labs are assigned biosafety levels (BSL) 1, 2, or 3.	BSL1 - organisms are not known to consistently cause disease in healthy adults and present minimal potential hazard to researchers and the environment	Non-pathogenic strains of *E. coli*
		BSL2 – organisms pose moderate hazards to researchers and the environment. The organisms are typically indigenous and associated with diseases of varying severity.	*Staphylococcus aureus*
		BSL3 - organisms can be either indigenous or exotic, and they can cause serious or potentially lethal disease through respiratory transmission. Respiratory transmission is the inhalation route of exposure.	*Mycobacterium tuberculosis*, the bacteria that causes tuberculosis
Compressed Gases	High pressure cylinders that contain gases. Cylinders are usually large and heavy. Gases may be harmless, toxic, flammable, or corrosive.	Physical hazard - potentially explosive or a projectile hazard Asphyxiant – gas may displace oxygen in the atmosphere	Nitrogen, oxygen, carbon dioxide

Radioactive Materials	Certain labs are approved for small scale work with radioisotopes but *minors are generally prohibited from working with these materials or in areas approved for this type of work.*	Tissue and organ damage with high doses.	Phosphorous 32 (P32)
Other Hazards	Exposure to noise, machinery, sharps, heat, cold, trip and slip hazards, etc.	Tissue damage, hearing loss, cuts, burns, scrapes, slips, trips, and falls.	Autoclaves, centrifuges, sonicators, blades/scalpels, wet floors, glass and plastic sharp items, etc.

General Rules for High School Students or Minors Performing Work in a Laboratory

- Never work in any laboratory environment without direct supervision from the Principal Investigator (PI)/Mentor or designated Supervisor. Direct supervision generally means to be physically present, or within an immediate distance, such as on the same floor and wing within the building, and available to respond to the needs of something or someone immediately.
- Never work alone when handling hazardous materials or performing hazardous operations. A trained and knowledgeable, UH, adult employee must be physically present in the lab during these operations.
- Complete all safety trainings.
- Always follow the instructions and obey rules.
- Always use the personal protective equipment (PPE) as trained and dispose of it appropriately. Personal protective equipment includes, but is not limited to, eye and/or face protection, gloves, coats/gowns, closed toe shoes.
- Always keep your hands away from your face and wash them well with soap and water after removing your PPE and before leaving any laboratory area.
- Do not touch your cell phone or other personal items with your gloves on. Remove your gloves and wash your hands before touching personal items.
- Never eat, drink, chew gum, apply lip balm, or touch contact lenses while in any laboratory environment.
- Do not store food/drink items in the laboratory.
- Always wear closed-toe shoes while in any laboratory.
- Always tie back long hair.
- Always wear clothing that reduces the amount of exposed skin.
- Always report any accident (regardless of severity) immediately to the PI or Supervisor.
- If an exposure occurs, wash immediately as trained and then report the incident to your PI/Supervisor.
- Always ask questions if you don’t understand the safety requirements.

Principal Investigator's or Sponsor's Assurance

I have read, understand, and will adhere to the MINORS & HIGH SCHOOL STUDENTS IN LABORATORIES Guidelines. The information provided above is accurate. The activities involved in the proposed work or learning activities are activities permitted under these Guidelines. I will ensure that the above-named student/minor receives task and site-specific training, in addition to the other trainings listed above, and training completions are documented.

Personal protective equipment appropriates for and specific to the laboratory hazards will be provided. The above-named student/minor will also be trained in the proper use of personal protective equipment, as well as any other equipment the student/minor will work with. While in the laboratory, the above name student/minor will be supervised at all times by a UH, adult employee who is trained and knowledgeable in the operations and hazards of the laboratory. My laboratory is in full compliance with all applicable University of Hawaii safety programs and regulations.

Printed Name of PI/Sponsor Date Signature of PI/Sponsor Date

Student's/Minor's Assurance

I have read, understand, and will adhere to the MINORS & HIGH SCHOOL STUDENTS IN UH LABORATORIES Guidelines. Attached is the completed Assumption of Risk Form.

Printed Name of Student/Minor Date Signature of Student/Minor Date

Parent's/Legal Guardian's Assurance

I have read, understand, and will adhere to the MINORS & HIGH SCHOOL STUDENTS IN UH LABORATORIES Guidelines. Attached is the completed Assumption of Risk Form.

Printed Name of Parent/Legal Guardian Date Signature of Parent/Legal Guardian Date

Authorization

Dean of the College / Unit Signature Date

APPENDIX I: Non-UH Entity Fee Schedule[6]

Service Fees	Non-UH Entity[1]
IBC Protocol Review	$2,500/3 years[2]
IBC Protocol Renewal Review	$2,500/3 years[3]
IBC Annual Facility Inspection (Oahu only)	$250/inspection
IBC Annual Inspection Transportation (Oahu only)	$100/inspection
IBC Inspection Travel Related Expenses (Oahu excluded)	Non-UH Entity Pays in Full
BSP Post-Approval Monitoring Inspection (Oahu only)	$250/inspection
BSP Post-Approval Monitoring Inspection Transportation (Oahu only)	$100/inspection
BSP Post-Approval Monitoring Inspection (Oahu excluded)	Non-UH Entity Pays in Full
BSP Post-Approval Monitoring Inspection Travel Related Expenses (Oahu excluded)	Non-UH Entity Pays in Full
Service Fees	**UH Entity**
IBC Annual Facility Inspection (Oahu excluded)	UH Entity Pays in Full[4,5]
BSP Post-Approval Monitoring (Oahu excluded)	UH Entity Pays in Full[4,5]

[1] Subject to Memorandum of Agreement between the University of Hawaii, Office of Research Compliance and UH Biosafety Program and the Non-UH entity.

[2] The IBC Protocol Review covers any reviews and/or amendments per protocol for a 3-year period. The fee is due in advance of a protocol review.

[3] Upon conclusion of the 3-year protocol approval period, if the non-UH Entity intends to continue work at UH, a new Memorandum of Agreement and resubmission of a full IACUC protocol is required. The IBC Protocol Renewal Review is subject to the $2,500/3 years fee.

[4] Subject to commercial round trip airfare, ground transportation, parking, mileage, per diem and meals and incidental (M&IE) expense rates. Current allowable per diem and M&IE rates are established by law or applicable collective bargaining contracts.

[5] In the event it is determined that a UH Entity requires additional oversight due to facility and/or program deficiencies, the UH Entity shall be required to pay for additional inspections and/or expenses associated with the additional BSP Post-Approval Monitoring oversight.

[6] Service Fee Rates effective 1 July 2018.

APPENDIX J. Biological Research in Foreign Countries

All biological research receiving funding through UH but conducted outside of the US must be registered with the IBC and comply with any rules of the host country.

Institutional approval may be required from the collaborating institution. This approval must be attached to your UH IBC Registration. The IBC policies apply to all research personnel engaged in activities and/or research involving recombinant or synthetic nucleic acid molecules, biohazard agents, materials and toxins that are:

- Sponsored by the University.
- Conducted by University research personnel.
- Conducted using the University's property, and facilities.
- Received, stored, used, transferred or disposed of at any of the University facilities.
- Research at other institutions conducted on behalf of the University

If your research is being "conducted entirely outside of UH and/or the U.S", and no work will be done on the UH campus, review by UH's IBC may not be needed. However, institutional approval must be obtained from the collaborating institution. A copy must be forwarded to IBC.

Those investigators must submit their research protocol along with an application to an IBC for approval before their research can begin. The IBC monitors and provides continuing approval throughout a study.

For more information contact your representative from the Office of Research Services.

Permits and Transport

If biological collecting specimen, ensure that all government agencies scientific collection permits are obtained. If shipping specimen back to UH, ensure export requirements from the country and obtained import requirements from federal and state. Federal or state import permits may be required for live organisms, including infectious clinical specimens All IATA/DOT transport must be adhered with for transporting biological materials. .

Before engaging in an international collaboration, the University needs to determine if export licenses are required and to verify that the foreign individual and/or organization are not blocked or sanctioned entities. Please contact UH Export Control Program. If there are any need for contractual agreement, UH

Office of Innovation and Commercialization (MTA NOA or other MOU, LOI IOA Unfunded Research Agreements, etc. information.

U.S. Embargoes and Sanction Programs

The Office of Foreign Assets Control (OFAC) is responsible for enforcing all U.S. embargoes and sanction programs. Depending on each country's embargo or sanction program, different activities may or may not be prohibited without a specific government authorization or license.

Reference:

University of Hawaii Global Sponsored Activities Guide (24 March 2015).

Risk Management: Sponsored International Study, Research and Training Involving UHM Student, Faculty and Staff (UHM Administrative Policy M2.401 13 Jan 2010)

APPENDIX K: Working Alone

Working alone, especially after hours, can be unsafe and should be avoided whenever possible. When it cannot be avoided, procedures to protect lab workers in the event of an emergency situation must be used. The Principal Investigator (PI) has the responsibility to ensure the safety of all lab workers in their laboratory, and after conducting a hazard review, can approve laboratory staff to work alone. Guidance is provided to develop a lab specific safety protocol for working alone. This policy applies to all work with biological materials or hazardous equipment in research laboratories.

The requirements are:

High School Students: Prohibited. Never permitted to work alone in laboratories, even with non-hazardous materials. They must always have a mentor/supervisor present. Review the Minors in Labs policy for additional information. No buddy system can be implemented.

Undergraduate Students: Never can work alone with biological materials, equipment, or operations that can result in injury or disease without prior written approval from the immediate PI or supervisor. Someone else with Biosafety Program required safety training must be in the lab or adjacent to the lab and be able to check on their safety. A strict buddy system can be used.

Graduate Students, Postdoctoral Fellows, Research Scientists, Technicians and Principal Investigators: These are considered full time laboratory workers, and laboratory training is integral to their professional training. They are permitted to work alone in a research laboratory after approval by the PI and following the lab's buddy system procedures.

Clinical Students, including Medical Students, Residents and Clinical Fellows: Since their laboratory training is only a portion of their professional training and work intermittently in a lab and have minimal laboratory experience, are not permitted to work alone in a lab with hazardous materials. They must use the "buddy system". Lab workers in this category, who have previous laboratory experience or where the non-clinical education is the primary laboratory training and experience, are permitted to work alone in a research laboratory after approval by the PI and following the lab's safety protocol for working alone.

Animal Work: Working alone with *in vivo* biological materials with animals is prohibited.

Faculty, staff, students, and visitors who works with (or intends to work with) potentially biological materials that may result injury or infection, even risk group 1, must discuss this activity with their Principal Investigator (PI) or supervisor prior to conducting the work alone and determine that the risk of working alone is controllable under the specific conditions established by the PI or supervisor for the work. If the PI or supervisor determines that the risk cannot be minimized to a controllable level, then the individual should perform the work only when others are present or a suitable alarm device is available that will summon help immediately. PI, Faculty and Supervisor are responsible for all activities; this cannot be relegated to staff (APT, RCUH, or students).

Laboratories should establish specific guidelines and standard operating procedures specifying when working alone is not allowed and develop notification procedures when working alone occurs, recommend the buddy system.

> BUDDY SYSTEM: If a laboratory worker determines it is necessary to work alone, consideration should be given to notifying someone else in the area – in an adjacent room, another lab on the same floor, or a lab on a different floor. It is recommended that a "buddy system" be established for regular, routine checks on personnel working alone, such as every 15-30 minutes, to ensure that no accidents have occurred. This could be accomplished by physically walking to the room where the lab worker is or through the use of a phone. A system of visual checks should be established to indicate there are no problems or to determine if help is needed. The buddy must be knowledgeable of the procedure that is being done and aware of the emergency procedures and location of emergency equipment.

Please note: For rooms that are locked due to security needs, prior arrangements need to be made to allow the designated buddy access. Be aware that Emergency Responders may not always have access to locked doors – which could result in a delay in response in the event of an emergency. Also understand that if the door to the lab does not have a window, or if the window is covered, then there is a chance that if something happened to a person working alone in a locked lab, then they may not be discovered until someone else from the lab goes into the room (which could be an hour or more).

Reference

CDC Morbidity and Mortality Weekly Report Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. 6 January 2012 61(01); 1-101.

- Working alone in the laboratory.
  No inherent biologic danger exists to a person working alone in the laboratory; however, the supervisor is responsible for knowing if and when a person is assigned to work alone. Because assigning a person to work alone is a facility-specific decision, a risk assessment should be conducted that accounts for all safety considerations, including type of work, physical safety, laboratory security, emergency response, potential exposure or injury, and other laboratory-specific issues.

APPENDIX L Transgenic Animal Use Guidelines

(revised November 2021)

Purpose

The purpose of this policy is to describe the UH Institutional Biosafety Committee (IBC) review and approval procedures required for all research or teaching activities that involve animals (vertebrate or invertebrate) in which the animal's genome will be altered by introduction of recombinant DNA or synthetic nucleic acid molecules into the germ-line (generation of transgenic animals).

Introduction

This policy refers to all research and instructional activities that involve whole genetically engineered (genetically modified, transgenic) animals (Tg). This includes any animal in which the genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids into the germ-line. This also includes the breeding, crossing and generation of genetically engineered (Tg) animals, including those referred typically as knock-in and knock-out.

Gene 'knock-in' experiments involving genes that are either exogenous to the wild-type rodent species or derived from any viral or prokaryotic genome that encodes a virulence factor, protein or toxin would trigger the submission of an IBC registration

This policy describes Principal Investigator (PI) responsibilities, institutional review and approval procedures, and animals' containment and disposal procedures required for all research or teaching activities involving animals in which the animal's genome will be altered by introduction of recombinant DNA or synthetic nucleic acid into the germ-line (production of transgenic, knock-out and knock -in animals)

Scope

Principle Investigators (PI) are required to be in compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules (https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf) and all applicable University policies. Research (with or without grant funding) and teaching activities that are conducted with the goal of producing transgenic animals using rDNA technologies must be reviewed and approved by the Institutional Biosafety Committee (IBC). Methods for transgenic animal production include DNA microinjection, retrovirus-mediated gene transfer, embryonic stem cell mediated gene transfer, CRISPR, Cre-Lox, and any new methods that develop in the future. IBC review and approval are required for transgenic animal breeding.

This policy defines animals as all organisms in the Kingdom Animalia. The policy applies to vertebrates, invertebrates, insects and all other members of the animal kingdom.

This policy applies to all PIs and University of Hawaii personnel at all campuses. Private companies operating in University facilities are expected to comply with the same standards and procedures as the University research community.

All vertebrate animal work must also be approved by the Institutional Animal Care and Use Committee (IACUC), unless the activity is deemed exempt, prior to study initiation.

Importation and use into Hawaii may require permits (US Dept. of Agriculture, Fish and Wildlife (NFWS), and/or Hawaii Department of Agriculture) and adherence to U.S. Department of Transportation requirements.

IACUC (for vertebrate animals only) and IBC registrations should be submitted and reviewed concurrently. Approval is required from both compliance committees; otherwise the activities are not permitted to commence.

The purchase or transfer of commercial whole transgenic rodents may be exempt from IBC review under the NIH Guidelines [Section III-D-4-c (2) and Appendix C-VII]; however, the PI must submit a minor amendment to his/her IBC registration.

Transgenic rodent breeding programs may or may not be exempt. Any unexpected pattern of adverse births, associated with the generation of Tg animal e.g., stillborn, birth defects, etc., must be reported to IBC. Any breeding of transgenic non-rodent animals will require written notification in a minor amendment to his/her IBC registration. Investigators are strongly encouraged to contact the BSO to discuss the appropriate review process for experiments that involve the breeding of transgenic animals.

Experiments for the creation or generation of transgenic animals are not exempt and must be reviewed by the IBC (see Section III-D-4 or III-E-3 of the NIH Guidelines) (UH Working Policy revised 2019). Methods for producing transgenic animals, includes but not limited to: DNA microinjection, retrovirus or other virus- mediated gene transfer and embryonic stem cell mediated gene transfer, CRISPR, Cre-Lox, and other new technologies.

The following table summarizes the category of experiments with Tg Rodents:

Table 1. Category of Experiments with Transgenic (Tg) Rodents

Category of Experiment	Minimum ABSL	NIH Guidelines[1]	Require IBC?
PURCHASE OR TRANSFER OF TRANSGENIC RODENTS[2]			
Purchase or transfer of Tg rodents that may be housed under BL1 containment if the research does not involve the use of recombinant or synthetic nucleic acid molecules	1	C-VII, III-D-4-c-(2), III-F	**Minor IBC amendment, possible T1 form**
Purchase or transfer of Tg rodents that may be housed under BL1 containment, if the subsequent research does involve the use of recombinant or synthetic nucleic acid molecules.	2 or higher	III-D-4	**Yes**
Purchase or transfer of Tg rodents that require BL2 or higher containment	2 or higher	III-D-4	**Yes**
BREEDING OF TRANSGENIC RODENTS [1,2]			
Breeding of two different Tg rodents or breeding of a Tg rodent and a non-Tg rodent with the intent of creating a new strain of Tg rodent that can be housed at BL1 containment if: (1) Both parental rodents can be housed under BL1 containment; and (2) neither parental Tg rodent contains the following genetic modifications: (i) incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or (ii) incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); and (3) the Tg rodent that results from this breeding is not expected to contain more than one-half of an exogenous viral genome from a single family of viruses.	1	III-E-3-a, C-VIII	**Minor IBC amendment**

[1] NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), April 2016 Department of Health and Human Services, National Institutes of Health

[2] FAQs for Research Subject to NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines): Genetically Modified Transgenic Animals and the Use of Recombinant or Synthetic Nucleic Acid Molecules in Animals, National Institutes of Health Office of Science Policy

Breeding rodents from two strains (generating new strain) if the parental rodent contains the following genetic modifications: (i) incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or (ii) incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); or (iii) the rodent that results from the breeding contains more than one-half of an exogenous viral genome from a single family of viruses and required to be housed under BL2 or BL3 containment	2 or higher	III-D-4	**Yes**
GENERATION OF TRANSGENIC RODENTS[2]			
Creation of a Tg or knock-out mice using CRISPR technology, where there is no introduction of recombinant or synthetic nucleic acid molecules into the animal's genome. And that can be housed under BL1 containment. CRISPR technology is regulated.	1	II-D-4	**Yes**
Creation of Tg or knockout rodents requiring housing under BL1 containment in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom. Also known as homologous recombineering. This includes CRE-LOX technology	1	III-D-4-c-(1), III-E-3	**Yes**
Creation of Tg or knock-out rodents requiring housing under BL2 or BL3 containment, in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefore, into the germ-line. Also known as homologous recombineering.	2 or higher	III-D-4	**Yes**
EXPERIMENTS WITH TRANSGENIC RODENTS[1]			
Experiments with Tg rodents that can be housed under BSL1 containment and does not involve the introduction of recombinant or synthetic nucleic acid molecules.	1	Appendix C-VIII	**Minor IBC amendment**
Experiments Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g. encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes		III-F-2	**Minor IBC amendment**
Experiments Those that consists solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.		III-F-3	**Minor IBC amendment**
Experiments Those that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or closely related strain of the same species), or when transferred to another host by well-established physiological means.		III-F-4	**Minor IBC amendment**
Experiments Those that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species.		III-F-5	**Minor IBC amendment**
Experiments Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent.		III-F-6	**Minor IBC amendment**
Experiments Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.		III-F-7	**Minor IBC amendment**
Experiments with Tg rodents that can be housed under BSL1 or higher containment involving the introduction of recombinant or synthetic nucleic acid molecules or nucleic acids derived therefrom into the germline (Tg animals) and experiments involving viable recombinant and synthetic nucleic acid molecule-modified microorganisms tested on whole animals. For the latter, other than viruses which are only vertically transmitted, a minimum containment of BSL2 is required.	2 or higher	III-D-4	**Yes**
Rodent study involving **viable recombinant or synthetic nucleic acid molecule-modified microorganism** tested on rodents	Refer to viral vector table		**Yes**

Rodent study involving **viable human materials such as human cells etc.** tested on rodents	2 or higher		**Yes**

Plant Experiments with Animals or Arthropods			
Experiments with microorganisms or insects containing recombinant DNA with the potential for detrimental impact to ecosystems.	BL3-P or BL2 P plus biological containment	III-D-5-a or III-D-5-b	Yes
Experiments with exotic infectious agents in the presence of arthropo vectors	BL4-P	III-D-5-c	Yes
Experiments with microbial pathogens of insects or small animals associated with plants with the potential for detrimental impact to ecosystems.	BL3-P or BL2 P plus biological containment	III-D-5-e	Yes
Small animals associated with recombinant DNA-modified plants.	BL1	III-E-2	Yes
Experiments with rDNA-modified arthropods or small animals associated with plants	BL1	III-E-2-b-(5)	Yes
Other			
Transfer of a drug resistance to microorganisms compromising the use in veterinary medicine	Set by NIH (case by case	III-A-1-a	Yes

SUMMARY

1 Before initiating any research project that is expected to generate Tg animals, the PI must do the following steps:

a. The PI must notify the Institutional Biological Safety Officer (IBSO) in writing about the proposed experiments. Written notification must include the purpose of the project and the following information:

1) animal species and specific strain (Tg, KO, KI),
2) transgene name,
3) transgene function,
4) transgene source,
5) vector(s) used,
6) method of animal transformation, and
7) physical location of the laboratories and research animals at the University. The PI should clearly indicate if the gene encodes a toxin or other hazardous agent.

b. The PI must submit a minor amendment to his/her IBC registration to include the proposed experiments.

c. Based on the written information from the PI, the BSO will determine the subsequent review procedures. In very rare cases, the project may need to be referred to the NIH Office of Biotechnology Activity for federal review. However, in most cases the BSO will determine that the project will require either: 1) submission of an IBC Registration for review and approval, OR 2) no further institutional review for the project and the IBC Chair can approve the minor amendment without full IBC review.

2. The NIH guidelines require the following provisions be met when generating or utilizing transgenic animals. These requirements are in addition to those listed in the Guide for Care and Use of Laboratory Animals.

a. Animal Facility Security

All facilities are maintained to minimize the possibility of theft, escape or accidental release of animals. Animal facilities housing transgenic mice are secured in accordance with NIH guidelines. Containment facilities are locked and access is restricted to research personnel and animal husbandry staff. Animal facilities are monitored on a regular basis by attending veterinarians, care staff and research personnel.

b. Animal Containment

The physical and biological containment levels for experiments involving genetically engineered animals must conform to Guidelines unless directed by the IBC. The containment levels required for research involving recombinant or synthetic nucleic acid molecules associated with or in animals are based on classification of experiments in NIH § III, Experiments Covered by the Guidelines. For the purpose of animal research, four containment levels are established in NIH Appendix G in the Guidelines for physical containment of smaller animals BL1-N through BL4-N. Because the University of Hawaii does not have an ABSL4 facility, no BL4-N work can be done. For larger animals such as cattle, swine, sheep, goats, horses, and poultry, they are outlined in Appendix Q.

c. Animal Disposal

As prescribed by the NIH, dead or euthanized animals are disposed of according to established guidelines. When a transgenic animal is euthanized or dies, the carcass must be disposed of by chemically digested or other method approved by the BSO. The BSO will determine whether the disposal method will be biomedical (e.g. Stericycle), non-hazardous chemically digested, or other methods suitable for the animal involved. This requirement for a particular method of disposal applies to transgenic animals, potentially transgenic animals, “no-takes” in the production of transgenic animals, and progeny of transgenic animals. No changes to the approved disposal protocol are allowed without prior review and written approval.

3. For projects involving the transfer of transgenic animals or tissues from such animals between University researchers and scientists, between UH buildings, or between other institutions or companies, animals and/or tissues must be clearly described, in advance of shipment, in a BSP2 application submitted to the BSO and/or T-1 form submitted to AVS. The cooperating institution, company or scientist must provide statements describing the transferred research materials and these documents must be attached to the BSP2 application and/or T-1 form. Examples of pertinent documents include, but are not limited to, copies of Material Transfer Agreements and statements from collaborators describing gene constructs, plasmids and genetic changes in the animals. International shipments may require special review due to export requirements (Material Transfer Agreement, Export Control/Dept. of Commerce).

4. The PI is responsible for reporting the inadvertent release of animals, improper disposal of transgenic animals or other incidents in the laboratory or classroom to the BSO. The BSO will report the incidents to the IBC.

5. The PI is responsible for training graduate students, teaching assistants, volunteers, and staff about the policies and procedures for Tg animal handling, incidents, and appropriate carcass disposal.

6. Contact the BSO when considering the use of Tg animals. The BSO will advise which category the Tg animal should be placed.
7. All additional strain(s) need to be registered with IBC.

Core Facilities

It is incumbent on the core facilities program to ensure that PI has IBC authorization. All transgenic animals must be used under an approved IBC registration, in addition to an approved IACUC protocol (vertebrate animals), unless the latter activity is deemed exempt.

Animal Facility

1. Access to the animal facility must be restricted to authorized persons. When the animal facility is unattended it must be kept locked.

2. Appropriate Personal Protective Equipment (PPE) must be worn within the facility.

3. A water supply and a sink must be available within the animal facility.

4. Hands must be disinfected or washed after handling animals or animal/laboratory waste

5. Eating, drinking, smoking, storing of food for human consumption and applying cosmetics is not permitted

6. Mouth pipetting must not take place

7. SOPs must be provided for the training of all routine operations that are carried out in the facility, for example, measures for limiting access to the unit, transport of Tgs within and outside of the unit, administration of drugs and where applicable the taking of blood, cleaning of equipment, operation, testing and maintenance of containment equipment, and disposal of waste.

8. Staff should be given appropriate training and instruction on the procedures to be carried out, and written records of training must be kept.

9. When an animal facility requires special provisions for entry (e.g., vaccination), a warning sign detailing the entry requirements must be posted on all access doors.

10. All accidents, including animal bites, scratches and stings, must be recorded andreported to the Biosafety Program.*

11. Pest control measures (barriers) must be in place to prevent the escape of Tg animals and the entry of wild species.

12. Animals must be transported to and from the facility in appropriate animal containers.

13. Security measures must be put in place in order to prevent theft or vandalism.

Animal Housing

1. All animals must be contained within an approved, UH IACUC enclosed cage/room/pen/tank to or Biosafety Level containment, to avoid the possibility ofunintentional release or theft.

2. Effective disinfectants must be available.

3. Animal housing must be well ventilated, easy to clean and disinfect.

4. Animal rooms/cages/tanks/pens must be disinfected as per the IBC approved registration.

5. Male and female animals should be separated to avoid unintentional or unwanted reproduction, unless reproductive studies are an approved element of the experiment.

6. All cages/pens/tanks must be appropriately labeled to reflect the content of each enclosure, in particular the number and sex of Tg animals contained therein, and the nature of the genetic modification should be recorded. (Not required, but suggested for small animals)

7. Full records of the receipt, breeding, movement, release and /or disposal of all transgenic animals must be kept.

8. The escape of a Tg animal from the animal facility must be reported to the Biosafety Program office within 24 hours of discovery.*

Waste

1. *A Tg animal presents no greater risk to human health or the environment than a non-Tg animal, however in the interest of public perception Tg animal carcasses must be decontaminated prior to disposal.

2. An autoclave for the decontamination of waste must be available on site. The off- site decontamination of Tg animal carcasses prior to disposal must comply with the requirements.

3. Waste being removed from the vivarium for the purposes of decontamination must be removed in closed, durable, leak-proof containers.

4. Waste material such as bedding, feces and urine, cage, feed and water are not considered to be hazardous waste, thereby, do not require additional measures.

5. Needles and syringes must be placed in a puncture resistant container and must be autoclaved prior to disposal.

6. When any transgenic animal is euthanized or dies, the carcass must be disposed of by incineration (recommended) or chemical digestion. This disposal requirement applies to transgenic animals, potentially transgenic animals, "no-takes" in the production of transgenic animals, and progeny of transgenic animals. There are no exceptions to this policy without review and written approval from the IBC.

7. For BL3-N (large animals), research records regarding experimental animal use and disposal must be maintained in a permanent record book.

Shipment

1. Before transgenic animals or their tissues can be shipped between UH facilities, or to or from the University or scientists at other institutions, the IBC registration form must clearly describe the animals and/or animal tissues. These include, but are not limited to, gene constructs, plasmids, and genetic changes in the animals. International shipments may

require special review due to export requirements. (Additional forms, including the T1 and BSP2 are required).

Aquatic animals - Transgenic Fish

1. The escape of transgenic fish and/or their gametes (developing fertilized eggs) from the tank must be prevented by placing appropriately sized filters over water entry/exit routes or drains. The top of the aquarium must also be securely covered to prevent the escape of the fish.

2. In the event of the tank leaking, rupturing or overflowing, the tank should be bounded or a secondary containment system should be used to contain spillage.

3. Experimental Tgs should be rendered biologically inactive by appropriate methods before disposal.

4. Security measures must be put in place in order to prevent theft or vandalism.

5. All water must be decontaminated prior to disposal into sewer.

Reference: NIH Division of Technical Resources, Technical News Bulletin, April – August 2012 Aquatic Facilities.

Invertebrates – Transgenic Fruit flies

The use of transgenic or genetically modified insects, including fruit flies, bees, ants and butterflies, in research is governed by the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH Guidelines). The NIH Guidelines detail procedures and practices for the containment and safe conduct of various forms of recombinant DNA research, including research involving genetically modified or transgenic insects. All researchers at UH must comply with the NIH Guidelines, even if their individual projects are not funded by NIH.

- ☐ The purchase or transfer of transgenic insects is not exempt from the NIH Guidelines.

- ☐ The creation, generation, breeding and propagation of transgenic insects are covered under Section III-D-4 of the NIH Guidelines. These activities are not exempt from the NIH Guidelines and must be reviewed by the IBC.

- ☐ Section III-D-5-e describes experiments involving genetically modified insects in conjunction with whole plants, which may have the potential for detrimental impact to agriculture or ecosystems. Section III-E-2-b-(5) describes experiments involving genetically modified insects in conjunction with whole plants which have no recognized potential for detrimental impact to ecosystems or agriculture.

- ☐ Per Section III-F-4 of the NIH Guidelines, experiments may be exempt when they involve recombinant or synthetic acid molecules that are entirely from a eukaryotic host (such as an insect), including its mitochondria or plasmids, when propagated only in that host or a closely related strain of the same species. However, at ASU, this research must also be submitted to the IBC for review.

- ☐ If you are manipulating insects that have mutations or genetic modifications that are the result of natural variation, chemical mutagenesis or radiation exposure, and that have not had any molecular manipulation, these may not need to be reviewed by the IBC. Please contact Biosafety & Biosecurity to discuss the details of your research.

- □ Knock-out (gene silencing, gene ablation, etc.) organisms may be exempt from IBC review if the method used to generate the knock-out does not leave any "new" genetic material or any markers behind in the genome after the procedure. If the recombinant or synthetic nucleic acid molecules that are used to create the knock-out are permanently inserted into the genome or if an *Escherichia coli* (*E. coli)* system is used to create the knock-out, the experiment must be reviewed by the IBC. Please contact Biosafety & Biosecurity to clarify your research.

- □ If there is any genetic marker from another source (not your insect), such as GFP, or if the genetic material is put into *E. coil* to amplify it, this research is subject to review by the IBC. Also, research or teaching activities involving the insertion of sequence elements which are engineered and did not originate in an organism or insertion of genes from another species that does not naturally exchange with your research species, must be reviewed by the IBC.

- □ Recombinant and synthetic nucleic acid molecule modifications to the somatic cells of non-transgenic insects may also be subject to the NIH Guidelines and review by the IBC.

A permit from the USDA is required for work with plant or animal pathogens and insects considered plant pests. An APHIS permit is required for the importation, movement or environmental release of genetically modified insects. Appropriate containment or confinement of the transformed organism is required whether the organism is released, imported or moved interstate.

1. Appropriate cages must be used in the insectaries.

2. In order to prevent entry by non-transgenic insects or the escape of transgenic insects, the use of secondary containment measures around the cages and the insectaries must be implemented (e.g. the use of gauze or mesh).

3. Security measures must be put in place in order to prevent theft or vandalism.

Invertebrates*: Caenorhabditis elegans*; *the earthworm, coelenterate - Hydra attenuate - the horse shoe crab - Limulus polyphemus etc.*

Must have a valid Conditional Animal import and use permit from Hawaii Department of Agriculture. Importation also requires a non-restricted microorganism permit for the import of *E. coli* (feed). *C. elegans* is used as model organisms for the investigation of a variety of biological processes. Storage of the worms is specifically restricted to the use and location as specified in your permit.

Definitions:

ANIMAL BIOSAFETY LEVEL 1 (ABSL1) is suitable for work in animals involving well-characterized agents that are not known to cause disease in immune-competent adult humans, and present minimal potential hazard to personnel and the environment. (See BMBL, 6th edition for specific details on ABSL1).

ANIMAL BIOSAFETY LEVEL 2 (ABSL2) builds upon the practices, procedures, containment equipment, and facility requirements of ABSL1. ABSL2 is suitable for work involving laboratory animals infected with agents associated with human disease and pose moderate hazards to personnel and the environment. It also addresses hazards from ingestion as well as from percutaneous and mucous membrane exposure. (See BMBL, 6th edition for specific details on ABSL2).

ANIMAL BIOSAFETY LEVEL 2N (ABSL2N) refers to containment of animals that cannot utilize an individually filtered enclosure, e.g. large animals.

ANIMAL BIOSAFETY LEVEL 3 (ABSL3) involves practices suitable for work with laboratory animals infected with indigenous or exotic agents, agents that present a potential for aerosol transmission, and agents causing serious or potentially lethal disease. ABSL3 builds upon the standard practices, procedures, containment equipment, and facility requirements of ABSL2. (see BMBL, 6th edition, for more details on ABSL3).

TRANSGENIC ANIMAL is an organism that carries a foreign gene that has been deliberately inserted into its genome. The foreign gene is constructed using recombinant DNA or synthetic nucleic acid technology. In addition to the gene itself, the DNA usually includes other sequences. The genetic material has been altered in a way that does not occur naturally by mating or natural recombination or by a combination of both.

KNOCK OUT/KNOCK IN. Techniques used to create a "knock-out" or "knock-in" may involve the stable introduction of recombinant or synthetic nucleic activity into the animal's genome, therefore, these animals are considered transgenic by NIH.

INVERTEBRATE ANIMALS: Animals having no backbone or spinal column. Working with or the production of genetically modified Drosophila melanogaster, Caenorhabditis elegans, and etc. must be approved prior to initiation of protocol.

R/SNA recombinant or synthetic nucleic acid molecules

REGISTRATION: An application to the Institutional Biosafety Committee in doing research, instructional or clinical use of recombinant activities or use of biological materials.

References:

1. FAQs for Research Subject to NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines): Genetically Modified Transgenic Animals and the Use of Recombinant or Synthetic Nucleic Acid Molecules in Animals, National Institutes of Health Office of Science Policy. Also Attached.

2. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), April 2016, Department of Health and Human Services, National Institutes of Health.

3. Biosafety in Microbiological and Biomedical Laboratories, 6th edition, June 2020, Department of Health and Human Services, Centers for Disease Control and Prevention, National Institutes of Health.

4. The Guide for the Care and Use of Laboratory Animals, 8th edition, 2011, The National Academies Press, Washington, D.C.

5. **FAQs** for Research Subject to NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines): Genetically Modified Transgenic Animals and the Use of Recombinant or Synthetic Nucleic Acid Molecules in Animals, National Institutes of Health Office of Science Policy. https://osp.od.nih.gov/biotechnology/faqs-on-genetically-modified-transgenic-animals-and-the-use-of-recombinant-or-synthetic-nucleic-acid-molecules-in-animals/

APPENDIX M DECOMMMISSIONG

Adopted by the UH IBC (UH System)

Prepared by: UH Environmental Health and Safety Office
Revision 1
Date: May 7, 2019

UNIVERSITY OF HAWAIʻI LABORATORY DECOMMISSIONING POLICY

I. POLICY STATEMENT:

Prior to laboratories being vacated, all equipment, chemicals, radioactive and biological materials must be properly transferred, removed, or disposed.

II. PURPOSE:

This policy is to prevent and minimize risk to the campus community, including cleaning and maintenance staff, contractors, and new occupants who may enter vacated laboratories containing abandoned hazardous material.

III. APPLICABILITY/SCOPE:

This policy applies to all laboratories and auxiliary spaces serving laboratories and provides for the removal of potentially hazardous material from these spaces when the user is planning to vacate the space. This includes terminating affiliation with the University, relocating to another laboratory space, major laboratory renovation requiring relocation of hazardous materials, and retirement from research activities. This policy applies to all units regardless of location on or off campus.This policy does not apply to facilities such as computer labs and music labs.

IV. DEFINITIONS:

A. Decommissioning – the formal deactivation of a laboratory.
B. Laboratory – a facility where quantities of hazardous chemicals, biological, and radiological materials are used in a non-production basis, including research labs, student teaching labs, and clinical labs.
C. Principal Investigator (PI) – faculty, staff, or researcher responsible for supervising activities within a laboratory.

V. RESPONSIBILITIES:

A. Deans/Directors are responsible for ensuring that departments and units are aware of and follow the procedures contained in this policy.
B. Department Chairs/Unit Heads are responsible for the following:
    1. Verify that PIs in their department/unit have notified the appropriate campus units, such as the Environmental Health and Safety Office (EHSO), Office of Research Compliance (ORC), and Campus Operations and Facilities (COF), when vacating or relocating a laboratory.

2. Inform appropriate campus units, such as EHSO, ORC, and COF of new laboratory assignments.
3. Accountable for costs, deficiencies, or regulatory actions or fines resulting from improper management or disposal of regulated materialsfrom laboratories that have not been properly decommissioned.
4. Ensure all assigned keys are returned to the University.

C. Principal Investigators (PIs) are responsible for the following:

1. Ensure enough lead time (at least one month) is given for proper management of materials. Required disposal time will vary depending on amount and type of materials involved.
2. Notify the appropriate departments (i.e., Radiation Safety, Hazardous Materials Management, Laboratory Safety, and Biosafety) when vacating or relocating a laboratory.
3. Complete the Laboratory Decommissioning Checklist (Attachment 1) and submit to the EHSO and ORC accordingly.
4. Take specific measures to transfer or dispose of hazardous, radioactive, and/or biological materials before vacating or relocating.
5. Ensure all equipment, such as fume hoods, biological safety cabinets, flammable or corrosive storage cabinets, freezers, incubators, scintillation counters, autoclaves, and centrifuges are emptied and decontaminated.
6. All research specific apparatus shall be dismantled, packaged, and removed.
7. All compressed gas cylinders shall be removed prior to closing of the laboratory.
8. All papers, books, rags, empty containers, boxes, bottles, glassware, plastic ware, etc., shall be properly disposed of prior to vacating the laboratory.
9. Return all assigned keys to the University.
10. If a vacated laboratory does not undergo decommissioning and becomes occupied by a new PI, all materials found within the laboratory become the responsibility of the new PI.

VI. PROCEDURES:

Refer to section V. RESPONSIBILITIES above.

VII. REFERENCES:

A. Laboratory Decommissioning Checklist – Attachment 1
B. Hazardous Materials (Chemical User) Disposal Close-out Procedures - Attachment 2
C. Biosafety Laboratories Close-Out Guidance Document- Attachment 3
D. Radioisotope Laboratories Close-out Procedures - Attachment 4
E. Guidance for other regulated and non-regulated items and waste (lab equipment, batteries, etc.) –Contact Your Campus EHSO

VIII. HISTORY:

Guidelines and procedures on hazardous waste handling have been in existence as listed above in REFERENCES (see B, C, D, and E, above). However, an official policy is warranted to ensure the health and safety of the campus community. This version replaces the previous AP dated March 18, 2011.

APPENDIX M ATTACHMENT 1
UNIVERSITY OF HAWAIʻI LABORATORY DECOMMISSIONING CHECKLIST

Principal Investigator:	Department:
Department Head/Chair:	Building:
Room Number:	Laboratory Closeout Date:

The purpose of this checklist is to assist Principal Investigators in safely removing hazardous materials from a laboratory and confirming that the area is free from contamination.

Chemicals and Hazardous Waste	**Yes**	**No**	**N/A**
Refrigerators, areas under sinks, fume hoods, cabinets, shelves, and bench tops have been checked for storage of hazardous materials (including shared spaces).	☐	☐	☐
All chemical containers have been labeled and made ready for disposal, transfer, or recycling in accordance with the University of Hawaiʻi Hazardous Materials Management & Disposal Guidelines.	☐	☐	☐
Refrigerators have been emptied, defrosted, and cleaned.	☐	☐	☐
Storage areas have been cleaned: chemical residues, drips, and spills have been appropriately decontaminated and cleaned.	☐	☐	☐
All benchtops have had disposable liners/covers removed from the work surface and surfaces have been cleaned.	☐	☐	☐
All keys to lockable chemical storage cabinets have been returned to the department.	☐	☐	☐
Controlled Substances	**Yes**	**No**	**N/A**
All storage areas are free of controlled substances.	☐	☐	☐
All controlled substances have been disposed of or transferred according to	☐	☐	☐

U.S. Drug Enforcement Agency regulations and requirements.			
Compressed Gas Cylinders	**Yes**	**No**	**N/A**
Cylinders have been properly labeled and secured.			
Cylinders not in use have been disconnected and capped.			
Arrangements have been made for returning empty cylinders to vendors.			
All cylinders have been labeled and readied for disposal, transfer, or recycling in accordance with the University of Hawai‘i Hazardous Materials Management and Disposal Guidelines.			
Radioactive Materials	**Yes**	**No**	**N/A**
Radioactive waste materials have been handled in accordance with the University of Hawai‘i Radioactive Waste Disposal Procedures.			
The removal of radioactive materials and termination surveys have been coordinated with the Radiation Safety Officer in accordance with the guidelines in the University of Hawai‘i Radiation Safety Manual.			
Biological Materials	**Yes**	**No**	**N/A**
All work surfaces and storage areas, including walk-in coolers, freezers, refrigerators and incubators, have been decontaminated.			
All inside working surfaces of the biological safety cabinets have been decontaminated.			
Certification of the biological safety cabinet is current.			
Arrangements have been made for the decontamination and replacement of the HEPA filter in the biological safety cabinet, if required.			
All sharps have been properly disinfected and placed in puncture-resistant containers for disposal.			
All biological waste has been autoclaved and properly disposed.			
Are there biological materials that need to be transferred to another location? If yes, contact the Biological Safety Program for transport information.			

The Responsible Official (Research Office) has been contacted to advise that experiments using Select Agents and/or Toxins will be terminated and the Select Agents and/or Toxins will be destroyed.	☐	☐	☐
Equipment	**Yes**	**No**	**N/A**
All equipment has been disinfected and decontaminated.	☐	☐	☐
Is any portable equipment going to be removed for disposal? If yes, submit a work request to Work Coordination Center.	☐	☐	☐
Is any permanently installed equipment (connected building systems) being removed for transfer with the exiting investigator? If yes, contact Facilities Management.	☐	☐	☐
Has all broken glass been placed in a rigid, puncture-resistant container? or cardboard box and sealed in preparation for disposal by Buildings and Grounds Management?	☐	☐	☐
Records	**Yes**	**No**	**N/A**
If any hazardous chemicals are remaining in the lab, has a copy of the current lab/chemical inventory been provided to the department head?	☐	☐	☐

I have, to the best of my knowledge, complied with the requirements of the University of Hawai'I Laboratory Decommissioning Checklist and am not aware of any other items or special circumstances that are not listed on this form.

Principal Investigator:_____ Date:_____

Department Chair:_____ Date:_____

Please submit this completed form to EHSO and ORC: Your Campus EHSO and biosafe@hawaii.edu

Inquires/Assistance:
Biosafety: 956-3197 biosafe@hawaii.edu

For EHSO/ORC Use Only Final Inspection Sign-Off

Chemical Hygiene Officer:_____ Date: _____

Biological Safety Officer:_____ Date: _____

Radiation Safety Officer:_____ Date: _____

APPENDIX M ATTACHMENT 2
HAZARDOUS MATERIALS (CHEMICAL USER) CLOSE-OUT PROCEDURES

Proper disposition of all hazardous materials used in the workplace is the responsibility of the chemical user or supervisor/Principal Investigator (PI) to whom a chemical use room/laboratory is assigned. Enforcement of this policy is the responsibility of the supervisor/PI. Proper disposition of hazardous materials is required whenever a chemical user leaves the University or transfers to a different laboratory/chemical use room. This process should be started at least a month prior to departure from the chemical use room/laboratory to allow ample time to properly dispose of all materials.

Hazardous waste pickup should be completed before the chemical use room/laboratory is vacated. The disposal must follow the University's Hazardous Materials Management Plan. The Laboratory Decommissioning Checklist (Attachment 1) should be completed prior to the chemical user's departure. Once completed, the checklist should be signed and submitted to the user's Dean or Director and to the Environmental Health and Safety Office (EHSO).

If periodic inspections by the EHSO reveal that proper close-out procedures have not been followed, the EHSO will oversee correction/remediation of any problems created by failure to follow those procedures, and the cost of correcting those problems will be charged to the budget of the Level V unit within which the problems were identified.

Contact the UH Chemical Hygiene Officer with questions or if assistance is needed.

UH EHSO Lab Safety Program Website: https://www.hawaii.edu/ehso/lab-safety/

APPENDIX M ATTACHMENT 3
GUIDANCE DOCUMENT: BIOSAFETY FACILITIES CLOSE-OUT

A. Documentation (Close-Out/Moving)

1. Provide a complete inventory of all biological commodities.

2. Submit inventory with a completed and signed BSP-2 form.

3. Attach copies of personally acquired federal and state permits and authorizations. (All federal and state agencies must be notified prior to move).

4. Follow close-out procedures.

5. Current Biological Shipping and Receiving training may be required.

Assess all biological materials (recombinant DNA materials, microorganisms, cells and cell lines, tissues, organs, body fluids, and biologically-derived or -contaminated media) and determine which materials will be moved to your new laboratory, transferred to another investigator or disposed of.

Dispose of the remaining materials as you would have during the course of experimentation. For example, solid materials (including Petri dishes and microfuge tubes) should be autoclaved and disposed of as biological contaminated waste.

B. Moving Biological Commodities from Lab

Many laboratory materials, including biological commodities, are regulated. Regulated biological commodities include all microorganisms: bacteria, fungi, virus, animals (vertebrate and invertebrate), plants, plant parts and seeds, human tissue, blood or body fluids, biological derived toxins and drugs, etc. Federal permits from USDA, CDC, DEA EPA, Commerce, Customs and DOT, as well as State HDOA and HDOH permits may be required prior to transport, transfer or destruction.

1. Cultures and Stocks of Microorganisms

Microorganisms are subject to the requirements of the U.S. DOT when being moved or shipped (Risk Group 2 or greater). HDOA must be notified if the microorganisms have an import or possession permit.

Federal agencies may require notification.

2. Human and Animal Materials (Blood, body fluids, cell line, organs)

We strongly encourage all laboratories working with human or animal materials (blood, sera, cell, tissue) to plan for the movement of these materials, whether at ambient temperatures or frozen. This will allow for an appropriate amount of time to clean incubators and other equipment, and go through the other requisite steps for the move.

3. Preserved Tissue and Specimens

Any tissue or biological specimen preserved in formaldehyde, mercuric chloride, 70% ethanol, glutaraldehyde, DMSO, or other preservatives should be included in your chemical inventory, using the preservative name and volume. These containers MUST be shipped as hazardous materials. All containers MUST be PROPERLY SEALED (so they cannot leak) and labeled with the full chemical name to be lab-packed and moved. Check directly with EHSO Hazardous Materials Management Program, if disposing.

4. Biological Contaminated Wastes

Decontaminate all wastes. Biological waste must not be transported. All sharps containers in use, whether or not they are full, must be disposed of as biological waste prior to the move. See biological wastes procedures.

5. Select Agents and Toxins

Select Agents or Toxins must not be moved by any outside contractors. All necessary federal requirements must be adhered to, including providing notice to USDA and completion of proper forms. Call OVCRGE Compliance for further information.

6. Biological Derived Toxins and Drugs

If they are controlled under Federal/State Drug Enforcement Agencies, the agencies must be notified prior to movement or disposal.

Disposal of biological toxins and drugs must be through an approved disposal method – either autoclaving or neutralization.

7. Animals

The transport of any live vertebrate animals used in teaching or research must be approved by and coordinated through the Animal and Veterinary Services (AVS) and IACUC.

The NFWS or DLNR must be notified for the transport of invertebrates permitted by the NFWS or DLNR.

C. Moving Equipment

All equipment, apparatuses, and fixed structures must be cleaned and decontaminated as necessary. Once decontamination is done, any work that could re-contaminate the premises is prohibited.

Decontaminate all surfaces (interior and exterior), first with soapy water and secondly with an appropriate working dilution of an appropriate disinfectant. Remember: Contact time of at least 10-15 minutes. Rinse with fresh water as some disinfectants are corrosive.

Tag equipment, instruments, and apparatuses "cleaned and decontaminated" (see "Equipment Owner Declaration" tag on page 5). Tag must be secured to the face of the equipment.

Remove any universal biohazard symbol.

1. **Equipment Needing Repair:** Contact the service company to determine if they require written verification of decontamination prior to servicing the equipment. The lab is responsible for certifying that equipment has been properly decontaminated. Consult the equipment manual for cleaning/decontamination procedures, policies, and chemical compatibility. If it is not possible to decontaminate the equipment, it must be properly packaged to prevent exposure and labeled to inform non-laboratory staff of the potential hazards present. When a person (University or outside contractor) services equipment in the laboratory:

    - Prepare a working area which is clean and free of hazards,
    - Clear enough space for easy access around the equipment,
    - Remove any hazardous items stored near, on, or under the equipment,
    - Inform the individual of potential hazards in the laboratory (training), and
    - Provide personal protective equipment if necessary.

2. **Centrifuge:** Clean and decontaminate chamber, cups, and rotors or other parts as instructed by manufacturer (consult manual).

3. **Water baths, bio-fermenters, aquariums, reactors, and incubators:** Flush out all drains. Water jackets must be drained and emptied. Prior to water disposal down a sanitary drain, the water should be decontaminated.

4. **Biosafety Cabinets:** All biological safety cabinets require a Biological Safety Program (BSP) evaluation to determine required decontamination, even if they are not moved. If it is moved, the equipment must be certified again after the move to ensure filter integrity. Decide for this work in advance to allow contractors to meet your schedule. All interior and exterior surfaces must be disinfected prior to moving them. This includes under the workbench/grille and the top of the BSC.

5. **Refrigerators:** Empty all refrigerators; clean and decontaminate inside and outside surfaces. Drain drip pans. Vacuum motor and grills.

6. **Freezers:** Freezers containing biological commodities may be moved without emptying them if they contain no infectious substances. If moving, complete inventory must be attached to the outside of the freezer.

Laboratory personnel are responsible for preparing freezers for the move, ensuring that all loose vials and containers are properly packaged using unbreakable containers (plastic, metal, or cardboard).

All spaces within the freezer must be filled with packing material to prevent the contents from shifting during transit.

Once the freezer is prepared to move, decontaminate the exterior of the freezer. Secure and lock down. The movers will secure the freezer lid with plastic straps before moving the freezer.

If freezer will be defrosted prior to move, water must be sterilized prior to draining.

Call vendor for proper instructions regarding liquid nitrogen freezers, cryostats, Dewar flasks, etc.

D. Decommissioning a Lab

All horizontal surfaces, including bench tops, floors, shelves, fire extinguishers, waste cans, electrical conduits, etc. should have been cleaned and decontaminated with appropriate disinfectant with appropriate contact time.

Sanitary drains must be flushed with bleach.

All universal biohazard symbols should be removed (entry doorway, wastes trash cans, bench tops).

E. New Location

The new location cannot be manipulated without proper federal, state and UH authorization. A new floor plan should have been submitted to the BSP. When the materials arrive at the new locations, lab personnel should check contents for breakage/damage. Open all parcels in a biosafety cabinet. All biosafety cabinets must be certified prior to use.

F. Post-Close-out/Move

If inspections by the BSP reveal that proper close-out procedures have not been followed, BSO will oversee the correction/remediation of any problems created by failure to follow those procedures, and the cost of correcting those problems will be charged to the budget of the Level V unit within which the problems were identified.

G. Equipment Owner Declaration Tag

Tag equipment, instruments, and apparatuses as cleaned and decontaminated. Tags should be printed on light green paper and secured to the face of the equipment being moved or relocated. Utilize printable "Equipment Owner Declaration" tags on page 5 (2 tags/page, form fillable).

Contact the UH Biosafety Officer at 956-3197 or email biosafe@hawaii.edu with questions or if assistance is needed.

UH ORS Biosafety Website: https://research.hawaii.edu/orc/programs/biological-safety/

Equipment Owner Declaration Tags

CLEANED

Equipment Owner Declaration

I have removed all known hazardous materials (biological commodities, chemicals and radioactive materials) from this equipment. All interior and exterior surfaces have been cleaned and decontaminated. To the best of my knowledge, this item is safe to handle, and does not pose a hazardous materials risk to personnel.

Equipment Type

Signature Date

Print Name

Department Phone

CLEANED

CLEANED

Equipment Owner Declaration

I have removed all known hazardous materials (biological commodities, chemicals and radioactive materials) from this equipment. All interior and exterior surfaces have been cleaned and decontaminated. To the best of my knowledge, this item is safe to handle, and does not pose a hazardous materials risk to personnel.

Equipment Type

Signature Date

Print Name

Department Phone

CLEANED

ATTACHMENT 4
CLOSEOUT PROCEDURES FOR RADIOISOTOPE LABORATORIES

MOVING TO ANOTHER LABORATORY

1. Submit an Amendment Application to Authorization Form, RSP-3a, to add a new laboratory location to your current authorization.

    a. Include floor plan of new lab space with areas marked for restricted area. Show where radioisotopes and radioactive waste will be stored on the floor plan.

    b. Show which sink will be the hot sink, if any.

2. Once new lab space is approved by the Radiation Safety Committee, do the following:

    a. Dispose of any radioactive waste by calling RSP for a waste pickup.
    b. If you need to move any radioisotopes to the new lab, call RSP to decide to move your material.
    c. Clear out all large equipment not being kept at old lab. Clear all lab benches of materials, supplies, chemicals, etc.
    d. Move refrigerators, freezers, LSCs, gamma counters, and glassware from lab benches.

3. Do a wipe test survey to ensure no contamination remains. Mark any fixed contamination that is present.

4. Call RSP to perform a final close out survey. If any contamination is found, you will have to decontaminate it and have RSP resurvey the area.

5. If you fail to clean up the contaminated areas identified, RSP will charge your departmentfor the time spent cleaning up the laboratory.

LEAVING THE UNIVERSITY OR STOPPING RADIOISOTOPE USE

1. Submit a memorandum to the RSO stating that you will close out your authorization.

2. Arrange to have radioisotopes transferred to another PI or university, or dispose of your radioisotopes and arrange for a waste pick up. The RSP will assist you with the paperwork to transfer your radioisotopes to another university.

3. Clean your lab equipment of any contamination and transfer equipment to another PI or have it disposed of. Notify RSP if giving fixed equipment to another PI.

4. Clear lab benches as much as possible of all lab supplies, which were used with radioisotopes.

5. Call RSP for a close out survey or decommissioning survey. If any contamination is found, you must decontaminate the areas and have RSP resurvey your lab. If you do not decontaminate the area, RSP will charge your department for the time spent cleaning up.

Contact the UH Radiation Safety Officer at 956-5097 or email ntg@hawaii.edu with questions or if assistance is needed.
UH EHSO Radiation Safety Program Website: https://www.hawaii.edu/ehso/radiation-safety/

ADDITIONAL INFORMATION

Please answer the following questions as thoroughly as possible for user's reference:

1) **What impact will this new or revised policy/procedure have on other UHM campus programs/departments/offices?** This updated policy will provide departments a clearer and up to date list of what is required to decommission a laboratory.

2) **What steps were taken to ensure all appropriate constituents were consulted (who was consulted, what concerns were raised, how were these concerns addressed, etc.)?** Internal review and comments were sought from the EHSO Director, relevant EHSO Program Managers and their respective staff, OCR staff, as well as the UH Chemical and Physical Hazards Committee (CPHC) which is comprised of VCR-appointed faculty. No major concerns were raised as this update clarified the decommissioning process, removed redundant language, provided a more concise checklist, and updated the policy with relevant departmental contact information. UHM Faculty from the CPHC noted the need to account for keys being returned at the end of a lab closeout. This policy was updated to reflect that feedback.

3) **Does this policy/procedure have a financial impact? If so, how?** No change in financial impact expected from the previous iteration of the policy.

4) **Does this policy/procedure affect space (classroom, research, etc.) on campus? If so, how?** This policy provides guidelines for the proper decommissioning of lab space and accounting of hazardous commodities prior to allocating space to a new user.

5) **Are there safety measures that need to be implemented prior to execution? If so, please specify. Who will be responsible to ensure safety standards?** The policy is geared around safety measures and serves as a mechanism for handling regulated hazardous commodities and lab equipment. The UH EHSO and ORC will be responsible for verifying that the required checklist is completed once submitted by the respective departments.

6) **What steps will be taken to ensure that proper clarification and training is provided to the appropriate campus representatives?** Notices will be sent out to Deans, Directors, Chairs, and PI's, as appropriate, to communicate the revised policy. Additionally, the policy will be made available on the EHSO website.

7) **What steps will be taken to ensure update and compliance of this policy?** Regular internal review will occur and subsequent changes based on regulatory agency requirements. Compliance with this policy will be a combined effort of the departments, ORC, and EHSO.

5 June 2020

Needles and Medical Sharps Handling and Disposal Guidance

Guideline 1.0 Version 1.0

Effective Date 1 Aug 2015

Improper disposal of discarded needles, other sharps and medical (auto-injectors, diabetic supplies, lancets, syringes, etc.) pose a health risk to the public, custodial workers and waste workers. Discarded needles expose waste workers to needle stick injuries and bloodborne infections when containers break open inside refuse trucks and custodians risk injury if sharps break through plastic garbage bags.

- ◻ Call the UH Mānoa Department of Public Safety at (808) 956-6911 immediately for assistance when a needle or any of the medical sharps are found on the grounds and facilities of the Mānoa campus.
- ◻ Only personnel instructed on the proper handling and disposal of needles and medical sharps should pick-up and dispose of these items.

Needles and Medical Sharps Handling and Disposal Procedure

- ◻ Put on gloves and safety glasses.
- ◻ Use only remote handling tool (tongs, forceps, etc.) to lift needle or sharp
- ◻ **Do Not Recap. Bend or Cut Needle.**
- ◻ Using remote handling tool, transfer needle to the sharp's container or plastic soft drink container and secure with cap. (Red sharps container can be found in biological laboratories or use a plastic bottle container with sealable cap
- ◻ Disinfect area with fresh household bleach solution (1:10 bleach/water solution) or other EPA registered disinfectant for no less than 10 minutes or manufacturer's instructions for other products.
- ◻ Wipe-up disinfectant solution with absorbent materials and dispose in the regular trash.
- ◻ Decontaminate remote handling tools and re-usable PPE and discard disposable PPE in regular trash.
- ◻ Re-apply disinfectant to ensure decontamination. Allow adequate contact time.
- ◻ Remove gloves and wash hands with soap and water.
- ◻ Call Biosafety Program, Office of Research Compliance at (808) 956-3197 (office) or 285-7619 (cellular) for further instructions.

Disposal reference is found in the UH Biological Materials Wastes Guidelines
http://manoa.hawaii.edu/researchcompliance/guidance-documents/uh-bio-waste-guidelines

Exposure to Blood and Other Potential Infectious Materials, go to your Department Exposure Control Plan or OSHA Template
https://www.osha.gov/OshDoc/Directive_pdf/CPL_2-2_69_APPD.pdf:

Reviewed by Buildings and Grounds, Environmental Health and Safety, Department of Public Safety, Work Coordination Center Jul 2015.

5 June 2020

Isolation of Select Agent (SA) in a non-Federal certified UH Facility

Guideline 1.0 Version 1.0

Effective Date 6 Aug 2006

1. The Laboratory Supervisor shall notify:

   Biosafety Officer, except CTHAR, CTAHR notifies their Responsible Official.Campus Security
   Chair, Dean, Unit Supervisor

2, CTAHR Responsible Officer shall notify (Biosafety Notification Tree Activated)

   Assistant RO
   Police, FBI and Homeland Security
   USDA (Local)
   Hawaii Department of Agriculture

2. The Laboratory Supervisor shall complete APHIS/CDC form 4, "Report of Identification of a Select Agent or Toxin in a Clinical or Diagnostic Laboratory":

   https://www.selectagents.gov/form4.html

   Fax or Scan and forward original, to RO and Biosafety Program, ORC, Honolulu HI 96822-2320, except JABSOM). **DO NOT SEND to USDA**.

4. Secure SA under lock and key all equipment that is storing SA.

5. Use the following procedures depending on intended disposition of the SA

   a. TRANSFER.

      Transfer to a secure federally authorized site. Form APHIS/CDC Form 2. "Transfer Select Agents and Toxins" must be completed and faxed to RO and Biosafety Program.

      A federal permit to transport is also required either: (a) USDA-APHIS VS Form 16-3, "Import Controlled Material or Transport Organisms or Vectors" for High Consequence Livestock Pathogens and Toxins/Select Agents (Overlap agents) or (b) PPQ Form 526, "Application to Move Live Plant Pests or Noxious Weeds."

      Once the permit to transfer is issued, the RO will notify facility's Laboratory Supervisor.

      BSP-2 form must be completed after notification and faxed to Biosafety Program.

      The package must meet IATA and DOT specifications. As this is a dangerous goods shipment, a "Dangerous Goods Declaration" is needed.

Use a parcel courier, no hand carrying on public transportation. Parcel must be shipped registered and certified with insurance.

Use must be Category A biological material transport trained.

b. RETAIN

All provisions of USDA and Health and Human Services (HHS) rules for the possession, use, and transfer of select agents and toxins (42 C.F.R. Part 73, 7 C.F.R. Part 331, and 9 C.F.R. Part 121) must be followed.

An IBC review must be conducted. Please submit appropriate Biosafety Program forms.

c. DESTROY

Notify RO of date of expected destruction.

Arrange for witness destruction by securing representatives from Biosafety, Police, FBI, Homeland Security, HDOA and USDA.

All agency representatives must sign the BSP-2 form acknowledging total destruction. Quality Controls (Biological Indicators, Chemical Indicator) must be run during the autoclave destruction.

Copies of the BSP-2 form with witnesses' signatures must be forwarded to RO and Biosafety Program

RO will notify appropriate agencies that the select agents have been destroyed.

5 June 2020

Reuse of Needles in Research Animals Guidance

Guideline 1.0 Version 1.0
Effective Date 1 March 2019

Purpose: Often for reasons of convenience and cost savings, syringes and needles used to inject research animals are often reused. This practice, while widespread, puts research animals at risk of disease from needle sharing, and also can cause unnecessary pain and distress from injections given with a dull needle. In addition, The Guide for the Care and Use of Laboratory Animals states that, "Aseptic technique is used to reduce microbial contamination to the lowest possible practical level."

DIRECTION:

In most instances the reuse of needles on multiple animals is not permitted. It can lead to dulling of the needle, increasing the discomfort associated with injections, and can lead to disease transmission and/or contamination of vials of material to be injected. In rare cases IACUC approval may be granted for needle reuse. **No disposable needle reuse is permitted in USDA-covered species (e.g., nonhuman primates, dogs, cats, hamsters, rabbits, etc.)**

Examples of Justification for Needle Reuse:

- Severely limited available volume of test article.
- Needles specifically designed for reuse (with appropriate sterilization).

General Consideration for Needle Reuse with Veterinary or IACUC Approval:

- A needle may not be used on more than five animals, and must be replaced before this point if there is evidence that it is becoming dull (e.g., needle is difficult to insert through skin).
- A needle should only be reused on animals from the same cage/group to avoid transmission of infectious diseases from one cage to the next.
- A needle and syringe used to treat an animal known to be sick may not be reused in any other animal.
- A needle used for intravenous (IV) or intraperitoneal (IP), intradermal, intramuscular or retro-orbital injection may not be used on more than one animal.
- A needle, once used on an animal, may not be reintroduced into the vial of material being injected to avoid the possibility of significant bacterial contamination at subsequent use.

If safety needles or sharps newer technology is available, this should be used instead of straight sharps.

5 June 2020

Earphones in Biological Laboratories Guidance

Guideline 1.0 Version 1.0

Effective Date 1 Jan 2019

Maintain awareness of your surroundings (no listening to music using headphones, earbuds); recognizes that many staff and students use audio equipment (audio-visual & multi-media production etc.) and other devices (MP3 players, iPods, etc.) with headphones/earphones/earbuds and that this may be directly associated with work or study. This information sheet aims to provide advice to ensure that the use of these devices does not impact on the health and safety of users and others at the University of Hawaii.

The following points should be considered by all University staff and students to minimize the potential health and safety impacts associated with the use of audio headphones/earphones/earbuds.

General

- If the wearer's situational awareness is reduced to the extent that their health and safety is compromised by the use of these devices e.g. they cannot hear emergency alarms, calls for help etc., then these devices must not be used.
- The use of high volumes can cause permanent noise-induced hearing loss. If someone standing nearby can hear what the wearer is listening to, the volume is too loud.
- Staff and students should consider using a single earpiece whenever possible, to assist in maintaining awareness of what is happening around them.
- Headphones/earphones/earbuds should be maintained in a clean and hygienic state. It is important to follow the manufacturer's instructions when cleaning these devices due to the potential for damage to the electrical/electronic components contained in the unit.
- Internal units such as earbuds should be single user only due to hygiene issues.

Activities requiring the use of headphones/earphones/earbuds

- Where activities require the wearing of headphones/earphones/earbuds, a risk assessment must be completed prior to their use. This is especially important in laboratories, workshops, studios or any other area where harmful biological, substances and materials e.g. infectious or toxic substances, etc. are used.
- If a risk assessment indicates there is no alternative but to use the headphones/earphones/earbuds, approval must be obtained from area managers, supervisors, etc., prior to the use of any such items in the workplace.
- Headphones/earphones/earbuds must be stored in such a way that minimizes the risk of them being contaminated by biological, chemical or other substances and materials.
- Ideally, external units such as headphones and earphones should be single user. Where this is not practical, it is important to ensure that the units are cleaned according to manufacturer's instructions prior to transfer between individuals.
- Headphones/earphones/earbuds must not be repeatedly touched, adjusted or re-fitted to the ear where there is risk of contamination from biological, chemical or other substances and materials.

5 June 2020

Styrofoam Dissecting Boards Guidance

Guideline 1.0, Version 1.o

Effective Date: 19 September 2018

The use of Styrofoam material or other porous material is generally not accepted for use as a specimen or necropsy dissecting board. The reason Styrofoam should be used with limitations is that the material cannot be autoclaved or chemically cleaned appropriately when cracked and/or punctured. Operators should consider using dissecting boards constructed of non-porous materials that can withstand autoclaving or chemical disinfectant treatment. However, Styrofoam can be used on as one time use board, decontaminated and disposed of after the activity.

Dissecting pins that are used to position the carcass must always be cleaned and stored; otherwise, pins may fall off of the dissecting board, thus, becoming displaced and a safety hazard.

Pursuant to the BMBL, because all procedure rooms are classified as BSL2/ABSL2 facilities, these Styrofoam boards must be completely cleaned after every use. Please be advised, equipment and work surfaces are required to be decontaminated with an appropriate disinfectant after work with an infectious agent, and after any spills, splashes, or other overt contamination.

5 June 2020

Guided Gene Drive Technology

Guideline 1.0, Version 1.o
Effective Date: 19 September 2018

PURPOSE

The purpose of this guideline is to describe the Institutional Biosafety Committee (IBC) review of gene drive technology.

INTRODUCTION

RNA-Guided Gene Drives, risk is not defined by the capability to infect and cause disease in a susceptible human or animal host, but instead, the main point of risk management is to consider effects to the natural ecosystem. Depending on the aim of the particular RNA-Guided Gene Drive, there is potential to alter populations of organisms in manners which could have positive effects on human health, but both direct and indirect effects on the environment and the living organisms that inhabit it (Wyss Institute Harvard University).

The **C**lustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeats (CRISPR)/Cas9) CRISPR-**a**ssociated protein **S**ystem is an incredibly powerful genome editing technology or other genome editing technologies such as Transcription Activator-Like Effector Nucleases (TALENS), Meganucleases (MGN) and Zinc Finger Nucleases (ZFN), are required to submit their research disclosures with the IBC registration.

Prior to CRISPR/Cas9, genome engineering approaches relied upon the use of customizable DNA-binding protein nucleases that required scientists to design and generate a new nuclease-pair for every genomic target. Largely due to its simplicity and adaptability, CRISPR has rapidly become one of the most popular approaches for genome engineering selectively activate or repress target genes, purify specific regions of DNA, and even image DNA in live cells using fluorescence microscopy (S. Moisyadi Jun 2016).

The greatest laboratory risks posed by CRISPR, other gene editing technologies, and also existing conventional rDNA research remain:

- Presence of replication competent viruses
- Insertion activation of oncogenes (more likely with MLV than lentiviruses)
- Risk of tumor suppressor gene inactivation
- Other (site-specific risk assessment)

Viral vectors, plasmids, and nanoparticles are being used to deliver CRISPR systems. CRISPR research is being performed in many organisms, from *E. coli* to human cells lines to animals.

Viral vectors, plasmids, and nanoparticles are being used to deliver CRISPR systems.
Mouse and human guide RNA will be used.
Off-target mutations may occur, or be unknown.
There may be unwanted immune system reactions.
Infection may be possible from viral vectors.

There may be challenges associated with CRISPR activity over time.

Some experiments have the Cas9 protein and gRNA being transiently expressed; the CRISPR DNA is not being stably integrated into the cell's genome.

In some experiments, targeted genes lead to reduced host fitness (e.g., slower growth rate); these strains would be less competitive if inadvertently released to natural environment.
OSHA Bloodborne Pathogens Standard followed for work with human materials (e.g., human cell lines). There is potential for needle sticks or other exposures. Eliminating needles and other sharps when doing the work is recommended.

BIOSAFETY REQUIREMENTS (University of Pittsburg Feb 2016)

- **BSL/ABSL-1: Recommended for non-viral, non-human cell use**

  The IBC will consider the use of gene drives in cell culture work viruses for use at BSL/ABSL-1:

  Transfection of cells in culture, except for human-derived cells

- **BSL/ABSL-2: Recommended for viruses or use in human cells***

  The IBC will consider the use of gene drives in cell culture work viruses for use at BSL/ABSL-2:

  Transfection in human-derived cells
  Transduction of cells in culture

*Viral vector must be at 3rd generation or later.,. 1st and 2nd generation may require containment BSL/ABSL 2+.

1) All work involving potential gene drive systems should be preceded by a thorough assessment by the relevant biosafety authorities of the risk of unwanted release from the laboratory. Seek guidance from external experts and make their evaluation available to others.

2) All laboratory gene drive experiments should employ at least two stringent confinement strategies (see the table) whenever possible to minimize the risk of altering wild populations. Using one form of confinement may be justified only if relevant biosafety authorities determine that it will reduce the probability of release to a level that is acceptably low. This probability must be defined on a case-by-case basis. The analyses necessary to confidently predict the efficacy of confinement strategies for gene drive systems are in a nascent form. Therefore, any proposal to use one rather than multiple forms of confinement requires even greater scrutiny and extensive deliberation between regulatory authorities and scientists.

3) Organisms carrying gene drive constructs that could spread if the reproductively capable life stages were to escape in transit should not be distributed to other institutions until formal biosafety

guidelines are established. Whenever possible, laboratories should instead send DNA constructs or information sufficient to reconstruct the gene drive. Protocols for distributing materials should be established in discussion with the wider research community and other relevant stakeholders.

BSL-1 or ABSL-1	Cas9 and gRNA on separate plasmid
	Plasmid or vector no capable of infecting human cells
	Standard cloning vector (<50% of Risk Group 2 pathogen)
	Research in non-pathogenic *E. coli* (K-12, other*) Saccharomyces cerevisiae, B. subtilis* , other Risk Group 1 cell lines)
	Replication defective Adeno Associated Virus Vector (AAV)
BSL-2 or ABSL-2	Cas9 and gRNA on same plasmid or vector
	Replication defective Adenovirus, Herpesvirus, ecotropic Retroviral vectors, other Risk Group defective vectors
	Research in human or non-human primate cell line (COS-7)
	Inserted nucleic acid targeting cell cycle or cell division, transcription, cell activators, cell growth
	Genes associated with toxicity or allergenicity
BSL-2+ or ABSL2+	Cas9 and gRNA on same plasmid or vector
	Lentiviral vectors
	Retroviral vectors with amphotropic packaging cell lines
	Vaccinia virus and VSV (lab strain) vector
	Large libraries targeting the human genome
	Human cellular or viral oncogene knock-in
	Tumor suppressor gene knock-out
BSL-3 or ABSL-3	Any research with CRSPR/Cas9 involving Risk Group 3 materials.

RISK ASSESSMENT

In order to perform a proper risk assessment, the researcher will provide the following:

1 Does your research involve CRISPR or another gene editing technology? If yes, you will need to describe the technology (e.g., CRISPR/Cas9, ZNF, TALENS, Meganucleases) that is being proposed.

2 For CRISPR systems, are the guide RNA (gRNA) and nuclease on the same plasmid, vector, or delivery vehicle?

If so, can this plasmid, vector, or delivery vehicle transfect or infect a human cell and can the gRNA or CRISPR nuclease be expressed in human cells?

3 For CRISPR research involving viral vectors, a Genome Target Scan (GT-Scan) for off target affects by your gRNA must be completed. This is necessary to determine if there is homology to human DNA and for assessing the risk of potential exposure in the event of an unanticipated incident. (**References:** Bae et al., 2014; O'Brien and Bailey, 2014

4 Will the genome editing technology be used in prokaryotes, eukaryotes, or mammalian cells? If so, please specify which.

5 How is the gene editing technology being delivered (e.g., nanoparticles, plasmid, lentivirus, adeno-associated virus, etc.)?

6 Will the gene editing technology target embryos or germ line cells? **

7 Will the gene editing technology be used for human gene transfer research? **

8 Will the research involve the creation of a gene drive experiment (i.e., a system that greatly increases the probably that a trait will be passed on to offspring) (**Reference:** Akbar et al., 2015).

**No gene editing of the germ line, human embryos, or germ cells for clinical application is allowed. Gene editing of human embryos and germ cells for scientific purpose may be allowed, but must be evaluated on a case- by-case basis by the appropriate federal and local scientific review committees.

Attach the following to your IBC Registration

1. **Project Description:** CRISPR specific for [insert species] will be used to inactivate [insert gene] to create a model for [insert disease]. Include how CRISPR will be dosed: viral vector, plasmid, liposome, etc.

2. **Containment Requirements:**

   Usually **BSL-1** biological practices, containment equipment, and facilities for all activities involving non-virus dosing.

   For virus-vectored CRISPR, **BSL-2** practices including biological safety cabinets are recommended. Centrifuge safety precautions, secondary containers for transport between incubator and BSC. Keep hands away from the eyes, nose and mouth in order to avoid potential exposure of the mucous membranes; eye goggles or face shields may assist in accomplishing this objective.

3. **CRISPR Injection dosing precautions:** The use of sharps should be minimized.

   Safe-sharp technology is highly recommended during animal dosing.

4. **Spills:**

   If non-virus vectored, cleanup per the biological spill plan.

   If virus vectored, the follow BSL-2 spill instructions.

5. **Biohazardous Waste:** Collect in double red bags and transport in a rigid container. Autoclave with appropriate time, pressure and temperature (with quality control)

6. **Approved Disinfectants:**

   Non-virus vectored siRNA: soap and water

   Virus-vectored; disinfectants appropriate for the virus.

7. **Disposal:**

   Non-virus vectored, as a biological spill plan

   Virus-vectored: Decontaminate before disposal; steam sterilization, incineration, chemical disinfection.

8. **Storage:**

   Store plasmids as per the chemical hygiene plan.

   Store virus vectors as BSL-2 organisms.

9. **Pathogenicity:** Mucous membranes, ingestion, broken skin and injection. Reasons can be sharps contact, failure to wash hands, skin contamination from dirty gloves or work surfaces.

10. **Modes of Transmission:** Liposomes and plasmids may cross the cell membrane of individual cells. If the gene target is present, it could result in silencing. Liposomes and plasmids are not infectious; once integrated into cells, they do not reproduce. For virus vectored, refer to appropriate virus vector sheet.

11. **Length of gene deletion:** In human and mammalian cells, as well as animals, CRISPR silencing is permanent. It is transmissible to off-spring.

12. **Communicability:** If virus vectored, accidental contact with live virus can result in CRISPR expression.

13. **Medical surveillance and clinical treatment procedure**: Immune suppression is required, as the silencing can affect the immune system. Clinical Operating Procedure “Virus Vectors” must be listed on risk assessment if used to vector CRISPR.

14. **Stability in Environment:** Refer to appropriate virus vector sheet.

15. **CRISPR concentration, dosage per experiment:** State your stock concentration and the amount used per experiment or kg animal weight.

16. **CRISPR shedding from animals:** Animals will not shed CRISPR if dosed with plasmid formulations. For viral vectors, refer to specific viral vector risk assessment.

17. **CRISPR Information:** Discuss the desired effect of gene editing on the animal or cell line. You must address the potential effects due to accidental worker exposure. If unknown, state that. Points to consider are:

a. Is the guide sequence specific to animals, humans or could it affect both? Similarity between human and animal guide sequences?

b. What is known about off-target effects?

c. How much genotype change (dose) is needed for a physical effect?

d. How does route of exposure affect outcome?

A good source for understanding the transgene being silenced or over-expressed is GENE CARDS

Potentially stringent confinement strategies for gene drive research

Multiple stringent confinement strategies should be used whenever possible.

TYPE	STRINGENT CONFINEMENT STRATEGY	EXAMPLES
Molecular	Separate components required for genetic drive	sgRNA and Cas9 in separate loci (*8*)
	Target synthetic sequences absent from wild organisms	Drive targets a sequence unique to laboratory organisms (*3*,*4*,*8*)
Ecological	Perform experiments outside the habitable range of the organism	*Anopheles* mosquitoes in Boston
	Perform experiments in areas without potential wild mates	*Anopheles* mosquitoes in Los Angeles
Reproductive	Use a laboratory strain that cannot reproduce with wild organisms	*Drosophila* with compound autosomes*
Barrier	Physical barriers between organisms and the environment	Triply nested containers, >3 doors (*6*)
	•Remove barriers only when organisms are inactive	Anesthetize before opening (*6*)
	•Impose environmental constraints	Low-temperature room, air-blast fans
	•Take precautions to minimize breaches due to human error	Keep careful records of organisms, one investigator performs all experiments (*6*)

*An example of reproductive confinement would be *Drosophila* laboratory strains with a compound autosome, where both copies of a large autosome are conjoined at a single centromere. These strains are fertile when crossed inter se but are sterile when outcrossed to any normal or wild-type strain because all progeny are monosomic or trisomic and die early in development.

Akbari et al. (2015). Safeguarding gene drive experiments in the laboratory. Science; 349(6251): 927-8. http://www.sciencemag.org.ezproxy1.lib.asu.edu/content/349/6251/927.full.pdf

What safeguards and confinement strategies are available?

Molecular confinement involves building gene drives that can spread through populations of transgenic laboratory organisms but not wild organisms. For example, an sgRNA-only drive will spread exclusively through populations that already express Cas9 from an unlinked locus, while a Cas9+sgRNA drive targeting a synthetic sequence will only spread in transgenic laboratory populations with that sequence. Both methods are easy to implement and have been tested in yeast.

Ecological confinement involves performing experiments in a geographic area where escaped organisms won't be able to find mates. For example, ongoing experiments attempting to build gene drives in tropical mosquito vectors of diseases such as malaria and dengue are currently being performed in regions that don't have resident populations of the relevant mosquito species.

Reproductive confinement involves working with laboratory organisms that can't reproduce with wild ones. For example, Drosophila lines with compound autosomes are completely infertile when mated to wild fruit flies. It's also worth noting that gene drive experiments are less hazardous in organisms that seldom reproduce sexually because the drive must be much more efficient and minimally harmful in order to spread.

Barrier confinement seeks to keep the organisms in the laboratory. It varies by organism, but your local biosafety officer should be familiar with appropriate measures. Barriers should be a component of all gene drive confinement strategies, but they should not be relied on exclusively because historical studies of pathogen research have conclusively shown that barrier protocols are vulnerable to human error. And with gene drives, one mistake can be enough.

Reversal drives are designed to overwrite a previous gene drive and thereby undo the genetic changes driven by the earlier intervention. While an initial reversal drive cannot restore the exact original sequence, it can restore the original protein-coding sequence using a recoding strategy; a subsequent drive can restore the wild-type sequence (save for the residual sgRNAs and possibly cas9 gene). An immunizing reversal drive is a variant that also spreads through the wild population and immunizes it against the first drive. Laboratories interested in building candidate gene drives intended for eventual release should consider building an appropriate immunizing reversal drive at the same time to mitigate the potential effects of an accidental release.