Lifespan System-wide Policy
RRC 003

Subject:

File under: ORA

Lifespan Institutional Biosafety Committee (IBC)

Issuing Department:
Lifespan Office of Research Administration

Latest revision date: May 2018

Original Policy Date:
December, 2010

Page 1 of 18

Approved by:

John Murphy, MD
Executive Vice President,
Physician Affairs

Revision Dates
August 7, 2017

Peggy McGill, MA, CRA
Vice President,
Research Administration

I. **Purpose:** The purpose of this policy and Procedure Manual is to define and describe the policies and procedures regulating the Lifespan Institutional Biosafety Committee (IBC)

II. **Eligibility:** The entire research community of the Rhode Island Hospital, The Miriam Hospital, Emma Pendleton Bradley Hospital, Newport Hospital, collectively known as Lifespan for the purposes of this manual.

III. **Content:** The Manual is attached.

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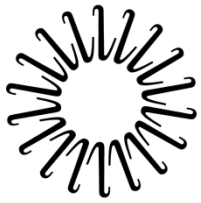

Lifespan

Institutional Biosafety Committee (IBC)

Policy and Procedure Manual

Contents

Institutional Biosafety Committee

IBC

Section 1: Introduction

1.1 Purpose

The purpose of the Institutional Biosafety Committee (IBC) is to assess appropriateness and adherence to Institutional guidelines of the proposed research activities utilizing recombinant DNA methods and materials, chemical hazards, and biological hazards in the laboratory setting.

1.2 Chemical and Biological Hazards

The purpose of IBC review regarding the use of potentially hazardous materials in the lab is to accomplish the following:

1. Assess and minimize risks of laboratory activities to the population within the Hospital (employees, patients and visitors).
2. Protect the research animal population from cross-contamination
3. Ensure compliance with pertinent codes and standards
4. To have in place a review mechanism as required by federal and state regulatory groups

For the purposes of IBC review; Hazardous Agents are defined as:

1. Chemical and biological agents that have been assigned a safety rating of 4 or greater in any category on the Safety Data Sheet (SDS)***
2. Any compound listed as a carcinogen, mutagen or teratogen in the Chemical Hygiene Plan
3. Any toxin including such proteins as ricin, cholera toxin and bacterial toxins
4. Any organism included in the list of Risk Group 2 (RG2) or higher or organisms in appendix B of the NIH Guidelines or organisms that require Biosafety Level Containment Level 2 (BSL2) or higher as defined by the Centers for Disease Control (CDC) manual Biosafety in Microbiological and Biomedical Laboratories (BMBL). Please note that at this time RIH does not have the facilities to handle Biosafety Level Containment Level 3 or 4.
5. Use of human source cells/tissue or any hazardous organism or chemical that will be administered to live animals as per IACUC protocol. Protocols with an animal component will submit a new (IBC) application every 3 years.

*** *See section 8.3* for the *list of commonly used hazardous agents created by the IBC committee that are considered exceptions and do not require review by the committee.*

1.3 Recombinant DNA

Recombinant DNA research conducted by the Lifespan research community must be conducted according to the most recent version of the NIH Guidelines For Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines). Recombinant DNA research conducted at Women & Infants Hospital is also assessed by this committee.

IBC review and approval is required before any project using recombinant DNA is initiated. This includes, but is not limited to: recombinant products, DNA probes, vector systems, and related materials received from outside sources. Additionally, projects which propose to administer agents created through recombinant methods to human subjects will also be reviewed by the IBC, even if those agents are determined to be Biohazard Level 1 (BL1).

Review by the IBC includes evaluation for compliance and conformance with the NIH Guidelines; assessment of the containment levels required by the Guidelines; assessment of the facilities, procedures and practices; and consideration of the training and expertise of personnel utilizing recombinant DNA.

1.3.a NIH Guidelines

The purpose of the *NIH Guidelines* is to specify practices for constructing and handling: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules. The *NIH Guidelines* detail safety practices and containment procedures for basic and clinical research involving recombinant DNA, including the creation and use of organisms and viruses containing recombinant DNA.

In the context of the NIH Guidelines, recombinant and synthetic nucleic acids are defined as: (i) molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids; (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or (iii) molecules that result from the replication of those described in (i) or (ii) above.

1.3.b Office of Biotechnology Activities (OBA) OBA

The NIH Office of Biotechnology Activities (OBA) promotes science, safety, and ethics in biotechnology through advancement of knowledge, enhancement of public understanding, and development of sound public policies. OBA accomplishes its mission through analysis, deliberation, and communication of scientific, medical, ethical, legal, and social issues. The Recombinant DNA Program within OBA promotes scientific advancement and safety in the conduct of basic and clinical recombinant DNA research. Institutional Biosafety Committees (IBCs) provide institutional oversight of recombinant DNA research governed by OBA and the *NIH Guidelines*.

Section 2: Institutional Biosafety Committee

2.1 Authority

Institutional Biosafety Committees (IBC's) derive their authority from the NIH. An institution must follow the *NIH Guidelines* if it receives any funding from the NIH for recombinant DNA research. Even if only one project of recombinant DNA research benefits from NIH support, all such projects conducted at or sponsored by that institution must comply with the *NIH Guidelines*. The Lifespan IBC is also charged with reviewing proposals for the use of potentially hazardous chemical and biological agents.

The President and CEO of Lifespan delegates authority through the Institutional Official (IO) to

appoint the chair(s) and members of the IBC. The Vice President, Research Administration is the appointed IO at Lifespan. The IO is given the administrative and operational authority to commit institutional resources to ensure compliance with the *NIH Guidelines* and other requirements.

The IBC's authority to review and approve protocols is independent of the IO, who may not overrule an IBC decision to withhold approval of a protocol. If the IBC approves a protocol, however, the Institution is not required or obligated to conduct the research activity. The Institution may also subject protocols to additional institutional review (e.g., department head, IRB, IACUC, etc.).

Lifespan has established an Institutional Biosafety Committee which is qualified through the experience and expertise of its members to oversee the Institution's program, facilities, and procedures.

The IBC Chairperson has the authority to immediately suspend any activity that endangers the facility or personnel safety. The suspension will be reported to the IBC for determination as to whether privileges will be reinstated or whether the suspension will be retained during the period of investigative review. A majority of members in attendance at a duly convened meeting at which quorum has been met are required to suspend research activities or research privileges. Suspension of privileges to use recombinant materials or methods, chemical hazards, or biological hazards will be reported in writing to the principal investigator, project sponsor, and NIH/OBA as applicable.

2.2 Composition

The IBC is composed of scientists and community members who review all research proposals involving recombinant DNA experiments, checmical hazards, or hazardous biological agents. The Committee shall consist of no less than 5 members recommended by their respective Department Head and appointed by the Institutional Official. At least two members shall not be affiliated with the institution and shall represent the interest of the surrounding community with respect to health and protection of the environment. Membership shall be qualified to meet the requirements for expertise as mandated by the *NIH Guidelines*. The Committee shall be known as the Lifespan Institutional Bisafety Committee (IBC) and shall meet once a month on an as-needed basis. The IBC will maintain certification of its membership with the NIH Office of Biotechnology Activities (OBA).

2.3 Responsibilities of the Committee

1. Review of research protocols which use recombinant DNA agents or methods, checmical hazards, and biological hazards in regards to containment levels, laboratory facilities, practices, and procedures.
2. Develop policies and procedures to address safety precautions to be taken for the use of specific agents (e.g. ether) or activities (e.g. lab construction, relocation, or renovation) as needed.
3. Notify the principal investigator of the results of the committee's review.
4. Ensure the research staff has adequate training and expertise to perform proposed research.

5. Ensure timely periodic inspections of laboratory facilities.
6. Maintain an inventory of Biohazard Level – 2 (BL-2) or higher biological agents used for recombinant research. [i.e. BL2 agents include viral vectors of any type, plasmids containing whole viral genomes, plasmids containing viral genes to be used for packaging, plasmids containing transforming genes (such as SV40 large T antigen), or stable cell lines containing any of these constructs, or bacterial agents that will be genetically modified.].
7. Serve as a resource for those investigators conducting research involving recombinant DNA and hazardous chemical and biological agents.
8. Report any significant problems with or violations of the NIH guidelines and any significant research-related accidents or illnesses to the appropriate institutional official and NIH/Office of Biotechnology Activities (OBA) within 30 days.
9. Address inquiries, complaints or problems regarding the use of recombinant agents, hazardous biological or chemical agents, laboratory activities, and the like.
10. Upon request, provide copies of IBC minutes and membership roster.

2.4 Responsibilities of Principal Investigators

The Principal Investigator is responsible for:

1. Fully complying with the NIH Guidelines in conducting any recombinant DNA research.
2. Registering all work involving all recombinant DNA agents or procedures and all work involving hazardous agents or procedures with the IBC.
3. Assuring that all review and approval requirements are fulfilled prior to initiating any new or modified research procedures.
4. Ensuring and documenting that employees are adequately trained in safe work practices and techniques, in the procedures for dealing with accidental spills and personal exposure, and that employees adhere to these procedures and practices.
5. Providing copies of the protocols and safety information sheets to laboratory staff.
6. Assuring that necessary safety precautions and containment are maintained within the laboratory.
7. Ensuring proper handling and disposal of biohazardous and chemical waste.
8. Maintaining current Safety Certifications for the laboratory.
9. Notifying the IBC of any significant changes in experimental protocol or location of the research.
10. Providing information to the IBC as necessary.
11. Maintaining current BL2 agent and Chemical Inventories and having them available upon request.

2.5 Conflict of Interest

No IBC member "may participate in the review or approval of an activity in which that member has a conflicting interest, (e.g. is personally involved in the activity) except to provide information requested by the IBC."

For a complete description of the Lifespan policy and procedure regarding the registration and management of conflicts of interest please refer to the policy, ORA GEN 003. The Project Director, Principal Investigator (PD/PI), and any other person, regardless of title or position, who is **responsible** for the design, conduct or reporting of research that is conducted at Lifespan must

report on their status of conflicts of interest at least annually. The Principal Investigators of each project are responsible for determining which people (e.g., co-investigators, collaborators, staff, trainees, consultants, etc.) meet the definition of "investigator" and are responsible for the filing of conflict of interest disclosures for each person. The Principal Investigators are also responsible for ensuring that all members of the research team have completed the required COI training.

When they have reviewed a disclosure that may impact the review of a protocol by the IBC, the Lifespan Research Conflicts of Interest Committee promptly communicates to the IBC in writing. The IBC may participate in the development of a management plan of the conflict, if appropriate. In no case may research proceed on a project until the disclosed conflict is reviewed and resolved by the Lifespan Research Conflicts of Interest Committee.

For additional guidance, Lifespan's Corporate Compliance Policy #46, "Interaction with Industry Representatives (Pharmaceutical, Medical, Device and Medical Supply Industries)", Lifespan's Corporate Compliance Policy #09, "Conflicts of Interest" and Lifespan's Materials Management Policy #150, "Institutional Purchasing: Conflict of Interest Guidelines" further describe Lifespan's position on conflicts of interest.

An IBC member may also have professional or personal conflicts of interest. An IBC member is said to have a conflict of interest whenever that person, his or her spouse/partner, or dependent child falls under any one of the above conditions, or:

- Is an investigator or sub-investigator on the protocol.
- Is involved in a potentially competing research program.
- Access to funding or intellectual information may provide an unfair competitive advantage.
- A member's personal biases may interfere with his or her impartial judgment.
- Has identified him or herself for any other reason as having a conflict of interest.

IBC members and consultants will not participate in any IBC action taken, including the initial and continuing review of any project, in which the member has a conflict of interest, except to provide information requested by the IBC. IBC members are expected to self-identify conflicts of interest on the COI form prepared for each full board meeting.

If the investigator submitting a protocol believes that an IBC member has a potential conflict, the investigator may request that the member be excluded. The Chair (or in his/her absence, the vice Chair or an Associate-Chair) will present the declared conflict and the Committee will determine whether a conflict exists. Should an IBC member declare involvement in any way in a research protocol under review by the IBC, or state a conflict of interest with the research protocol, then the member(s):

- Decline to serve as a primary reviewer of the application
- May remain in the meeting room to provide information requested by the IBC;
- Leave the meeting room for discussion and voting; and
- Are not counted towards quorum.

2.6 Quorum Requirements

Lifespan defines a "quorum" as more than half of the regular IBC voting members.

A protocol is approved only if a quorum is present, and if more than 50% of the quorum votes in favor of protocol approval. For reasons other than conflict of interest, abstentions from voting do not alter the quorum or change the number of votes required. For example: If the IBC has 15 voting members, at least 8 members must be present at a convened meeting to constitute a quorum and approval of a protocol would require a minimum of 5 of those 8 votes whether or not there were abstentions.

2.7. Public Access

IBC meetings are open to the public upon request. Meeting dates and contact information for the IBC Chairperson, Manager, and Coordinator are posted on the IBC website.

Upon request, the institution shall make IBC meeting minutes available to the public in either paper or electronic format. Although not typically included in the minutes, any proprietary information contained therein would be redacted before release.

Questions or comments about the committee should be referred to the Manager, Coordinator, or Chair who will bring this to the full committee at the next meeting to formulate a response. Any relevant comments will be forwarded to the OBA.

3. Review Procedures

The IBC review is conducted by way of a convened meeting, with some members participating by teleconference. Application forms for recombinant DNA and chemical/biological hazards are accessed from the electronic protocol management system. Research proposals are then submitted through the electronic system and will be processed for review by IBC staff.

Minutes of Committee meetings will be recorded, transcribed and maintained for inspection by IBC staff. Notice of meeting schedule and application due dates will be posted in the electronic protocol management system, and also on the Office of Research Administration website https://www.lifespan.org/office-research-administration/institutional-biosafety-committee-ibc.

3.1 New Applications

3.1.a Recombinant DNA

Recombinant DNA applications that are thought to be exempt will be forwarded to the Chair for review. If the research is determined to be exempt according to NIH Guidelines, the investigator will receive a notice of review status from IBC staff. If the Chair determines that the research does not meet the definition of exempt research as described in the NIH Guidelines, the application will be processed for full board review by the convened committee. For applications that require full board review, two primary reviewers will be assigned to review the protocol. If the assigned reviewer feels he/she has a conflict of interest, or lacks sufficient expertise to review the protocol, an alternate reviewer may be requested. All IBC members will have access to the application through the electronic protocol management system. The principal investigator or a

representative who is knowledgeable about the proposed research and competent to discuss the protocol will be asked to appear before the Committee at the next monthly meeting to present the research for review. After committee review is complete, the members will vote to approve, approve with modifications required to secure approval, or defer the proposal for further consideration at a later date. In some cases, the committee may feel the proposal should not be implemented and will so indicate.

3.1.b. Biological and Chemical Hazards

Applications to use chemical or biological hazards must include information with regard to the agents used, their hazards, and precautions planned.

Expedited Review

A list of commonly used hazardous agents has been created by the committee to be reviewed on an expedited basis. (See section 8.3.)

For proposals that are eligible for expedited review, the signed expedited application form is sent to the Chair or designee for review. The reviewer will then return any comments, corrections, or concerns. The reviewer has the authority to approve, approve with minor modification, or defer to the full board any expedited application.

Full Board Review

For proposals that require full board review by the convened committee, all IBC members will have access to the application through the electronic protocol management system. The investigator may be asked to appear before the Committee at the next monthly meeting to present the research for review.

3.2 Continuing Review

3.2.a. Recombinant DNA

Those protocols that use BL-2 or higher microorganisms, as determined by the IBC, will be reviewed at least once annually and more frequently if the Committee feels it appropriate. The investigator will be required to complete a progress report for continuing review. Reminder notices will be sent 90, 60, and 30 days before the expiration date. Failure to submit a complete progress report will result in expiration of IBC approval of the research protocol until the report is filed, reviewed and approved for continuation. Failure to submit a complete progress report within 30 days of the expiration notice will result in termination of the project. Those protocols deemed exempt will not be required to undergo continuing review.

3.2.b. Biological or Chemical Hazards de novo Review- animal protocols

Approval to use biological or chemical hazardous agents in animals must be renewed every 3 years through the submission of a new application.

3.4 Changes to Protocol

It is the responsibility of the investigator to notify the IBC in writing of any substantive intended change in the approved research activity. For example, the addition of a new viral vector, new

cell line, or new bacterial strain with a different safety profile would be considered to be substantive changes which require review and approval by the IBC prior to initiation. Requests for revision must be submitted through the electronic protocol management system, using the designated form. Such requests that do not appear to directly involve handling of recombinant DNA material or hazardous agents, and do not appear to involve patient/personnel/animal safety, will be forwarded to the Chair or Vice Chair in the Chair for expedited review. The Chair/Vice Chair will review the requested change and determine whether it requires review by the full committee and/or any change in the original biosafety classification. The reviewer has the authority to approve, approve with minor modification, or defer to the full board any request for revision to protocol. The Committee will be notified of all expedited reviews on the next agenda. Work on the amended protocol will not be undertaken until a letter of approval is issued by the Committee for the requested change.

3.5 Administrative Review

Should an investigator submit a DNA protocol to more than one funding agency, the initial application will be given a full review by the Committee. Subsequent submissions will be given an Administrative Review provided the investigator notifies the Chair in writing that the recombinant DNA portions of the subsequent application(s) are indistinguishable from the original, noting the date of the original approval. The Chair will review the application and approve the subsequent application(s) without requiring a review by the primary reviewers or full committee. An approval letter will be issued for each subsequent application. If the original application requires a continuing review then that review must be current (within the last 12 months).

Section 4: Reporting Incidents, Accidents and Violations

4.1 Accidental Exposure

Personnel exposed to recombinant DNA materials or other hazardous agents through splash, spills, needle sticks, inhalation, or other routes must report immediately to Employee and Occupational Health Services. If the incident occurs outside of routine business hours, then the individual must go to the Emergency Department. Principal Investigators are required to maintain Safety Information Sheets for the recombinant BL2 agents in use and Safety Data Sheets (SDS) for hazardous chemical agents. These forms must be readily available to staff and include information regarding toxicity, infectivity, and replication competence. Personnel should bring a copy of the Safety Information Sheet for the agent to assist medical personnel who will provide treatment for the accidental exposure. The PI must report accidental exposures to the IBC as an unanticipated problem.

4.2 Types of incidents involving recombinant DNA that must be reported to the NIH OBA

Under Section IV-B-2-b-(7) of the *NIH Guidelines* states that IBCs should report "...any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses" to NIH OBA within 30 days. Appendix G of the *NIH Guidelines* specifies certain types of accidents that must be reported on a more expedited basis. According to Appendix G-II-B-2-k, spills or accidents in BL2 laboratories resulting in an overt exposure must be immediately reported to NIH OBA (as well as the IBC). According to Appendix G-II-C-2-q

and Appendix G-II-D-2-k, spills or accidents occurring in high containment (BL3 or BL4) laboratories resulting in an overt or potential exposure must be immediately reported to NIH OBA (as well as the IBC, and Biological Safety Officer (BSO).

Minor spills of low-risk agents not involving a breach of containment that were properly cleaned and decontaminated generally do not need to be reported. OBA staff should be consulted if IBCs, investigators, or other institutional staff are uncertain whether the nature or severity of the incident warrants reporting to OBA.

4.3 Responsibility to report

Reporting to NIH OBA is the responsibility of institution's, IBC Chair, BSOs, and PIs under Sections IV-B-1-j, IV-B-3-c-(2), and IV-B-7-a-(3), respectively. Institutions have the discretion to determine which party should make these reports, and one report for each incident or set of information is generally sufficient.

4.4 Information to be included within an incident report

Incident reports should include sufficient information to allow for an understanding of the nature and consequences of the incident, as well as its cause. A detailed report should also include the measures that the institution took in response to mitigate the problem and to preclude its reoccurrence.

Office of Biotechnology Activities
National Institutes of Health
6705 Rockledge Dr., Suite 750
Bethesda, MD 20892-7985
Phone: (301)-496-9838
Fax: (301) 496-9839

Section 5: Special Topics

5.1 Review of Research Utilizing Gene Transfer Technology

The IBC recognizes that research utilizing gene transfer technology in human subjects requires additional considerations for review and monitoring. Research involving human subjects treated with gene transfer methods will be reviewed by both the IBC and the Institutional Review Board (IRB). IBC responsibility for the review of gene transfer technology protocols includes, but is not limited to, safety and efficacy of the virus in human subjects and occupational safety of research and hospital staff.

All human gene transfer studies should if appropriate, be reviewed and approved by the Recombinant DNA Advisory Committee (RAC) at the NIH Office of Biotechnology (OBA) prior to initiation. All serious adverse events must also be reported to RAC.

The IBC requires a written report on: (1) any serious adverse event that is both unexpected and associated with the use of a gene transfer product; and (2) any finding from tests in laboratory animals that suggest a significant risk for human research participants. Furthermore, all other relevant committees and agencies must be included in the

appropriate content, format and time frame for each committee or agency respectively. The time frame for reporting a verbal report to all agencies is within 24 hours of event with a written report submitted by 48 hours from onset of event. Any study will go on automatic hold at time of serious adverse event until fully investigated and cleared by all relevant agencies and committees.

The IBC encourages the use of the GeMCRIS database for reporting adverse events on human gene transfer trials. For more information regarding GeMCRIS please visit: http://oba.od.nih.gov/rdna/adverse_event_oba.html

The IBC primary reviewers assigned to examine the application with regard to recombinant DNA issues will be available to the IRB as scientific consultants. The IBC reviewers or the Chair will be available to present the recombinant DNA perspective to the IRB upon request. In return, the IBC may request that the IRB primary reviewers or designates be available to advise the IBC of human subjects protection concerns. Joint review will be coordinated by the Compliance Manager or the IBC Coordinator. Adverse events involving research participants involved in gene transfer technology protocols will be reviewed by both the IRB and the IBC, in accordance with IRB adverse event reporting policy.

5.2 Use of hazardous chemical and biological agents in animals

Each Principal Investigator is responsible for the care of animals in areas where hazardous agents are used and is responsible for ensuring that laboratory staff are supervised and trained. PIs or their designee must provide at least one week's notice to CRF Management before using the hazardous agent in live animals to allow for training of CRF animal care staff. The PI or an appropriate designee must also be present and assist with training CRF animal care staff in the proper handling and containment of the hazards before any use in animals. IBC approval documents will not be released until appropriate training for lab personnel and CRF animal care staff has been documented and submitted to the Committee Coordinator.

5.3 Use of recombinant DNA BL1 and BL2 Agents in Animals

All projects involving both recombinant DNA and animals will be designated BL-1 or BL-2 by the IBC at the time of initial review.

Requirement for BL-1 Agents:

Work involving non-human source cells previously modified in culture by the introduction of replication incompetent retroviral vectors would be considered animal level BL-1, as described in NIH Guidelines for Research Involving Recombinant DNA (NIH Guidelines), Section III-D-4-a. Standard CRF housing and husbandry procedures will be followed for animals on BL-1 protocols.

Requirements for BL-2 containment:

Genetic engineering has made viral vectors safer by designing them to be replication defective outside of specialized packaging cell lines. This greatly limits the possibility of generating replication competent virus which poses a higher risk of infection.

Replication defective viral vectors are handled at BL-2 in the laboratory because of their potential to enter human cells, deliver genetic material, and elicit an immune response. Viral vectors in this category include adenovirus, adeno-associated virus, lentivirus, and retrovirus.

Administration of viral vectors in animals likewise must be performed in an animal BL-2 animal holding room. Data has shown that shedding (excretion) of virus particles significantly decreases after 72 hours, post inoculation.

The IBC requires that animal work done by personnel from a laboratory that is directly administering viral vectors or BL-2 agents be conducted under NIH precautions for Animal Biosafety Level 2 (BL-2). Rodents involved in this research will be housed in an appropriate animal room of the Central Animal Facility (CAF). The animal handling and husbandry procedures for Animal Biosafety Level 2 (ABLS2) are described in the CAF Policy and Procedure Manual.

5.4 Inspection of Laboratory Facilities

The Safety Officer is charged with performing periodic inspections to ensure that laboratory standards are rigorously followed. Any significant problems relating to chemical, biological hazards, or recombinant DNA research that are encountered as a result of these inspections should be promptly reported to the IBC.
In conjunction with the laboratory inspections conducted by the chemical hygiene officer the IBC will ensure that annual inspections are conducted in those laboratories performing recombinant DNA research to ensure that laboratory standards are rigorously followed. The IBC will maintain and update a list of laboratories that conduct recombinant DNA research.

5.5 Inventory of Material Transfer Agreements and Distribution of BL-2 (and Higher) Biological Agents

The *NIH Guidelines* for Recombinant DNA Research requires that the IBC monitor the use of vectors derived from viruses and/or cell lines with incorporated viral sequences. To comply with this requirement, the Office of Research Administration (ORA) will maintain a file of material transfer agreements. The investigator is required to maintain an inventory of BL-2 agents that are used within the lab. The inventory will be updated at the time of annual laboratory inspection and the investigator will be responsible for final accountability of the inventory at the time he/she leaves the institution.

5.6 Waste disposal of recombinant DNA materials

Recombinant DNA materials must be disposed of by following hospital disposal regulations. All sharps, including pipet tips, must be disposed of in sharps containers. Lab waste must be disposed of in red bag waste container. Liquid waste from cultures must be treated with the addition of stabilized sodium hypochlorite such as Dispatch, or freshly prepared bleach to a final concentration of 10% and allowed to sit for at least 5 minutes before disposal down the sink.

5.7 Screening for Replication Competent Viruses

Recombination events or contamination with wild type viruses can result in the production of replication competent virus (RCV) in a population of replication deficient viral stocks. The IBC

requires testing for the presence of RCV in viral stocks and the method of testing must be indicated in the appropriate section of the application. For each category of viral vector, (e.g.: adenoviral viral, retroviral vector or lentivirus derived vector) refer to Section 7.3 for links to the recommended procedures for the detection of RCV.

Section 6: Education and Training

Principal Investigators (PIs) are responsible for providing specific training to their staff regarding the agents to be used in the lab (e.g. BL-2 agents, chemical and biological hazards). PIs must maintain documentation of this training, and provide it with all new and continuing applications. In addition the IBC will on an as-needed basis, provide interested members of the research community with additional educational and training information necessary for the investigator to maintain a safe laboratory environment and to ensure research conducted in the laboratory is within the *NIH Guidelines*.

A member of the IBC will be present and assist with training of laboratory staff and CRF animal care staff on hazardous agents that will be used in live animals. Approval documents will not be released until training of lab personnel has been documented.

6.1 Training Requirements

Recombinant agents:
The IBC has created an on-line training program that should be completed by all investigators and research staff in the laboratory before initiating recombinant DNA work.
See www.citiprogram.org, Lifespan Recombinant DNA and Biosafety Course.

Hazardous Chemical and Biological Agents:
PIs are to provide specific training for employees regarding:

-Hazardous agents used in their departments
-OSHA's Hazard Communication Standard
-Interpreting Safety Data Sheets
-How to interpret cautionary information on container labels
-How to protect themselves and others when using hazardous materials
-How to deal with a hazardous materials spill, accident, or other emergency
-Applicable Lifespan and departmental policies and procedures concerning hazardous materials including proper disposal of hazardous waste

Employee's educational background and past experience are taken into consideration when developing training plans. Supplemental training takes place if new hazardous substances are used in the work area and general precautions and procedures are reviewed annually. Employees are to be familiar with important concepts, understand them, and demonstrate that they know how to safely handle and use workplace chemicals.

PIs must keep attendance records on all employees who receive training or retraining involving hazardous substances. These records must be available upon request and at the time of annual lab inspections.

Section 7: Noncompliance with IBC Protocol;, Policies, Procedures, or Decisions

Protocol non-compliance occurs when procedures or policies approved by the IBC are not being followed. Examples include performing unauthorized procedures, unauthorized persons participating in a research project, or the use of hazardous agents that the IBC has not approved. When faced with protocol non-compliance, the IBC's first step will be to investigate the incident. When non-compliance is confirmed then it will be determined if there was intentional, unintentional or continuing non-compliance.

Based on this determination the following steps will be taken with the goal of bringing the protocol into compliance as quickly as possible:

Unintentional non-compliance

If a clearly minor and unintentional misinterpretation of an IBC policy that has created no problem for human health or welfare is noted, an explanation describing the problem and the corrective steps taken will be requested.

Intentional or continuing non-compliance

When it has been determined by the IBC that an offense was intentional or continuing non-compliance, the response will be based upon the severity of the event and may include:

- Written warning to the PI
- Mandatory retraining for the PI and their research staff
- Required attendance at a convened meeting of the IBC to explain corrective actions taken to prevent a recurrence of the incident
- Implementing measures to prevent recurrence
- Suspension of privileges regarding the use of hazardous agents
- Notifying the PI's department head
- Notifying the Institutional Offical

Section 8: Resources

8.1 Member Roster

Please contact the Committee Coordinator for the most recent list of IBC members
(kbrilliant@lifespan.org, 444-2093)

8.2 FORMS:

Please be sure to download the most recent version of the forms for all submissions from the electronic protocol management system (www.IRBNet.org)

Recombinant DNA forms

- Recombinant DNA Application
- Progress Report

- BL-2 Employee Training
- Safety Information Sheets for Recombinant DNA Materials
  - Viral
  - Non-viral

Recombinant DNA Guidance Documents

- Recommended Testing Procedures for Adenoviral Vectors and Replication Competent Virus - Annual Requirement for Biosafety 2 Approval
  - Adenovirus
  - Retrovirus
- S.O.P. for Handling and Storage of Human Subject Study Reagents Utilizing Recombinant DNA in Viral Vectors
  - guidance

Chemical and Biological Hazard forms

- Biohazards and Lab Safety Application form
- BSL2 Training Document

8.3 Expedited Review List

Chemical hazards

1. Bromodeoxyuridine (Brdu) when used in animals
2. 5-ethynyl-2'-deoxyuridine (EdU) when used in animals
3. Cisplatin
4. Doxorubicin
5. Streptozotocin (STZ)
6. Tamoxifen

Biological hazards

1. Human Primary cells, cell lines and tissues when used in animals
2. Lipopolysaccharide (LPS) when used in animals

Commonly used hazardous agents not needing review

1. Formalin
2. Paraformaldehyde

8.4 Safety Resources

Please refer to the Environmental Safety Department website for additional information.