

SAFETY OF PERSONNEL ENGAGED IN RESEARCH

- 1. REASON FOR ISSUE.** This Veterans Health Administration (VHA) Handbook establishes policies for ensuring the safety of personnel engaged in research.
- 2. SUMMARY OF MAJOR CHANGES.** There are no major changes.
- 3. RELATED DIRECTIVE.** VHA Directive 1200.
- 4. RESPONSIBLE OFFICE.** The VHA Office of Research and Development (12) is responsible for the contents of this VHA Handbook. Questions may be addressed to (202) 461-1690.
- 5. RESCISSION.** VHA Handbook 1200.8 dated June 7, 2002, is rescinded.
- 6. RECERTIFICATION.** This VHA Handbook is scheduled for recertification on or before the last working day of March 2010.

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DISTRIBUTION: CO: E-mailed 3/10/2009
FLD: VISN, MA, DO, OC, OCRO, and 200 – E-mail 3/10/2009

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SAFETY OF PERSONNEL ENGAGED IN RESEARCH

1. PURPOSE

Ensuring personnel safety in Veterans Health Administration (VHA) research necessitates oversight at the national and local levels. This VHA Handbook prescribes procedures involving the use of potential hazards encountered in these settings, including, but not limited to:

- a. Biohazards, such as:
 - (1) Pathogens and etiologic agents corresponding to Biosafety Levels (BSL) 1-4, and
 - (2) Organisms and viruses containing recombinant deoxyribonucleic acid (DNA) molecules.
- b. Chemical hazards.
- c. Physical hazards.

NOTE: This Handbook covers safety issues in research laboratories. It is not intended to replace general occupational safety and health policy applicable to all Department of Veterans Affairs (VA) employees, whether or not involved with research, or to replace specific regulatory programs mandated by law.

2. DEFINITION OF HAZARD CATEGORIES

NOTE: Hazards encountered in research laboratories vary among medical centers according to the nature of research being conducted. This variability does not affect the mandatory policies described in this Handbook.

- a. **Biohazards.** Biohazards include, but are not limited to, the following:
 - (1) Pathogens and etiologic agents, human and non-human primate tissues including blood and body secretions, and human cell lines corresponding to BSL 1-4 (see subpar. 10a);
 - (2) Toxins produced by microbial organisms (see subpar. 10a);
 - (3) Poisonous, toxic, parasitic, and venomous animals or plants;
 - (4) Recombinant DNA molecules (see subpar. 6g.);
 - (5) Select agents, as specified in Title 42 Code of Federal Regulations (CFR) Part 73; 7 CFR 331; and 9 CFR 121; and
 - (6) Animals experimentally or naturally exposed to any of the preceding (see subpar. 10a).

b. **Chemical Hazards.** Chemical hazards include any substance or mixture of substances with properties capable of producing adverse effects on the health and safety of humans (see subpar. 3a(2)). Chemical hazard categories include, but are not limited to, the following:

- (1) Corrosives;
- (2) Toxic substances (poisons, irritants, asphyxiates);
- (3) Sensitizers;
- (4) Carcinogens, mutagens, and teratogens;
- (5) Flammables; and
- (6) Explosives.

c. **Physical Hazards.** Physical hazards include, but are not limited to, the following (see subpar. 3a(3)):

- (1) Ionizing and non-ionizing radiation (see App. D),
- (2) Noise,
- (3) Vibration,
- (4) Extremes of temperature and pressure,
- (5) Explosive hazards,
- (6) Electrical hazards, and
- (7) Mechanical hazards.

3. SCOPE

a. Research laboratories are included in the medical center-wide written occupational safety and health program. The role and responsibilities of the Research Office is defined within this program. Research offices must maintain a Research Safety Program that is consistent with VA policies, Federal statutes and regulations from Occupational Safety and Health Administration (OSHA), the Environmental Protection Agency (EPA), the Nuclear Regulatory Commission (NRC), etc., and any applicable State and local requirements. All applicable National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC) guidelines must be followed (see subpar. 10a).

(1) **Biohazards.** The medical center research office must develop a service-wide safety manual. It shall include a description of biohazard controls (e.g., engineering, procedures, and personal protective equipment), emergency procedures, and an emergency cascade phone list

specific to the facility. This document must be updated, reviewed, and approved annually by the Subcommittee on Research Safety (SRS) and forwarded to the Research and Development (R&D) Committee for approval. Individual laboratories must adhere to CDC and NIH safety and health guidelines. Those laboratories that work at BSL 3 containment (see App. A) must maintain a separate, written, regularly updated laboratory manual that includes standard operating procedures and emergency procedures, and includes, but is not limited to a: spill, power outage, or breach of security.

(a) Bloodborne Pathogens. The risk of exposure to bloodborne pathogens will be minimized in the research setting by ensuring that all research personnel are aware of, and utilize, universal precautions in the handling of biologic fluids of any type according to the specifications of the Bloodborne Pathogen Standard (see subpar. 10e(6)). Similarly, the risk of exposure to airborne pathogens such as Mycobacterium tuberculosis must be minimized and strict adherence to all applicable Federal statutes, regulations, policies and guidelines must be rigorously upheld.

(b) Recombinant DNA Research

1. VA investigators planning to conduct recombinant DNA research must comply with the most current Guidelines for Research involving Recombinant DNA Molecules (see subpar. 6g), regardless of the source of research funding.

2. VA investigators should note that all funded and unfunded projects and proposals must be reviewed and approved according to the procedures described in the most current NIH Guidelines for Research involving Recombinant DNA Molecules. Local SRS and R&D Committee approvals are also required.

(2) **Hazardous Chemicals and Waste**. This Handbook does not address the policies relating to the management of hazardous chemicals and waste in detail. However, the research laboratory program must ensure that all Federal and State occupational safety and health, transportation and shipping, and environmental regulations are adequately addressed. As an example, Federal regulations (see subpar. 10e(8)) require the development of a “chemical hygiene plan” and the administration of this plan by a “chemical hygiene officer.”

(3) **Physical Hazards**. Physical hazards are addressed in the Research Safety program to minimize risk and ensure regulatory compliance. Routine laboratory inspections by facility safety personnel and research personnel must include a review of all potential physical hazards. As needed, inspections must be coordinated with program managers and technical experts such as the Radiation Safety Officer.

b. The provisions of this handbook apply to all research that is conducted completely or partially in VA facilities, conducted in approved off-site locations and facilities, or conducted by VA researchers while on VA official duty time. The research may be VA funded, funded from extra-VA sources, or conducted without direct funding. As a minimum, facility safety personnel must verify that other or remote facilities adhere to health and safety standards that are equivalent to VA standards.

4. RESPONSIBILITIES OF THE FACILITY DIRECTOR

The facility Director is responsible for:

a. Ensuring that the research safety program is staffed adequately and that resources are available to maintain full compliance with all applicable regulations and standards of safety.

b. Ensuring that all Research personnel are included in the facility Occupational Safety and Health program and that research space is included in annual workplace inspections.

NOTE: Research personnel must be covered by all other facility safety programs (e.g., the Respiratory Protection program, the Fire Safety program, etc.)

c. Ensuring the resolution of any facilities-related deficiencies identified in inspections.

d. Providing engineering support in conducting ventilation maintenance and validation of required specifications.

e. Providing the technical assistance of facility safety and health professionals as needed.

f. In cooperation with the Associate Chief of Staff (ACOS) for R&D or Coordinator for Research (C for R&D), ensuring that measures for the security of the research laboratories and surrounding space is developed (see App. E).

g. Providing adequate administrative support for SRS, including:

(1) Space sufficient to provide privacy for conducting sensitive duties related to biosafety,

(2) The personnel to support the review and record-keeping functions of SRS, and

(3) Support for the timely preparation of investigator correspondence and other documents.

5. RESPONSIBILITIES OF THE ASSOCIATE CHIEF OF STAFF FOR RESEARCH AND DEVELOPMENT OR THE COORDINATOR FOR RESEARCH AND DEVELOPMENT

The ACOS for R&D or C for R&D is responsible for:

a. Ensuring that safety related communications from the Chief Research and Development Officer (CRADO) are disseminated to appropriate personnel on time after receipt.

b. Ensuring the responses to safety “holds.”

c. Ensuring that research activity ceases until a particular “hold” is lifted.

d. Ensuring continuous development and evaluation of performance standards of the Research Safety program.

6. RESPONSIBILITIES OF THE RESEARCH AND DEVELOPMENT COMMITTEE

a. The R&D Committee must establish either an SRS or multiple subcommittees dealing with different aspects of research safety. In some instances alternate safety oversight and review mechanisms may be developed with an affiliate safety committee or committees.

(1) Pre-approval by the CRADO is required to use such an alternate mechanism.

(2) The alternate mechanism does not absolve the R&D Committee from any responsibilities related to the SRS functions.

(3) If using the services of an external subcommittee, VA interests must be adequately represented by the inclusion of at least one VA employee with appropriate qualifications.

(4) The SRS must meet the requirements found in Appendix B.

b. The R&D Committee is responsible for:

(1) Reviewing all R&D proposals.

(a) Ensuring the SRS review of those protocols and submissions for funding that involve safety hazards to personnel and the environment.

(b) Prior to review of a proposal, ensuring that a complete list of chemicals designated or identified by OSHA or EPA as “hazardous” (see subpar. 10e(4), subpar. 10e(7), or applicable State requirements) has been reviewed and approved by the Safety Officer. **NOTE:** *This chemical inventory is reviewed and maintained locally; and it is not submitted along with the research proposal submitted to Office of Research and Development (ORD) for funding consideration.*

(2) Acting upon SRS recommendations for approval or non-approval of reviewed proposals submitted to ORD for funding consideration.

(3) Reviewing and acting upon SRS minutes.

(4) Appointing a Research Safety Coordinator who is responsible for supervising and operating the Research Safety Program. Specific responsibilities for this position must be specified in the written local policy of the Research Safety Program. **NOTE:** *The ACOS for R&D or C for R&D generally assumes this role.*

(5) Appointing a Biological Safety Officer, if research is conducted at the facility involving:

(a) The use of recombinant DNA at BSL 3 or 4, or

(b) Large scale (greater than 10 liters of culture) research or production activities involving viable organisms containing recombinant DNA molecules (see subpar. 10h).

NOTE: This may require establishing a “Biosafety Committee” according to the National Institutes of Health (NIH) Guidelines, which may be merged into the SRS, if all specifications are met. In all cases this committee or subcommittee must report to the R&D Committee following review of protocols involving recombinant DNA that are covered by NIH Guidelines for Research Involving Recombinant DNA.

- (6) Ensuring the development and implementation of the laboratory Chemical Hygiene Plan.
- (7) Appointing a Chemical Hygiene Officer to provide technical guidance on the implementation of the Plan. The Chemical Hygiene Officer should be a standing member of the SRS.
- (8) Overseeing compliance with this VHA Handbook by Principal Investigators (PIs) conducting research at the facility.
- (9) Ensuring the development and implementation of safety protocols by the PI for individual research projects as needed.
- (10) Ensuring that the Research Office provides support to the SRS to assist in their functions.
- (11) Ensuring that the minutes of SRS meetings are documented correctly (see App. D), and maintained by the Research Office.
- (12) Providing the ACOS for R&D or C for R&D, and facility, or Veterans Integrated Service Network (VISN) safety officials with adequate information to evaluate the performance of the R&D safety program.
- (13) Ensuring coordination with other regulatory programs or committees such as the Radiation Safety Officer or Radiation Safety Committee.
- (14) Reviewing accident and injury trends reported by SRS. Recommending and ensuring the implementation of corrective action.
- (15) Reviewing all citations issued by regulatory agencies and ensuring that appropriate committee members and PIs take prompt corrective actions, and coordinating the necessary responses to regulatory agencies.

7. RESPONSIBILITIES OF THE SUBCOMMITTEE ON RESEARCH SAFETY

The SRS is responsible for:

- a. Reviewing all research activities involving biological, chemical, physical, and radiation hazards for compliance with all applicable regulations, policies, and guidelines prior to submission for R&D funding. This includes a review of all research applications for funding that will be conducted at the VA facility or by VA personnel with VA funding located off-site.

(1) The review VA Form 10-0398, Research Protocol Safety Survey (RPSS), (see App. F) must include a risk assessment of the facilities, level of containment, laboratory procedures, practices, training and expertise of personnel involved in the specific research conducted including recombinant DNA research (see App. A).

(2) All research projects involving biological, chemical, physical, and radiation hazards must be approved by SRS and then by the R&D Committee prior to commencement. SRS must review proposed research at convened meetings at which a quorum (majority of voting members) is present. *NOTE: For the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. A quorum must be maintained for each vote to occur. If a quorum is not maintained, the protocol must be tabled and only non-protocol related issues may be discussed.*

b. Providing written notification of the results of SRS review to the R&D Committee, the Research Office, and the PI.

c. Reviewing annually all active research protocols involving biological, chemical, physical, and radiation hazards, regardless of funding status or source. The date of continuing review will be based on the date of SRS approval. Research protocol changes not included in the original application must be documented on an amended RPSS (see App. F) and must be submitted to and reviewed by SRS prior to the implementation of the changes.

d. Ensuring that a complete list of all products containing chemicals designated or identified by OSHA or EPA as “hazardous” (see subpar. 6c (8), subpar. 6e (2), or applicable State requirements) has been submitted to the Safety Officer for review and approval prior to the submission of a protocol for local review.

e. Coordinating all safety-related activities in research laboratories including mandatory and non-mandatory training, safety inspections, accident reporting, and liaison activities with all facility safety committees and officials to include:

(1) Coordinating follow-up evaluations to ensure that deficiencies cited during inspections are permanently and effectively abated, and

(2) Reporting follow-up results to the R&D Committee.

f. Reporting operational problems or violations of directives to the Research Office within 30 days of occurrence or detection, unless SRS determines that a report has been previously filed by the PI.

g. Identifying the need for health surveillance of personnel involved in individual research projects; and if appropriate, advising the R&D Committee and Employee Health Practitioner on the need for such surveillance.

h. Maintaining adequate documentation of all the SRS or equivalent subcommittee activities.

i. Forwarding minutes of SRS to the Research Office (see App. C).

- j. Ensuring that all laboratory personnel receive annual research specific safety training.
- k. Holding SRS meetings at least quarterly.
- l. Ensuring coordination with other regulatory programs, personnel, or committees such as the Radiation Safety Officer or Radiation Safety Committee.
- m. Ensuring the collection of appropriate personnel samples to make employee exposure determinations whenever the proposed use of laboratory chemicals may potentially exceed OSHA Permissible Exposure Limits or Action Levels.
- n. Evaluating annually the effectiveness of the laboratory's Chemical Hygiene Plan and making necessary revisions.
- o. Ensuring the review of investigation reports of all lost-time injuries and all significant adverse environmental events.
- p. Ensuring the proper reporting of injury and illness trends to the R&D Committee, as appropriate.
- q. Requesting, when appropriate, the appointment of an ad hoc committee (consisting of members with appropriate expertise) to investigate and report on occupational injuries, illnesses, and adverse environmental events.
- r. Ensuring the development of a policy for the preservation of employee medical and OSHA exposure records (see subpar 6c(6)) and environmental records (i.e., hazardous waste, air monitoring).
- s. Cooperating with appropriate medical center personnel to review the quantity and type of hazardous waste generated by each PI annually.
- t. Providing technical assistance, where appropriate, in recycling programs and reduction of the quantity of waste and.

8. RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR OR LABORATORY DIRECTOR

The PI or Laboratory Director is responsible for research activities conducted in assigned space, including:

- a. Submitting a completed VA Form 10-0398 (see App. F) to the medical center Research Office along with each research proposal to be submitted for funding.
 - (1) The "Work Proposed" section of the research proposal must accompany the survey.
 - (2) The Research Office arranges for review of the proposal and evaluation by SRS.

(3) A complete list of chemicals defined as “hazardous” to be used must be submitted with each research proposal. **NOTE:** *Not submitting such a list will result in failure to obtain approval by the facility Safety Officer. Review and approval by the Safety Officer is required prior to local review of protocols by the R&D Committee.*

NOTE: *This chemical inventory is reviewed and maintained locally by the Laboratory Director.*

- b. Ensuring that active protocols and new pilot projects have been reviewed by SRS, regardless of funding status or source.
- c. Identifying laboratory specific hazards, and:
 - (1) Ensuring that all personnel receive training specific to the hazard(s).
 - (2) Advising laboratory personnel of any potential risk to themselves or the research environment.
 - (3) Establishing and enforcing standards of practice which minimize employee exposures to biological, chemical, physical, and radiation hazards.
- d. Supervising the performance of the laboratory staff to ensure the correct use of required safety practices and techniques (including personal protective equipment).
- e. Ensuring that Biological Safety Cabinets are certified annually. **NOTE:** *In research settings involving airborne pathogens, certification must be performed on a semi-annual basis.*
- f. Reporting problems and concerns about operation and containment practices and procedures to the Research Safety Coordinator, facility Safety Officer, Veterinary Medical Officer (VMO) or Veterinary Medical Consultant (VMC) (if applicable), Radiation Safety Officer (if applicable), and other appropriate authorities.
- g. Ensuring that all accidents are reported to the Employee Health Office and the facility safety office using appropriate VHA forms.
- h. Securing approval of the R&D Committee through the SRS for any significant changes made in the original research plan.
- i. Coordinating with appropriate safety staff such as the Radiation Safety Officer for removal or disposal of all chemicals, biological agents, radioisotopes, and waste generated by these materials.
- j. Notifying all pertinent personnel prior to departure from the laboratory.
- k. Notifying all pertinent personnel prior to relocating the research laboratory space.

l. Ensuring that a copy of the laboratory's Chemical Hygiene Plan is readily available to all employees in their work area, that employees have been trained in the contents of the Plan, and that all provisions of the Plan are implemented in all laboratories under the PI's supervision.

m. Maintaining employee exposure to hazardous chemicals in laboratory activities at the lowest possible levels. At no time may employee exposures to chemicals exceed the Permissible Exposure Limits established by OSHA (see subpar. 6e(3)).

n. Maintaining an up-to-date inventory of all hazardous chemicals located in the laboratory.

(1) Ensuring that all laboratory personnel know the location of this inventory.

(2) Providing this inventory to the facility Safety Officer.

o. Managing all biological and chemical waste in accordance with Federal, State, and local regulations and all VA, VHA, and facility policies.

(1) Seeking technical assistance when needed to ensure proper waste management.

(2) Implementing waste reduction techniques, where appropriate.

p. Investigating the deficiencies cited during all inspections of work areas. Submitting a written abatement plan for all deficiencies cited during inspections to SRS within the specified time limits.

9. CRADO RISK MANAGEMENT POLICIES

The CRADO is responsible for:

a. Requiring the review of mandatory safety surveys by the Biosafety Office prior to release of funding for any approved research proposals (see App. F). **NOTE:** *Alternate safety surveys may be submitted following a complete audit and approval of the local research safety program by the CRADO.*

b. Establishing standards for acceptance or non-acceptance of submitted forms. **NOTE:** *Failure to meet these standards will result in an administrative "hold."* The following is required:

(1) VA Form 10-0398 is required for all submissions for funding.

(2) Title of submission must correspond to the title listed on the form.

(3) Information, including negative responses, must be completely and accurately entered on the form. No blank fields will be acceptable for submission.

(4) All authorized signatures and dates must be present and approval must be within 12 months of submission.

c. Establishing procedures for the field to respond to a Hazard “hold.”

(1) The VA medical center receiving notification of the “hold” must respond within 12 weeks of receipt.

(2) Responses must be forwarded to the ORD service that placed the hold.

(3) Resubmission of a research proposal does not qualify as a response, and will result in an automatic “hold.” Review for that funding cycle will proceed, but the application will not be reviewed in the following cycle until a response to the original “hold” has been received and approved by the Biosafety Office.

d. Requesting copies of SRS meeting minutes for review. The Biosafety Office must review SRS minutes.

e. Scheduling site visits when operational deficiencies in the safety program are detected following new construction or renovation, or as appropriate. Failure to correct deficiencies will result in withholding research funds.

f. Responding to a CDC notice of failure to comply with the Select Agent Laboratory Registration Program. This is accomplished by a site visit or by withholding research funds or both for the specific research program. Failure to correct deficiencies will result in withholding research funds.

10. REFERENCES

a. CDC-NIH. Biosafety in Microbiological and Biomedical Laboratories 4th Edition. CDC-NIH, Washington, DC, 1999 <http://bmbi.od.nih.gov/> .

b. Title 42 CFR Part 73.

c. Title 7 CFR 331.

d. Title 9 CFR 121.

e. Title 29 CFR Part 1910, Occupational Safety and Health Standards.

(1) CFR 1910.38, Emergency Actions Plans.

(2) CFR 1910.39, Fire Prevention Plans.

(3) CFR 1910.269, Electric Power Generation, Transmission, and Distribution.

(4) CFR 1910.1000, Subpart Z – Toxic and Hazardous Substances.

(5) CFR 1910.1020, Access to Employee Exposure and Medical Records.

- (6) CFR 1910.1030, Bloodborne Pathogens.
- (7) CFR 1910.1200, Hazard Communication.
- (8) CFR 1910.1450, Occupational Exposure to Hazardous Chemicals in Laboratories.
- f. Title 10 CFR Chapter 1, Nuclear Regulatory Commission, Parts 0-199.
 - (1) CFR 19, Notices, Instructions and Reports to Workers; Inspections and Investigations.
 - (2) CFR 20, Standards for Protection Against Radiation.
 - (3) CFR 35, Medical Use of Byproduct Material.
- g. Title 40 CFR Chapter 1, Environmental Protection Agency Parts 1-1299.
 - (1) CFR 260, Hazardous Waste Management System: General.
 - (2) CFR 261, Identification and Listing of Hazardous Waste.
 - (3) CFR 262, Standards Applicable to Generators of Hazardous Waste.
- h. “National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules,” NIH Guidelines. National Institutes of Health, Bethesda, MD, May 11, 1999
<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>.
- i. VHA Directive 1105.1, Management of Radioactive Materials
<http://www1.va.gov/vhapublications/index.cfm>.
- j. VHA Handbook 1105.1, Procedures for Management of Radioactive Materials
<http://www1.va.gov/vhapublications/index.cfm>.
- k. VA Directive 7700, Occupational Safety and Health
<http://www1.va.gov/vhapublications/index.cfm>.
- l. National Council on Radiation Protection and Measurements reports:
 - (1) Number 107, Implementation of the Principle of As Low as Reasonably Achievable (ALARA) for Medical and Dental Personnel (Bethesda, MD, 1990)
<http://www.ncrponline.org/Publications/Publications.html>, and
 - (2) Number 116, Limitation of Exposure to Ionizing Radiation (Bethesda, MD, 1993)
<http://www.ncrponline.org/Publications/Publications.html>.

INFECTIOUS DISEASES RISK ASSESSMENT

1. RISK. Risk implies the probability that harm, injury, or disease will occur. In the context of the microbiological and biomedical laboratories, the assessment of risk focuses primarily on the prevention of laboratory-associated infections. Choosing the proper level of containment is very important to reduce the employee's and the environment's risk of exposure to an agent to an absolute minimum. Risk assessment can be quantitative or qualitative. If the hazard is known (e.g., residual levels of formaldehyde gas after a laboratory decontamination), a quantitative assessment is possible. For the most part, it is not possible to do a quantitative assessment of biohazardous agents. A number of factors and considerations for a qualitative risk assessment follow:

2. ASSESSMENT OF RISK. The Laboratory Director or Principal Investigator (PI) is responsible for assessing risks.

a. **Factors of Interest.** The factors of interest must include:

- (1) Pathogenicity of the infectious or suspected infectious agent,
- (2) Route of transmission,
- (3) Agent stability,
- (4) Infectious dose,
- (5) Concentration,
- (6) Origin,
- (7) Availability of data from animal studies,
- (8) Availability of an effective prophylaxis,
- (9) Medical surveillance, and
- (10) An evaluation of experience and skill level of at-risk personnel.

b. **Materials Containing Known Infectious Agents.** Use the:

(1) Information obtained from laboratory investigations, disease surveillance, and epidemiological studies.

(2) Infectious agents listed in Agent Summary Statements (Section VII) of Biosafety in Microbiological and Biomedical Laboratories 4th Edition and American Public Health Association's manual, Control of Communicable Diseases.

c. **Materials Containing Unknown Infectious Agents.** Questions to be considered in establishing the appropriate biosafety level include:

- (1) Why is an infectious agent suspected?
- (2) What epidemiological data is available?
- (3) What route of transmission is indicated?
- (4) What is the associated morbidity or mortality rate or both?
- (5) What medical data is available?

d. **Materials Containing Recombinant Deoxyribonucleic Acid (DNA) Molecules.**

NOTE: This includes microorganisms that have been genetically modified through recombinant DNA technologies.

- (1) Use the appropriate reference for establishing appropriate biosafety level: National Institutes of Health publication, Guidelines for Research Involving Recombinant DNA Molecules.
- (2) Evaluate the potential increased biohazard associated with a particular genetic modification.
- (3) Select the appropriate biosafety level beginning with the classification of a non-modified virus. Carefully consider the nature of genetic modification and quantity of virus when selecting the appropriate biosafety level.
- (4) Consider the following points:
 - (a) Does the inserted gene encode known toxin or relatively uncharacterized toxin?
 - (b) Does the modification have the potential to alter the host range or cell tropism of virus?
 - (c) Does the modification have the potential to increase the replication capacity of virus?
 - (d) Does viral DNA integrate into the host genome?
 - (e) What is probability of generating replication-competent viruses?

e. **Materials that May or May Not Contain Unknown Infectious Agents.** Always use universal precautions when there is no information that an infectious agent is suspected.

f. **Animal Studies.** Animal studies:

- (1) May present many different kinds of physical, environmental, and biological hazards.
- (2) Are unique according to species involved and the nature of the research.
- (3) Need to focus on the animal facility's potential for increased exposure to both human pathogens and to zoonotic agents.
- (4) Need to consider that latent infections most common in field-captured animals or animals that come from unscreened herds.
- (5) Must consider animal routes of transmission.

NOTE: The described risk assessment process also applies to laboratory operations other than those involving use of primary agents of human disease such as chemical hazards.

INFRASTRUCTURE OF SUBCOMMITTEE ON RESEARCH SAFETY (SRS)

It is recommended that the Subcommittee on Research Safety (SRS) include member(s) from the facility safety committee, such as the Safety Officer or the Facility Infection Control Committee; the Institutional Animal Care and Use Committee (IACUC); the Radiological Safety Officer; and a liaison from an affiliated university Institutional Biosafety Committee. **NOTE:** *individuals may be included in the core five members referred to in subparagraph 1a of this appendix.*

1. NUMBER AND QUALIFICATION OF MEMBERS

a. Each SRS must have at least five members, exclusive of ex-officio members; when the research reviewed involves recombinant deoxyribonucleic acid (DNA) not exempt from the current NIH Guidelines for Research Involving Recombinant DNA Molecules. The SRS must include two members not affiliated with the Institution.

b. It is usually necessary for the SRS membership to possess expertise in:

(1) Etiologic agents, including bloodborne and airborne pathogens.

(2) Chemical carcinogens and other chemical hazards.

(3) Physical and radiation hazards.

c. It is recommended that at least one SRS member possess specific occupational safety and health, environmental, and Department of Transportation expertise to ensure that all pertinent hazards in protocols are identified. It is also advisable this member have first-hand knowledge of the space and facilities assigned to each Principal Investigator (PI) to ensure that research operations can be conducted safely.

d. It is highly desirable that the Veterinary Medical Officer (VMO), Veterinary Medical Consultant (VMC), or a member of the IACUC be appointed to SRS.

2. EX-OFFICIO MEMBERS. Ex-officio members must include:

a. A liaison member from the local Research and Development (R&D) Committee (voting).

b. The Chemical Hygiene Officer (appointed by the R&D Committee) (voting).

c. The Administrative Officer (AO) for R&D or other non-voting representative from the R&D office.

d. An employee union safety representative, or other union designee, whose voting status is determined by the applicable union contract.

3. APPOINTMENT OF MEMBERS

a. SRS members and R&D Committee members forward the names of nominees for membership in SRS to the medical center Director. The medical center Director must officially appoint members in writing. *NOTE: In addition, the length of the appointment needs to be specified.*

b. The facility Director appoints the SRS chairperson for the term of 1 year. The SRS Chairperson may be re-appointed without any lapse in time; however, the SRS chairperson may not simultaneously chair the R&D Committee or another research subcommittee.

4. REPRESENTATIVES FROM OTHER MEDICAL CENTER COMMITTEES AND OFFICES. If research with recombinant DNA is conducted in the facility, the facility Director must comply with all requirements with respect to composition of an Institutional Biosafety Committee as specified in the NIH Guidelines.

**FORMAT FOR SUBCOMMITTEE ON RESEARCH SAFETY MEETING
AGENDAS AND MINUTES**

Agendas and minutes of the Subcommittee on Research Safety (SRS) must be prepared according to the following format.

1. AGENDA. An agenda is to be developed before each SRS meeting and distributed to SRS members at least 3 working days before the meeting. At a minimum, the agenda is to include:

a. **Approval of Minutes.** Approval of minutes of previous meeting (date).

b. **Unfinished Business.** List pending items and individual responsible.

c. **New Business.** Identify individual responsible when necessary.

(1) **Standing Recurring Reports.** Identify individual responsible.

(2) **Issues.** Any issues not previously addressed by the body.

(3) **Other.** Any other item that warrants review or discussion by the committee and is not routinely reviewed by the committee.

d. **Announcements**

e. **Next Meeting.** Date, time, and place of the next meeting.

2. MINUTES. Minutes of all SRS meetings must be prepared according to the following format.

a. Identification of the subcommittee to be centered at the top of the page, including the Department of Veterans Affairs (VA) medical center name and number.

b. The first paragraph is to include:

(1) Place, date, and time of the meeting.

(2) Name of presiding officer (chairperson).

(3) The attendance record, which must list all individuals identified as members. Members are to be marked "Absent," if the Chairperson or recorder has not been notified in advance. Members are to be marked "Excused," if the Chairman or recorder was notified in advance. For each member, note their role on the committee and whether they are voting or nonvoting.

(4) Indication that a quorum is present. **NOTE:** *A quorum is defined as more than 50 percent of the voting members are present.*

c. Succeeding paragraphs are to identify the recommendations, date of the meeting when the recommendation was initially made, action taken to date or a realistic date to expect resolution, and the status as “Closed” or “Pending.” For each project under consideration, list the name of the Principal Investigator (PI) and the complete name of the project.

NOTE: A recommendation is not to be carried for more than two meetings awaiting a resolution unless there is clear documentation that a plan of action is being followed and an anticipated date for resolution is noted.

d. Minutes are not to be recorded verbatim except for recommendations; however, the substance of the discussion is to be reported clearly and concisely. After summation of the discussion, the minutes must reflect:

(1) **Conclusion.** This indicates what was concluded from the discussion; for example, “The follow-up action plan was ineffective, and the issue is not considered resolved at this time.” If analysis of the data occurred in the meeting, then the conclusion of the analysis needs to be in the minutes.

(2) **Recommendation.** This includes who or what is expected to change.

(3) **Action.** This includes what action is appropriate in view of the cause, scope, and severity of the problem, and who is responsible for implementing the action.

(4) **Follow-Up or Evaluation.** This identifies the date a status report is due on the action plan, the date the action plan will be implemented, or the date the action plan will be evaluated for accomplishment of expected outcome or impact of the changes made.

e. For each new project, the motion passed by the committee (approved, approved pending clarification, deferred, disapproved) must be recorded with the exact vote; this must include the number voting for the motion, the number voting against the motion, and the number abstaining from voting on the motion. *NOTE: The motion needs to be worded in such a way that it is clear which members will review revisions and have the authority to grant approval.*

f. The minutes must note which members excused themselves from voting on which project(s) to prevent conflicts of interest.

g. Copies of any internal or external reports or correspondence with outside agencies referenced in the minutes need to be attached to the minutes if they are important to understanding the conduct of business.

h. SRS members having a scientific or monetary conflict of interest for the protocol under consideration may provide information helpful to the SRS prior to deliberations, but must excuse themselves from the meeting once deliberations begin.

i. Minutes must be written and published within 3 weeks of the meeting date.

- j. Minutes must be signed by the Chairperson of the SRS.

- k. Approved minutes must be forwarded to the Research and Development (R&D) Committee for review and approval. The R&D Committee may review the minutes for content regarding committee functions, protocol review, education of members, and preparation of minutes. Recommendations for changes or improvements in SRS procedures may be made, but the R&D Committee may not alter the SRS minutes.

- l. Minutes must be maintained by the R&D Office and made available to VA Central Office upon request.

RADIATION SAFETY

1. FACILITY REQUIREMENTS. The use of radioactive materials within Department of Veterans Affairs (VA) facilities must comply with the statutory and regulatory requirements of the Nuclear Regulatory Commission (NRC) and with Veterans Health Administration (VHA) policies and procedures for the safety and control of such materials. These policies, procedures, and regulations collectively control the receipt, uses, and disposal of radioactive materials in VHA research programs.

2. RADIATION SAFETY COMMITTEE (RSC) AND RADIATION SAFETY OFFICER (RSO). X-ray devices and their uses, while generally not subject to regulation in Federal facilities, are nevertheless subject to actual standards of practice and the important recommendations of influential national and international councils and commissions. Specific details of local facility requirements are approved and published by a facility RSC and implemented by the RSO. The RSC and the RSO are the primary facility resources for ensuring safe and effective uses of ionizing radiation in research and always need to be consulted.

3. AS LOW AS REASONABLY ACHIEVABLE (ALARA). While Federal regulation and the weight of authoritative commissions establish upper limits for the permissible radiation dose to workers and the public, one of the most effective tools for education on dosage is the facility specific ALARA programs. This is a mandatory commitment to maintain individual and collective radiation doses as low as reasonably achievable and requires participation of management, safety personnel, and individual research users.

4. REFERENCES

- a. VHA Directive and Handbook 1105.1, Management of Radioactive Materials
<http://www1.va.gov/vhapublications/index.cfm>.
- b. Title 10 Code of Federal Regulations (CFR) Chapter 1, Nuclear Regulatory Commission, Parts 0-199.
 - (1) CFR 19, Notices, Instructions and Reports to Workers: Inspections, and Investigations.
 - (2) CFR 20, Standards for Protection Against Radiation.
 - (3) CFR 35, Medical Use of Byproduct Material.

LABORATORY SECURITY AND EMERGENCY RESPONSE FOR MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES

The following procedures are offered for laboratories using biological agents or toxins capable of causing serious or fatal illness to humans or animals and for the use of radioactive materials. Research, clinical, and production laboratories working with newly-identified human pathogens, high-level animal pathogens, or toxins not covered by Biosafety Level (BSL) 3 or 4 recommendations, need to follow these procedures in order to minimize opportunities for accidental or intentional removal of these agents from the laboratory.

1. RECOGNIZE THAT LABORATORY SECURITY IS RELATED TO, BUT DIFFERENT FROM, LABORATORY SAFTEY

a. Review safety policies and procedures regularly.

(1) Management needs to review policies to ensure that they are adequate for current conditions and consistent with other facility-wide policies and procedures.

(2) Laboratory supervisors need to ensure that all laboratory workers and visitors understand security requirements and are trained and equipped to follow established procedures.

b. Review safety policies and procedures whenever an incident occurs, or a new threat is identified.

2. CONTROL ACCESS TO AREAS WHERE BIOLOGICAL AGENTS OR TOXINS ARE USED AND STORED

a. Laboratory and animal care areas are to be locked at all times.

b. Card-keys or similar devices are to be used to permit entry to laboratory and animal care areas.

c. Only workers required to perform a job are to be allowed in laboratory areas, and workers need to be allowed only in areas and at hours required to perform their particular job.

(1) Access for students, visiting scientists, etc., is to be limited to hours when regular employees are present.

(2) Access for routine cleaning, maintenance, and repairs is to be limited to hours when regular employees are present.

d. Freezers, refrigerators, cabinets, and other containers where stocks of biological agents, hazardous chemicals, or radioactive materials are stored are to be locked when they are not in direct view of workers (e.g., when located in unattended storage areas).

3. KNOW WHO IS IN THE LABORATORY AREA

- a. All workers are to be known to facility administrators and laboratory directors.
- b. All workers (including students, visiting scientists, and other short-term workers) are to wear visible identification badges.
- c. Guests are to be issued identification badges, and escorted or cleared for entry using the same procedures as for regular workers.
- d. All workers are to challenge or question unknown, unfamiliar, or unidentified persons in the laboratory area.

4. KNOW WHAT MATERIALS ARE BEING BROUGHT INTO THE LABORATORY AREA. Packages containing specimens, bacterial or virus isolates, or toxins are to be opened in a safety cabinet or other appropriate containment device.

5. KNOW WHAT MATERIALS ARE BEING REMOVED FROM THE LABORATORY AREA

a. Biological materials and toxins for shipment to other laboratories are to be packaged and labeled in conformance with all applicable local, Federal, and international shipping regulations.

(1) Required permits (e.g., Public Health Service, Department of Transportation, Department of Commerce, Department of Agriculture) are to be in hand before materials are prepared for shipment.

(2) The recipient (preferably) or receiving facility is to be known to the sender, and the sender is to make an effort to ensure that materials are shipped to a facility equipped to handle those materials safely.

b. Hand carrying of microbiological materials and toxins to other facilities is rarely appropriate. If biological materials or toxins are to be hand carried by common carriers, all applicable regulations must be followed.

c. Contamination or possibly contaminated materials are to be decontaminated before they leave the laboratory area. Chemicals and radioactive materials must be disposed of in accordance with local, State, and Federal regulations.

6. HAVE AN EMERGENCY PLAN

a. Control of access to laboratory areas can make an emergency response more difficult. This must be considered when emergency plans are developed.

(1) An evaluation of the laboratory area is to be made by appropriate facility personnel, with outside experts if necessary, to identify both safety and security concerns needs before an emergency plan is developed.

(2) Facility administrators, laboratory directors, principal investigators, laboratory workers, the facility safety office, and facility security officials need to be involved in emergency planning.

(3) Police, fire, and other emergency responders need to be informed as to the types of biological radioactive and chemical materials in use in the laboratory areas; these responders need assistance in planning their responses to emergencies in the laboratory areas.

(4) Plans are to include provision for immediate notification of (and response by) laboratory directors, laboratory workers, safety office personnel, or other knowledgeable individuals when an emergency occurs, so that biosafety issues can be dealt with, if they occur.

b. In accordance with standards established by the Occupational Safety and Health Administration (OSHA), the emergency plan must include, at a minimum, the following elements (see Title 29 Code of Federal Regulations (CFR) 1910.38, Subpart E Appendix):

(1) Emergency escape procedures and emergency escape route assignments;

(2) Procedures to be followed by employees who remain to operate critical plan operations before they evacuate;

(3) Procedures to account for all employees after an emergency evaluation has been completed;

(4) Rescue and medical duties for those employees who are to perform them;

(5) The preferred means of reporting fires and other emergencies; and

(6) Names or regular job titles of persons or departments who can be contacted for further information or explanation of duties under the plan.

c. Laboratory emergency planning is to be coordinated with facility-wide plans. Such factors as bomb threats, severe weather (hurricanes, floods), earthquakes, power outages, and other natural (or unnatural) disasters need to be considered when developing laboratory emergency plans.

7. HAVE A PROTOCOL FOR REPORTING INCIDENTS. Laboratory directors, in cooperation with facility safety and security officials, are to have policies and procedures in place for reporting and investigating incidents, or possible incidents (e.g., undocumented visitors, missing chemicals, unusual or threatening phone calls, etc.).

VA FORM 10-0398, RESEARCH PROTOCOL SAFETY SURVEY

VA Form 10-0398, Research Protocol Safety Survey can also be found on the Veterans Health Administration (VHA) Forms Intranet at <http://vaww.va.gov/vaforms>. This is to be used for local reproduction. Since this is a low use form, it will not be stocked by the Forms and Publications Depot.



VA Form
10-0398.pdf

SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR INFECTIOUS AGENTS

| Bio-Safety Level (BSL) | Agents | Practices | Safety Equipment (Primary Barriers) | Facilities (Secondary Barriers) |
|------------------------|---|---|--|--|
| 1 | Not known to consistently cause disease in healthy adults. | Standard Microbiological Practices | None required | Open bench top sink required |
| 2 | Associated with human disease. Hazard: percutaneous injury; ingestion; mucous membrane exposure. | BSL-1 practices plus: a. Limited access. b. Biohazard warning signs. c. “Sharps” precautions. d. Biosafety manual defining any needed waste decontamination or medical surveillance policies. | Primary barriers = Class I or II Biosafety Cabinet (BSC)s or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials; Personal Protective Equipment (PPE)s: laboratory coats; gloves; face protection as needed. | BSL-1 plus: Autoclave available |
| 3 | Indigenous or exotic agents with potential for aerosol transmission; disease may have serious or lethal consequences. | BSL-2 practices plus: a. Controlled access. b. Decontamination of all waste. c. Decontamination of lab clothing before laundering. d. Baseline serum. | Primary barriers = Class I or II BSCs or other physical containment devices used for all open manipulations of agents; PPEs: protective lab clothing; gloves; respiratory protection as needed. | BSL-2 plus: a. Physical separation from access corridors. b. Self-closing, double-door access. c. Exhausted air not recirculated. d. Negative airflow into laboratory. |
| 4 | Dangerous or exotic agents which pose high risk of life-threatening disease; aerosol-transmitted lab infections; or related agents with unknown risk of transmission. | BSL-3 practices plus: a. Clothing change before entering. b. Shower on exit. c. All material decontaminated on exit from facility. | Primary barriers = All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full- body; air-supplied, positive pressure personnel suit. | BSL-3 plus: a. Separate building or isolated zone. b. Dedicated supply and exhaust, vacuum, and decontamination systems. c. Other requirements outlined in the text. |

NOTE: Text taken from Biosafety in Microbiological and Biomedical Laboratories; 15th Edition, Pub. May 1999, Pg. 75.

**SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR ACTIVITIES
IN WHICH EXPERIMENTALLY OR NATURALLY INFECTED VERTEBRATE ANIMALS ARE USED**

| BSL | Agents | Practices | Safety Equipment (Primary Barriers) | Facilities (Secondary Barriers) |
|-----|--|---|--|--|
| 1 | Not known to consistently cause disease in healthy human adults. | Standard animal care and management practices, including appropriate medical surveillance programs. | As required for normal care of each species. | Standard animal facility: a. No recirculation of exhaust air. b. Directional air flow recommended. c. Hand washing sink recommended. |
| 2 | Associated with human disease. Hazard: percutaneous exposure; ingestion; mucous membrane exposure. | Animal Biosafety Level (ABSL)-1 practices plus: a. Limited access. b. Biohazard warning signs. c. "Sharps" precautions. d. Biosafety manual. e. Decontamination of all infectious wastes and of animal cages prior to washing. | ABSL-1 equipment plus primary barriers: Have containment equipment appropriate for animal species; PPEs: laboratory coats, gloves, face and respiratory protection as needed. | ABSL-1 facility plus: a. Autoclave available. b. Hand washing sink available in the animal room. c. Mechanical cage washer used. |
| 3 | Indigenous or exotic agents with potential for aerosol transmission; disease may have serious health effects. | ABSL-2 practices plus: a. Controlled access. b. Decontamination of clothing before laundering. c. Cages decontaminated before bedding removed. d. Disinfectant foot bath as needed. | ABSL-2 equipment plus: a. Containment equipment for housing animals and cage dumping activities. b. Class I or II BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. PPEs: appropriate respiratory protection. | ABSL-2 facility plus: a. Physical separation from access corridors. b. Self-closing, double-door access. c. Sealed penetrations. d. Sealed windows. e. Autoclave available in facility. |
| 4 | Dangerous or exotic agents that pose high risk of life-threatening disease; aerosol transmission; or related agents with unknown risk of transmission. | ABSL-3 practices plus: a. Entrance through change room where personal clothing is removed and laboratory clothing is put on; shower on exiting. b. All wastes are decontaminated before removal from the facility. | ABSL-3 equipment plus: Maximum containment equipment (i.e., Class III BSC or partial containment equipment in combination with full body, air-supplied positive-pressure personnel suit) used for all procedures and activities. | ABSL-3 facility plus: a. Separate building or isolated zone. b. Dedicated supply and exhaust, vacuum, and decontamination systems. c. Other requirements outlined in the text. |

NOTE: Text taken from *Biosafety in Microbiological and Biomedical Laboratories; 16th Edition, Pub. May 1999, Pg. 75.*