NIH POLICY MANUAL

3035- Working Safely With Hazardous Biological Materials
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1. Explanation of Material Transmitted:

This chapter updates the NIH policy on working with hazardous biological materials in the NIH research environment and instructions for transferring Select Agents and Toxins as defined in 42 CFR 73. 42 CFR 73 supersedes 42 CFR 72.6 and implements provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the Act) and is designed to protect public health and safety.

2. Filing Instructions:

Remove: NIH Manual Chapter 3035 dated 05/06/1998

Insert: NIH Manual Chapter 3035 dated 3/25/2008

PLEASE NOTE: For information on:

- Content of this chapter, contact the issuing office listed above.
- NIH Manual System, contact the Office of Management Assessment, OM, on (301) 496-4606.
- Online information, enter this URL: http://www1.od.nih.gov/oma/manualchapters/

WORKING SAFELY WITH HAZARDOUS BIOLOGICAL MATERIALS

A. PURPOSE

This chapter establishes the National Institutes of Health (NIH) policy governing the conduct of work with hazardous biological materials in the research environment. This includes recombinant DNA materials, toxins, human pathogens classified at Biosafety Level 2 (BSL-2) and higher and Select Agents as defined in 42 CFR 73, "Select Agents and Toxins".

B. BACKGROUND

The safe handling of hazardous biological materials in the biomedical research setting has been and will continue to be a concern. The emergence of the human immunodeficiency virus (HIV) prompted public awareness and enhanced the need for guidelines relative to the handling of potentially infectious materials. The Centers for Disease Control and Prevention (CDC)/NIH publication, *Biosafety in Microbiological and Biomedical Laboratories (BMBL),* serves as the primary resource guide on biological safety issues. It describes biosafety levels for work with infectious agents and infected animals, risk assessment criteria, and biological agent summary statements.

The Occupational Safety and Health Administration (OSHA) promulgated a standard on working safely with human blood and body fluids (29 CFR 1910.1030, "Occupational Exposure to Bloodborne Pathogens"). This standard applies to research laboratories and outlines the requirements for working with human body fluids, tissues, and potential bloodborne pathogens. The standard provides information concerning facility requirements, safe work practices, medical surveillance, personal protection, first aid procedures, and worker training. In addition, it provides standards for packaging and handling materials during transport to protect both the employee and the public.

The U.S. Department of Transportation (DOT) identifies infectious substances as Hazardous Materials. These materials are regulated during transport (49 CFR 171 – 178). Once these materials are placed into transport via air, either domestically or internationally, they are governed by the International Air Transport Association (IATA) *Dangerous Goods Regulations*.

The CDC and U.S. Department of Agriculture (USDA) implemented regulations that govern the possession, use and transfer of certain biological agents and toxins, defined as Select Agents (42 CFR part 73, 7 CFR part 331 and 9 CFR 121). NIH facilities that apply to possess, use, or transfer these agents must demonstrate capabilities for handling these agents in accordance with the appropriate biosafety level and the NIH Manual Chapter "1743- Keeping and Destroying Records" (see Section E. Records Retention and Disposal). These facilities are subject to periodic CDC and USDA site inspections. Concerns about the potential use of certain biological agents for terrorist purposes caused the U.S. Congress to enact Public Law 104-132, "The Antiterrorism

and Effective Death Penalty Act of 1996". Section 511 of the Act required the Secretary of Health and Human Services to regulate the transfer of Select Agents.

The Director, Division of Occupational Health and Safety (DOHS), ORS, or his/her designee, is the Responsible Official for the implementation, development and management of the Select Agent Program at the NIH per 42 CFR Part 73, 7 CFR part 331 and 9 CFR 121. A list of the agents can be found in Appendix 1, Part 73, CFR 42. The CDC provides an updated list of Select Agents on the CDC webpage at http://www.cdc.gov/od/sap/docs/salist.pdf.

C. POLICY

The policy of the NIH is to ensure that all biomedical research involving hazardous biological materials, including recombinant DNA molecules and human pathogens classified at BSL-2 and higher, is conducted in a manner that will protect research personnel, support staff, and the environment. The DOHS is responsible for managing biological safety at the NIH, in addition to providing a broad range of support services, consultation and assistance.

All work with hazardous biological materials will be conducted in compliance with the current edition of the CDC/NIH publication *Biosafety in Microbiological and Biomedical Laboratories* (BMBL). The policy for working with bloodborne pathogens is set forth in the *NIH Bloodborne Pathogen Exposure Control Plan for Non-Hospital Personnel*. Copies of these documents may be obtained from the DOHS webpage at http://dohs.ors.od.nih.gov/publications.htm.

It is a requirement of the biological safety program at the NIH that Principal Investigators (PIs) register work creating, manipulating, or using recombinant DNA products with the DOHS by submitting a recombinant DNA registration document, or 'RD' (see subparagraph 1). In addition, work involving potentially infectious materials and human pathogens, human and non-human primate blood, tissues, and body fluids, including primary human cell cultures require the submission of a human pathogen registration document, or 'HPRD' (see subparagraph 2). PIs are required to complete these forms, described below, and submit them to the Institutional Biosafety Committee (IBC). DOHS safety specialists assigned to each IC are available to assist PIs in processing these registrations.

1. *Registration Document for Recombinant DNA Experiments*, NIH Form 2690, http://forms.nih.gov/adobe/misc/NH2690.PDF , is used to register all work with recombinant DNA. PIs creating, manipulating or using recombinant DNA must complete this form and submit it to the Executive Secretary of the IBC for approval (Bldg.13, Room 3K04).

The PI is responsible for complying with the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (the Guidelines), ensuring that appropriate reviews and approvals are obtained for all recombinant DNA experiments, and supplying updated information annually (e.g., personnel changes, amendments) to the IBC. The NIH IBC, whose functions are defined under the Guidelines, reviews and approves research protocols involving the use of recombinant DNA techniques as well as materials potentially infectious to humans.

2. *Registration of Materials (Potentially) Infectious for Humans*, (HPRD form)http://dohs.ors.od.nih.gov/forms.htm, is used to register work involving human pathogens, human or non-human primate blood, tissues, and body fluids, including primary human cell cultures. The PI must complete the form and forward the document to the IBC Executive Secretary (Bldg. 13, Room 3K04) for review and approval. The PIs must review and update these documents annually.

For research work involving Select Agents, as defined per 42 CFR Part 73, 7 CFR part 331 and 9 CFR 121, the PI must contact the NIH Responsible Official designated as the Director, DOHS, ORS or his/her designee; at (301)-496-2960 for assistance and final approval.

Employee training is an important component in the safe conduct of work with biological materials. Mandatory training is provided by DOHS to help supervisors fulfill basic lab safety orientation and the training requirements. Requirements, course information and schedules are available on the DOHS website at http://www.ors.od.nih.gov/labsafety/. Supervisors are responsible for providing the site specific training and ensuring that annual retraining of their employees is completed. Also, supervisors are responsible for ensuring that their employees are advised of the potential hazards associated with infectious agents and the proper use of laboratory equipment, including containment devices. This includes all visiting scientists, summer research associates, trainees, fellows, special volunteers and summer students.

In accordance with the BMBL, laboratories working at BSL-1 and higher must be posted with proper signage. The biosafety sign is obtained from the assigned IC safety specialist. The sign must indicate the assigned biosafety level, biological material(s) in use, special procedures or precautions for entry, required immunizations (if any), name of the PI, and both work and emergency phone numbers.

All registered laboratories must be surveyed by DOHS staff prior to posting the biosafety sign and at least annually thereafter to ensure that the facility is operating properly for the biosafety level and that appropriate practices and procedures are observed.

Principal Investigators operating or working in a BSL-3 laboratory must secure all potentially infectious materials appropriately and disinfect surfaces prior to allowing entry of support

personnel, such as maintenance employees. All laboratory components (sinks, countertops, etc.) and equipment scheduled for repair or servicing must be thoroughly decontaminated by research personnel prior to initiation of the maintenance or repair work. A staff member familiar with the operation of the laboratory must be present during normal working hours whenever maintenance or repair work is being conducted.

In the event of an after-hours emergency in a BSL-3 laboratory, the PI must be contacted prior to entry by non-laboratory personnel. The emergency contact information posted on the biosafety sign on the laboratory door must be kept current to facilitate emergency response.

All NIH personnel must comply with the NIH Policy Manual 1340-1, "Permits for Import or Export of Biological Materials", when shipping hazardous materials. All infectious or hazardous materials must be shipped through the NIH Office of Logistics and Acquisition Operations (OLAO), Freight Forwarding Team. See the following website: http://www.olao.od.nih.gov/Transportation/ShipmentServices/OtherThanHouseholdGoods/.

The DOHS provides training on shipping biological materials. Information on the training and how to register for a class can be found on the DOHS website at http://dohs.ors.od.nih.gov/training.htm.

The transport (on or off campus) of Select Agents is subject to prior approval by the NIH Select Agent Program, an extension of Federal Law as explained in Section B. Background, and the CDC or USDA, Animal and Plant Health Inspection Service (APHIS). Contact the NIH DOHS at (301)-496-2960 for approval and further assistance.

Anyone at the NIH wishing to personally transport material via air must have the hazardous material packaged by a trained shipper, following IATA packaging instructions. The hazardous material must be declared prior to departure.

Transfer of research materials to anyone outside the NIH, including other federal agencies, may involve intellectual property and technology transfer issues. For further information, contact the Technology Development Coordinator (TDC) for the NIH Institute/Center. A list of the TDC's and their contact information may be found at http://www.ott.nih.gov/nih_staff/tdc.html

NIH employees may not transport hazardous materials in a privately owned vehicle (POV): a government vehicle must be used. All applicable packaging requirements of the Department of Transportation regulations found in 49 CFR Parts 171-178 must be followed.

The movement of infectious or potentially infectious materials within an NIH site or building requires packaging designed to reduce or eliminate potential spillage and leakage. Packaging must include a primary container within a watertight, unbreakable secondary container. There must be enough absorbent between the primary and secondary container to absorb all liquids in the primary

container in the event of breakage of the primary container. Information on shipping biological materials can be found on the DOHS website at http://dohs.ors.od.nih.gov/training.htm.

D. REFERENCES

References and copies of registration forms are available from the DOHS website http://dohs.ors.od.nih.gov/forms.htm. OSHA references are available on the OSHA website http://www.osha.gov.

1. Select Agents and Toxins. Centers for Disease Control and Prevention 42 CFR 73, Federal Register, December 13, 2002 (67 FR 76886).
2. Biosafety in Microbiological and Biomedical Laboratories. Centers for Disease Control and Prevention/National Institutes of Health. Current edition.
3. NIH Bloodborne Pathogen Exposure Control Plan for Non-Hospital Personnel. Prepared in compliance with 29 CFR 1910.1030.
4. NIH Guidelines for Research Involving Recombinant DNA Molecules (the Guidelines). Federal Register, July 5, 1994 (59 FR 34496). Amendment - Federal Register, FR, January 5, 2001 (66 FR 1146) and all current amendments.
5. Occupational Exposure to Bloodborne Pathogens. Occupational Safety and Health Administration Standard 29 CFR 1910.1030, 66 FR 5325 January 18. 2001.
6. Animals and Plant Products, U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS), Title 9, Parts 101-123. http://www.aphis.usda.gov/
7. *Dangerous Goods Regulations*, IATA. http://www.iata.org/index.htm
8. NIH Manual Chapter 1340-1, Permits for Import and Export of Biological Materials http://www1.od.nih.gov/oma/manualchapters/management/1340-1/
9. NIH Manual Chapter 26101-42-F, Shipping Policies and Procedures http://www1.od.nih.gov/oma/manualchapters/acquisitions/26101-42-F/
10. NIH Manual Chapter 3050, Intellectual Property and Technology Transfer (pending release
11. NIH Manual Chapter 1743, Keeping and Destroying Records http://www1.od.nih.gov/oma/manualchapters/management/1743/

E. RECORDS RETENTION AND DISPOSAL

All records (e-mail and non-e-mail) pertaining to this chapter must be retained and disposed of under the authority of the NIH Manual Chapter 1743, "Keeping and Destroying Records,"

Appendix 1, NIH Records Control Schedule, Sections 7000, PART 4 Protection from Biohazards Contaminants, Pollutants and Research Risks**,** B. Biohazards and C. Environmental Impact; 1300 Station Management, B. Safety; and 2600 Procurement, Property and Supply Management, C. Property, and Supply Management including all other items that apply.

NIH e-mail messages: NIH e-mail messages (messages, including attachments, that are created on the NIH computer systems or transmitted over the NIH networks) that are evidence of the activities of the agency or have informational value are considered Federal records. These records must be maintained in accordance with current NIH Records Management guidelines. Contact your IC Records Officer for additional information.

All e-mail messages are considered Government property, and if requested for a legitimate Government purpose, must be provided to the requester. Employees' supervisors, the NIH staff conducting official reviews or investigations, and the Office of Inspector General may request access to or copies of the e-mail messages.

E-mail messages must also be provided to the Congressional Oversight Committees, if requested, and are subject to the Freedom of Information Act requests. Since most e-mail systems have back-up files that are retained for significant periods of time, e-mail messages and attachments are likely to be retrievable from a back-up file after they have been deleted from an individual's computer. The back-up files are subject to the same requests as the original messages.

F. MANAGEMENT CONTROLS

The purpose of this Manual Chapter is to establish the NIH policy for working with hazardous biological materials in the research environment, including recombinant DNA materials, toxins and human pathogens classified at Biosafety Level 1 and higher, and Select Agents as defined in 42 CFR 73, Possession, Use, and Transfer of Select Agents and Toxins. NIH maintains an inventory of Select Agents transferred, received, or stored in its laboratories.

1. Office Responsible for Reviewing Management Controls Relative to this Chapter (Issuing Office): Through this manual issuance, the DOHS, ORS is accountable for the method used to ensure that management controls are implemented and working.

2. Frequency of Review (in years): Annual.

3. Method of Review: The DOHS will maintain oversight and ensure effective implementation and compliance with this policy. This shall be accomplished through the continuous review of Animal Study Proposals; annual surveys of all laboratories working with human pathogens; human blood, body fluids and tissues; recombinant DNA registrations; and Select Agent material quarterly inventories.

The DOHS maintains a database of all hazardous biological materials and laboratory locations from two separate sources: the *Registration Document for Recombinant DNA Experiments and* the *Registration of Materials (Potentially) Infectious for Humans.*

Any discrepancies in documentation will be clarified with the PI. Appropriate forms for registering and updating registered experiments are available on the DOHS website http://dohs.ors.od.nih.gov/forms.htm

4. Review Reports are sent to: An annual summary detailing the total number of registrations, surveys and reviewed animal study proposals will be sent to the Director, DOHS; the Associate Director for Research Services, the Deputy Director for Intramural Research; and the Deputy Director for Management. Issues of concern will be brought to the attention of the Associate Director for Research Services.

WORKING SAFELY WITH HAZARDOUS BIOLOGICAL MATERIALS

Appendix 1

Excerpted from Part 73, CFR 42 Possession, Use, or Transfer of Select Agents and Toxins; DHHS Select Agents and Overlap Agents.

Part 331 CFR 7 and Part 121 CFR 9 Agricultural Bioterrorism Protection Act of 2002; Possession, Use, and Transfer of Biological Agents and Toxins; USDA High Consequence Livestock Pathogen or Toxin

DHHS SELECT AGENTS

Viruses

Cercopithecine herpes virus1 (Herpes B virus)

Crimean-Congo haemorrhagic fever virus

Ebola viruses

Lassa fever virus

Marburg virus

Monkeypox virus

South American haemorrhagic fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)

Tick-borne encephalitis complex (flavi) viruses (Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis, Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever)

Variola major virus (Smallpox virus)

Variola minor (Alastrim)

Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 InfluenzaVirus)

Toxins

Abrin

Conotoxins

Diacetoxyscirpenol

Ricin

Saxitoxin

Shiga-like ribosome inactivating proteins

Tetrodotoxin

Appendix 1
(continued)

Bacteria

Rickettsia prowazekii
Rickettsia rickettsii
Yersinia pestis

Fungi

Coccidioides posadasii

DHHS-USDA OVERLAP AGENTS

Viruses

Eastern equine encephalitis virus
Nipah virus
Hendra virus
Rift Valley fever virus
Venezuelan equine encephalitis virus

Bacteria

Bacillus anthracis
Botulinum neurotoxin producing strains of *Clostridium*
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei
Burkholderia pseudomallei
Coxiella burnetii
Francisella tularensis

Toxins

Botulinum neurotoxins
Clostridium perfringens epsilon toxin
Shigatoxin
Staphylococcal enterotoxins
T– 2 toxin

Appendix 1
(continued)

Fungi

Coccidioides immitis

APHIS PLANT PATHOGENS

Liberobacter africanus,
Liberobacter asiaticus
Ralstonia solanacearum Race 3
Peronosclerospora philippinensis
Sclerophthora rayssiae var zeae
Xanthomonas oryzae pv. oryzicola
Xylella fastidiosa (citrus variegated chlorosis strain)

USDA High Consequence Livestock Pathogen or Toxin

African horse sickness virus
African swine fever virus
Akabane virus
Avian influenza virus (highly pathogenic)
Blue tongue virus (exotic)
Bovine spongiform encephalopathy agent
Camel pox virus
Classical swine fever virus
Foot and mouth disease virus
Goat pox virus
Japanese encephalitis virus
Lumpy skin disease virus
Malignant catarrhal fever
Menangle virus
Newcastle disease virus (exotic)
Peste des petits ruminants
Rinderpest virus

Appendix 1 (continued)

USDA High Consequence Livestock Pathogen or Toxin (continued)

Sheep pox

Swine vesicular disease virus

Vesicular stomatitis virus (exotic)

Cowdria Ruminantium (Heartwater)

Mycoplasma capricolu/M. F38/*M. mycoides capri* (contagious caprine pleuropneumonia agent)

Mycoplasma mycoides mycoides (contagious bovine pleuropneumonia agent)