



LABORATORY BIOSAFETY ISSUES

**BIO Safety & Security Committee
June 2002**



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I. INTRODUCTION

The intensified concern over bioterrorism in the aftermath of September 11, 2002, and the subsequent anthrax mail attacks have caused Congress, Federal regulators and Federal law enforcement authorities to increase their scrutiny of potential sources of biohazardous materials, including the nation's scientific research laboratories. This document addresses the existing regulatory scheme that governs the transportation, handling and use of certain etiologic agents, as well as current legislative efforts to impose stricter standards on facilities that transport, handle and use such agents.

The first section of this document addresses transportation regulations applicable to laboratories handling certain etiologic agents. This section first covers the Centers for Disease Control & Prevention (the "CDC") regulations governing the interstate shipment of etiologic agents. These regulations create a list of so-called "select agents," require facilities that transfer or receive those select agents to register with the CDC and impose certain transfer requirements. This section then provides a brief overview of the more comprehensive transportation regulations promulgated by the Department of Transportation ("DOT") and the interaction of those regulations with international standards. Also provided is a high level overview of potentially relevant permit requirements addressing the importation of etiologic agents, plant material, animals and genetically engineered organisms.

The second section of this document provides an overview of other Federal regulations and sources of guidance applicable to facilities that handle etiologic agents. ^{1/} The following regulations and guidance are discussed below: (1) NIH's Recombinant DNA Guidelines; (2) Occupational Health and Safety Act standards, with a particular emphasis on Bloodborne Pathogens and Exposure to Hazardous Chemicals in Laboratories; and (3) various environmental laws including:

^{1/} There are also numerous State environmental laws and regulations that are beyond the scope of this document.

- the Resource Conservation and Recovery Act ("RCRA");
- the Toxic Substances Control Act ("TSCA");
- the Federal Clean Air Act ("CAA");
- the Federal Clean Water Act ("CWA"); and
- the Emergency Planning Community Right to Know Act ("EPCRA") and the Comprehensive Environmental Response, Compensation and Liability Act ("CERCLA").

The third section of the document addresses recent Federal legislative initiatives in the area of biosafety. First, we address the USA PATRIOT Act, which was enacted in October 2001 and that creates new biosafety-related criminal offenses. Second, we provide a brief summary of biosafety legislation that has been passed in two slightly different versions by the House and Senate and the final language of which has yet to be officially decided through conference proceedings. Although there has yet to be an official conference for this Bill, we are including a summary of compromise language that had been included in the recently enacted Department of Defense Appropriations Bill, but that was deleted for technical reasons. It is our understanding, however, that the language in the appropriations bill represents agreed upon language.

This document is provided as a guide; it is not intended to constitute legal advice on the rules, regulations or laws discussed here in.

II. TRANSPORTATION REGULATIONS

A. The CDC Regulations

In 1996, Congress enacted the Antiterrorism and Effective Death Penalty Act of 1996 (the "Act"), Pub. L. No. 104-132, which was a broad-ranging statute that sought to deter terrorism by expanding the circumstances under which countries that support terrorists could be sued, making it more difficult for terrorists to obtain financial support, and strengthening immigration laws to prevent terrorist infiltrations into the United States. From the perspective of biosafety, the Act required the Secretary of the Department of Health and Human Services ("HHS") to promulgate regulations that would create a list of biological agents that posed a severe risk to the public's health and safety, establish and enforce safety procedures governing the transportation of certain agents, implement safeguards to prevent unauthorized access to such agents, and ensure the appropriate availability of regulated agents for research, educational and other legitimate purposes.

HHS delegated the above-referenced responsibility to the CDC, which issued regulations now set forth within 42 C.F.R. Part 72. We address each of the major elements of the CDC regulations below.

1. Select Agents

In accordance with its statutory mandate, the CDC prepared a list of over thirty viruses, bacteria, rickettsiae, fungi and toxins that are considered to be "select agents." See 42 C.F.R. Part 72, Appendix A. Among the select agents are:

- Viruses – Eastern Equine Encephalitis, Ebola, Yellow Fever;
- Bacteria – *Bacillus Anthracis*;
- Rickettsiae; and
- Toxins – Botulinum, Ricin.

2. Registration Requirements

In order to transfer or receive a select agent lawfully, a facility 2/ must register with an approved entity 3/ or be approved by the CDC as being equipped to handle select agents at Biosafety Levels 2 – 4, depending on the agent being handled. When seeking to become a registered facility, an applicant must provide the reviewer with sufficient information to determine whether it is equipped to handle agents at Biosafety Levels 2 – 4, depending on the agent and the work contemplated, and also must agree to submit to potential inspections. Once registered, the facility receives a unique

2/ A "facility" is defined as "any individual or government agency, university, corporation, company, partnership, society, association, firm, or other legal entity located at a single geographic site that may transfer or receive through any means a select agent" 42 C.F.R. § 72.6(j).

3/ The CDC may authorize either a State or private entity to register facilities handling select agents. The CDC will authorize such entities to register facilities only if the registering entity's criteria for determining whether the applicant's biosafety standards are consistent with a CDC publication entitled "*Biosafety in Microbiological and Biomedical Laboratories*". The biosafety standards and requirements set forth in that publication for operations at biosafety levels 2 – 4 have been incorporated by reference into 42 C.F.R. Part 72.

registration number. Moreover, a registered facility is subject to additional inspections to ensure that it remains capable of handling select agents. 4/

Once obtained, a registration remains in effect until relinquished by the facility or withdrawn by the CDC. 5/ Grounds for withdrawal of a registration include:

- Evidence that the facility is no longer capable of handling select agents at the applicable biosafety level;
- Evidence that the facility has handled select agents in a manner contrary to applicable biosafety level requirements;
- Evidence that the facility has or intends to utilize select agents in a manner harmful to humans;
- Evidence that the facility has failed to comply with the CDC regulations; or
- Failure to pay a registration fee. 6/

A facility that has its registration application denied or that has an existing registration withdrawn may appeal such a decision to the Secretary of HHS. Any appeal must be filed within 14 days of the date on which the adverse decision occurred and must set forth in detail the reasons why the decision was erroneous.

3. Requests for Select Agents

Prior to transferring 7/ any select agent, a facility must complete a CDC Form EA-101, which requires:

4/ Inspections may be random or for cause and may include an examination of relevant documents and records and/or review of the mechanisms used by the facility to track intrafacility transfers, as well as disposal procedures.

5/ The CDC's laboratory registration application states that a facility will receive a registration certificate valid for three years.

6/ The requirement to pay a site registration fee is currently suspended.

7/ A "transfer" is defined as "[t]he conveyance or movement from a point of origination to a point of destination either: (i) [f]rom one state or territory to another or (ii) [e]ntirely within one contiguous state or territory." 42 C.F.R. § 72.6(j). The CDC regulations also note that an intrafacility transfer within a registered facility located at a single geographic site is not covered by the

[Footnote continued]

- The name of the requestor and requesting facility;
- The name of the transferor and transferring facility;
- The names of the responsible facility officials §/ for both the transferor and the requestor;
- The requesting facility's registration number;
- The transferring facility's registration number;
- The name of the agent being shipped;
- The proposed use of the agent; and
- The quantity being shipped.

The EA-101 must be signed by both the transferor and the requestor, as well as by the responsible facility officials from both entities. Both facilities are required to maintain the EA-101 for a period of five years after the date of shipment or for five years after the select agents were consumed or disposed of, whichever is greater. Moreover, facilities are required to produce an EA-101 form when requested by Federal and authorized local law enforcement authorities, officials authorized by the Secretary of HHS and officials of the registering entity.

[Footnote continued]

regulations addressing requests for agents, verification of registration and transfer, each of which is discussed in detail below. However, in order for this exemption to apply, the intended use of the agent must be consistent with the most current transfer form and the facility must maintain records of the name and location of the recipient, as well as the amount of agent transferred and the date of the transfer.

§/ A "responsible facility official" is defined as "an official authorized to transfer and receive select agents covered by this part on behalf of the transferor's and/or requestor's facility. This person should be either a safety officer, a senior management official of the facility or both. The responsible facility official should not be an individual who actually transfers or receives an agent at the facility." 42 C.F.R. § 72.6(j).

4. Verification of Registration

Prior to transferring a select agent, the transferor's responsible facility official is required to verify with the requestor's responsible facility official that:

- The requesting facility possesses a valid registration;
- The requestor is an employee of the requesting facility; and
- The EA-101 accurately reflects the proposed use of the select agent being transferred.

If the transferor facility is unable to verify any of the above-referenced information, or suspects that any of the information received is incorrect, the transferor facility must notify the CDC.

5. Transfer of Select Agents

Only after the proper completion of an EA-101 and verification of the requesting facility's registration may the transfer of a select agent occur. There are a series of specific packaging requirements applicable to the transfer of etiologic agents. ^{9/} For example, material (including diagnostic specimens and biological products) that may contain an etiologic agent may not be transferred without packing the material in such a manner as to prevent leaks, as well as to ensure that the material can withstand shocks, pressure changes and other stresses.

In addition to the packaging instructions, the CDC regulations also set forth certain verification of delivery requirements:

- A sender of certain specified agents (those that must be sent by registered mail or its equivalent) must notify the CDC if the sender fails to receive notice of delivery within five days of the anticipated delivery date.
- Similarly, the requesting facility's responsible facility official must acknowledge receipt of the select agent either telephonically or by other

^{9/} These requirements apply to a broader spectrum of agents than the "select agents" listed in Appendix A to 42 C.F.R. Part 72. That is because 42 C.F.R. § 72.6, which addresses select agents, was, as stated above, promulgated in response to the Antiterrorism and Effective Death Penalty Act of 1996 and was intended to bolster the already existing regulations in 42 C.F.R. Part 72.

electronic means within 36 hours of receipt and provide a paper copy or facsimile transmission of the receipt to the transferor within three business days of receipt of the agent.

- Within 24 hours of being notified by the requestor that the select agent has been received, the transferor is required to provide a paper copy or facsimile transmission of the relevant EA-101 to the entity holding the transferor's registration. This copy will be maintained in the registering entity's central registry.

6. Disposal of Select Agents

If a facility completes a project involving a select agent without completely consuming all of the agent, the facility must take appropriate steps to dispose of the remainder. This can be accomplished by securely storing the agent in accordance with prudent laboratory practices, transferring the agent to another registered facility or destroying the agent on-site using autoclaving, incineration or some other recognized sterilization or neutralization process. Once the select agent has been entirely consumed or destroyed, the responsible facility official must formally notify the cognizant registering entity. This notification must be included on the EA-101, a copy of which must be retained for five years.

7. Exemptions

In some instances, a facility may be exempt from certain requirements of the CDC regulations. The first exemption provides that clinical laboratories certified under the Clinical Laboratories Improvement Amendments ("CLIA") of 1988 that use select agents for diagnostic, reference, verification, or proficiency testing purposes are exempt from the provisions of 42 C.F.R. § 72.6. The second exemption provides that a select agent is exempt from 42 C.F.R. Part 72 10/ if it meets one of three tests:

10/ It is noteworthy that the plain reading of this exemption suggests that if a select agent meets one of the three criteria it is exempt from 42 C.F.R. Part 72 in its entirety. This is, of course, inconsistent with the CLIA exemption that would exempt certain laboratories from Section 72.6, but not the rest of Part 72. To clarify this apparent inconsistency, we interviewed a representative of the CDC who informed us that the CDC views both exemptions as essentially allowing a laboratory to forego the registration requirements of Section 72.6. In other words, if a laboratory is going to work with only a particular select agent that has been inactivated for use in a vaccine, that facility would not have to register with the CDC. The CDC also noted that regardless of whether the packaging provisions of

[Footnote continued]

- The agent is part of a clinical specimen intended for diagnostic, reference or verification purposes;
- The agent is a toxin having an LD sub50 for vertebrates of more than 100 nanograms per kilogram of body weight, which is used for legitimate medical purposes or biomedical research, or is one of the listed toxins, which has been inactivated for use as a vaccine or otherwise detoxified for use in biomedical research procedures; or
- The agent is on specified in Appendix A to the CDC regulations and/or CDC Form EA-101 as being exempt.

8. Penalties

Failure to comply with the CDC regulations can result in substantial civil and/or criminal penalties:

- Individuals may be penalized by a fine of up to \$250,000 and/or one year in jail. Organizations are subject to a fine of up to \$500,000 per event.
- Likewise, making a false, fictitious or fraudulent statement or representation on any of the forms required by the CDC regulations could result in an individual receiving a jail sentence of up to five years or a fine; an organization would be subject to a fine.

B. DOT Regulations

In addition to the CDC regulations governing the interstate shipment of etiologic agents, other entities have promulgated regulations addressing the transportation of hazardous materials. For example, DOT has promulgated the Hazardous Materials Regulations ("HMR"), 49 C.F.R. Parts 171 – 180, that address, among other issues, the classification and packaging of certain hazardous materials for intrastate, interstate and overseas transportation. Additionally, the International Civil Aviation Organization (the "ICAO"), which has jurisdiction over international civil aviation matters, has published

[Footnote continued]

Part 72 apply, a facility transporting an etiologic agent would have to comply with the stringent DOT transportation regulations discussed below.

the "Technical Instructions for the Safe Transport of Dangerous Goods by Air", which are based on United Nations recommendations. 11/ The HMR recognize the ICAO standards and provide that in many instances, a hazardous material may be legally transported by air (with either prior or subsequent transportation by vehicle) if the shipment is made in accordance with the ICAO standards. However, the HMR note that although they are based on UN recommendations, and are generally consistent with the ICAO standards, compliance with the HMR will not "guarantee acceptance by regulatory bodies outside of the United States." 49 C.F.R. § 173.1(d). 12/

The general regulatory scheme set forth in the HMR mandates that "[n]o person may offer or accept a hazardous material for transportation in commerce unless . . . the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment" 49 C.F.R. § 171.2(a). The specific regulations set forth detailed guidance regarding:

- The preparation of shipping papers;
- Marking, labeling and placarding responsibilities;
- Emergency response information; and
- Training materials.

The HMR also provide detailed instructions on how to classify hazardous materials and specific instructions pertaining to the transportation of such materials by rail, aircraft, vessel and public highway. The remaining sections of the HMR set forth specifications for the actual packages used to transport hazardous materials and for tank cars used for that purpose.

Failure to comply with the HMR can result in significant penalties that can be compounded (i.e., each breach is considered a violation, thereby resulting in a single

11/ The International Air Transportation Association has published the "Dangerous Goods Regulations", which present a somewhat "simplified" and more "user friendly" version of the ICAO standards.

12/ Although beyond the scope of this memorandum, laboratories that are exporting human, animal or plant materials should be aware of the Export Administration Regulations ("EAR"), 15 C.F.R. Parts 730-774, and the International Arms Control Regulations ("ITAR"), 22 C.F.R. Parts 120-130, administered by the Department of Commerce's Bureau of Export Controls and the State Department Office of Defense Trade Controls, respectively.

package potentially causing numerous violations). Moreover, a willful violation of the HMR can lead to criminal penalties.

C. Permit Requirements 13/

1. Etiologic Agents, Hosts and Vectors

Etiologic agents, hosts and vectors (organisms such as mosquitoes, ticks or snails with the capacity to transmit infectious diseases) are often imported into the United States for research purposes. However, pursuant to 42 C.F.R. § 71.54, no person may

import into the United States, nor distribute after importation, any etiologic agent or any arthropod or other animal host or vector of human disease, or any exotic living arthropod or other animal capable of being a host or vector of human disease unless accompanied by a permit [issued by the CDC].

Such a permit may be issued only to the importer who will be considered legally responsible for ensuring that the foreign shipper packages, labels and ships the material in accordance with applicable regulations. When the importer receives the permit, it will be accompanied by shipping labels that must be sent by the importer, along with a copy of the permit, to the shipper.

Among the information that a permit applicant must provide is the following:

- The applicant's name (the applicant should be knowledgeable and skilled in handling infectious agents or biological material, directly responsible for the contemplated work and located at the address where the work will be performed);
- The complete name, address, telephone and facsimile numbers of the shipper;
- A description of the sample, the host source and the etiologic agent (if appropriate);

13/ Compliance with the permitting regulations discussed below does not ensure compliance with other potentially applicable permit requirements, such as those promulgated by the Fish and Wildlife Service or the EPA.

- Method of transport;
- Quantity of material being imported;
- Proposed use;
- The biosafety level of the laboratory where the work will occur; and
- Qualifications and experience of technical personnel (including, if pertinent, a list of publications).

2. Vectors and Organisms

The Department of Agriculture has promulgated regulations, set forth at 9 C.F.R. Part 122, that generally prohibit the importation of vectors and organisms 14/ into the United States without a permit. A permit applicant must provide

- the name and address of the consignee,
- the true name and character of each of the organisms or vectors; and
- the use to which each will be put.

In order to obtain a permit, an applicant must also agree to comply with specified safeguards.

3. Plant Pest Permits

The Department of Agriculture has issued regulations, 7 C.F.R. Part 330, governing the movement of plant pests, which are defined as:

any living stage of insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof, viruses, or any organisms similar to or allied with any of the foregoing, or any infectious substances of the aforementioned which are

14/ A "vector" is defined as "all animals (including poultry) . . . which have been treated or inoculated with organisms, or which are diseased or infected with any contagious, infectious, or communicable disease of animals or poultry or which have been exposed to any such disease." 9 C.F.R. § 122.1. An "organism" is "all cultures or collections of organisms or their derivatives, which may introduce or disseminate any contagious or infectious disease of animals (including poultry)." Id.

not genetically engineered as defined in 7 C.F.R. § 340.1 which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants. 15/

Under the terms of these regulations, it is generally prohibited to knowingly move a plant pest into or through the United States from outside the country, in interstate commerce, or to accept delivery of a plant pest unless the movement was authorized by a permit. However, biological specimens of plant pests that are preserved or dried may be imported without a permit, although they are subject to inspection on arrival.

Permits to move plant pests into or through the United States will only be granted to United States residents. To obtain such a permit, one must provide the Plant Protection and Quarantine Programs the following information (to the extent it is known):

- Scientific name of the pest;
- Stage, quantity, origin and destination;
- Whether the pest is established in the State, Territory or other jurisdiction of destination in the United States;
- Method of shipment, proposed port of first arrival in the United States (or of export if permit is for moving through the United States), approximate date of arrival and number of parcels expected to be moved;
- Intended use;
- Measures to be employed to prevent danger of plant pest dissemination; and
- Method of final disposition.

Additionally, if host material must accompany the plant pest, the application is required to state the name of the host material and why it is necessary.

Permits to move plant pests in interstate commerce also require submission of an application, which should contain all of the pertinent information set forth above. In addition, the applicant should provide the approximate dates the movement will occur.

15/ 7 C.F.R. § 330.100.

If the interstate movement is to a port for export purposes, the application should include:

- Scientific name of the pest;
- Stage, quantity, origin and destination;
- Method of shipment, proposed port of export, approximate date of the movement and number of parcels expected to be moved;
- Proposed use; and
- Measures to be employed to prevent danger of plant pest dissemination during the interstate movement.

The regulations also provide a series of requirements governing packing materials and containers for plant pest movement. Among these requirements is a general mandate that plant pests must be free of soil and must be contained in approved packing materials. Containers holding plant pests must be "stoutly constructed so as to prevent breakage while in transit and danger of plant pest dissemination." 7 C.F.R. § 330.210. They must also meet applicable labeling requirements.

4. Permits for Genetically Engineered Organisms

Regulations promulgated by the Department of Agriculture, 7 C.F.R. Part 340, govern the importation, interstate movement or release into the environment of "regulated articles" into the United States. Regulated articles are considered to be:

an organism that has been genetically engineered (via recombinant DNA techniques) from a donor organism, recipient organism, vector, or vector agent that is a plant pest or contains plant pest components. APHIS [Animal and Plant Health Inspection Service] regulations in 7 C.F.R. 340.2 list such organisms. Other genetically engineered organisms may be regulated articles if they have been genetically engineered using an unclassified organism or if the Director of Biotechnology and Scientific Services determines that the genetically engineered organism is a regulated article. 16/

16/ Department of Agriculture, Animal and Plant Health Inspection Service
Questions and Answers on General Regulatory Authority Under 7 C.F.R. 340.

A permit is not required if an otherwise regulated article is exempted from coverage or can meet a complex six-part test authorizing introduction by notification, as well as the related performance standards. 17/

There are several different types of permits, including:

- Permits for releases into the environment, applications for which must be submitted at least 120 days before the proposed release. Among the information that must be provided is the following:

- (1) name, title, address, telephone number and signature;
- (2) all scientific and trade names and all designations needed to identify the (i) donor organism, (ii) recipient organism, (iii) vector or vector agent, (iv) constituent of each regulated article which is a product, and (v) the regulated article;
- (3) names, addresses and telephone numbers of the persons who developed or supplied the regulated article;
- (4) a description of the means of movement;
- (5) a description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs from the expression in the non-modified parental organism;
- (6) A detailed description of the molecular biology of the system;
- (7) Country and locality where the donor organism, recipient organism, vector or vector agent, and regulated article were collected, developed, and produced;
- (8) A detailed description of the purpose for the introduction of the regulated article including a detailed description of the proposed experimental and/or production design;
- (9) The quantity of the regulated article to be introduced and proposed schedule and number of introductions;
- (10) A detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in the United States to prevent contamination, release, and dissemination in the production of the: Donor organism; recipient organism; vector or

17/ The introduction by notification test is set forth at 7 C.F.R. § 340.3.

vector agent; constituent of each regulated article which is a product; and regulated article;

(11) A detailed description of the intended destination (including final and all intermediate destinations), uses, and/or distribution of the regulated article;

(12) A detailed description of the proposed procedures, processes, and safeguards, which will be used to prevent escape and dissemination of the regulated article at each of the intended destinations;

(13) A detailed description of any biological material accompanying the regulated article during movement; and

(14) A detailed description of the proposed method of final disposition of the regulated article.

- Limited Permits for interstate movement or importation of a regulated article, applications for which must be submitted at least 60 days before the first proposed interstate movement or importation. If a person is seeking a limited permit for interstate movement, a permit can be obtained for the interstate movement of multiple regulated articles. If the permit is sought for the purpose of multiple interstate movements between contained facilities, the applicant must specify (i) the regulated articles to be moved, (ii) the origins and destinations of the proposed shipments, (iii) a description of the contained facilities where the regulated articles will be utilized, and (iv) a description of the containers that will be used. Limited permit applications also include the information set forth above in paragraphs 1, 2, 4, 6, 7, 9 and 11-14.

The genetically engineered organism regulations also provide that any permits issued will include conditions, with which the permit holder must comply, intended to prevent the dissemination and establishment of plant pests. Likewise, certain marking and packaging requirements are set forth.

III. OTHER SOURCES OF REGULATION 18/

A. NIH's Recombinant DNA Guidelines

The "NIH Guidelines for Research Involving Recombinant DNA Molecules" were enacted to provide guidance regarding the construction and handling of recombinant DNA molecules, as well as organisms and viruses that contain recombinant DNA molecules. The Guidelines define recombinant DNA molecules as "(i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above." Guidelines § 1-B. 19/ The Guidelines apply to all NIH-funded and non-NIH funded gene transfer projects that are conducted at or sponsored by an organization that receives NIH support for recombinant DNA research. Failure to comply with the Guidelines can jeopardize a facility's recombinant DNA research funding.

The Guidelines require facilities engaged in recombinant DNA experiments to establish and implement policies and procedures that will ensure the safe conduct of covered research. To accomplish that goal, the Guidelines set forth mechanisms to assist researchers in assessing the risk associated with working with a particular agent and to use that assessment to implement appropriate safeguards. One key element of the Guidelines is the requirement that an institution conducting recombinant DNA research

18/ Each of these sources contains a multitude of specific requirements that are essentially of a "checklist" nature. This memorandum is not intended to provide a comprehensive treatment of all requirements that are potentially applicable to a particular laboratory. Rather, this memorandum provides an overview of each source that is intended to present the reader with a sense of the types of specific requirements that may be applicable to a particular laboratory.

19/ The CDC's select agent list notes that recombinant organisms/molecules include "[g]enetically modified microorganisms or genetic elements from organisms on Appendix A [the select agent list], shown to produce or encode for a factor associated with a disease . . . [or] [g]enetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins listed in this Appendix, or their toxic subunits." 42 C.F.R. Part 72, Appendix A.

assemble an Institutional Biosafety Committee ("IBC") that is charged with reviewing and approving all experiments that are not exempt from the Guidelines. 20/

B. OSHA Standards

The Occupational Safety and Health Act of 1970 (the "Act") was passed by Congress to ensure safe and healthful working conditions. Under the authority of the Act, the Occupational Health & Safety Administration ("OSHA") has promulgated numerous standards, each of which is directed toward a specific workplace hazard. Of these standards, two are particularly relevant to laboratories – the Bloodborne Pathogens Standard and the Standard for Exposure to Hazardous Chemicals in the Laboratory. We first address those two standards and then provide brief summaries of some of the other potentially relevant standards.

1. The Bloodborne Pathogens Standard

The Bloodborne Pathogens Standard, 29 C.F.R. § 1910.1030, applies to occupational exposures to “blood” or “other potentially infectious materials.” “Blood” means “human blood, human blood components, and products made from human blood.” 29 C.F.R. § 1910.1030(b). “Other potentially infectious materials” means

- (1) The following human body fluids: semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, pericardial fluid, peritoneal fluid, amniotic fluid, saliva in dental procedures, any body fluid that is visibly contaminated with blood, and all body fluids in situations where it is difficult or impossible to differentiate between body fluids;
- (2) Any unfixed tissue or organ (other than intact skin) from a human (living or dead); and (3) HIV-containing cell or tissue cultures, organ cultures, and HIV- or HBV-containing culture medium or other solutions; and blood, organs, or other tissues from experimental animals infected with HIV or HBV.

Likewise, the term of "occupational exposure" means "reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials that may result from the performance of an employee's duties." Id.

20/ There are certain types of experiments that require additional approval from NIH's Recombinant DNA Advisory Committee and/or by NIH's Office of Biotechnology Activities.

If the Bloodborne Pathogens Standard applies, an employer is required to establish a written Exposure Control Plan that is designed to eliminate or minimize employee exposures. Such a plan is required to include the following elements:

- An exposure determination, which sets forth a list of job classifications in which some or all employees have occupational exposure, as well as a list of tasks and procedures in which occupational exposure occurs and that are performed by employees in the listed job classifications;
- Procedures for evaluating exposure incidents; and
- A schedule and methods of implementation addressing how the employer will meet (i) the Standard's requirements regarding general protective measures (known as "methods of compliance"), (ii) the portion of the Standard governing HIV and HBV Research Laboratories and Production Facilities, (iii) the portion of the Standard governing Hepatitis B Vaccination and Post Exposure Evaluation and Follow-up, (iii) the Standard's requirements concerning the communication of hazards to employees; and (iv) recordkeeping requirements.
- Methods of compliance include engineering and work practice controls (such as handwashing, prohibitions against eating, smoking, and applying cosmetics where occupational exposure is reasonably likely to occur), container labeling and storage requirements, and housekeeping requirements. (d). Where occupational exposure remains after institution of these controls, personal protective equipment (e.g. gloves, gowns, ventilation devices) also must be used. (d)(3).

Once implemented, the Exposure Control Plan must be made available to employees and must be reviewed and updated at least annually. Moreover, the plan must be updated to reflect new or modified tasks or procedures that affect occupational exposure, or whenever new or revised employee positions involve occupational exposure.

2. The Standard for Exposure to Hazardous Chemicals in Laboratories

The OSHA Standard for Exposure to Hazardous Chemicals in Laboratories, 29 C.F.R. § 1910.1450, applies to any employer who engages in the "laboratory use of

hazardous chemicals," 21/ a term that is defined to mean the handling or using of such chemicals under all of the following conditions:

- Chemical manipulations are carried out on a "laboratory scale" (i.e., where the project is designed to be easily and safely handled by one person, and not where the function of the workplace is to produce commercial quantities of materials);
- Multiple chemical procedures or chemicals are used;
- The procedures involved are not part of a production process, nor in any way simulate a production process; and
- Protective laboratory practices and equipment are available and in common use to minimize the potential for employee exposure to hazardous chemicals.

If the OSHA standard applies to a particular laboratory, there are certain safeguards that must be put into practice. Primarily, employers are required to implement a Chemical Hygiene Plan that is capable of protecting employees from the dangers associated with the use of hazardous chemicals in the laboratory and that will maintain exposures below applicable limits.

There are several required elements of such a plan:

- Standard operating procedures ("SOPs") to be followed when laboratory work involves hazardous chemicals;
- Criteria to be used by the employer to develop control procedures to reduce employee exposure to hazardous chemicals (these measures should include engineering controls, the use of protective equipment and personal hygiene practices);
- A requirement that fume hoods and other protective equipment operate properly and procedures to be implemented if they are not;
- Provisions for employee training and information;

21/ A "hazardous chemical" is "a chemical for which there is statistically significant evidence based on at least one study conducted in accordance with established scientific principles that acute or chronic health effects may occur in exposed employees." 29 C.F.R. § 1910.1450(b).

- Circumstances when a particular procedure will require prior approval from the employer;
- Provisions to ensure appropriate medical care for employees;
- Designation of those individuals who will carry out the plan and the appointment of a Chemical Hygiene Officer (and, if necessary, a Chemical Hygiene Committee); and
- Specific provisions addressing the use of particularly hazardous substances (i.e., use of such substances would be restricted to a particular area, identification of containment devices, and procedures to remove waste and to carry out a decontamination).

Once implemented, the Chemical Hygiene Plan must be made available to employees and their representatives, as well as, on request, to the Assistant Secretary for Occupational Safety and Health, Department of Labor. Moreover, employers must review the plan at least annually for the purpose of making any necessary updates.

3. The Hazard Communication Standard

The Hazard Communication Standard is set forth at 29 C.F.R. § 1910.1200 and is intended "to ensure that the hazards of all chemicals produced or imported are evaluated, and that information concerning their hazards is transmitted to employers and employees." 29 C.F.R. § 1910.1200(a)(1). The Hazard Communication Standard applies to any hazardous chemical 22/ known to be present in the workplace in a manner that employees may be exposed to it under normal conditions of use or in a foreseeable emergency. The Hazard Communication Standard rules contain five major requirements:

- Hazard determination. Chemical manufacturers and importers must determine the hazards of their products.
- Labeling. Manufacturers, importers and distributors must label containers of chemicals determined to be hazardous with the chemical identity and appropriate hazard warnings. Employers are required to ensure that the labels on incoming hazardous chemicals are neither removed nor defaced.

22/ A chemical is hazardous if it presents either a health or a physical hazard. 29 C.F.R. § 1910.1200(c).

- Material Safety Data Sheets (“MSDSs”). Employers must maintain all material safety data sheets that are received by the laboratory with shipments of hazardous chemicals, and ensure that the MSDSs are available to employees when they are in their work areas.
- Employee Information and Training. Employees must be provided with comprehensive information and training concerning workplace hazards. This training must be offered at the time an initial assignment is made, as well as when a new hazard is introduced into the workplace. The program must include, among other elements: (i) identification of operations in the employee's work area where hazardous chemicals are present, (ii) methods to detect the presence or release of hazardous chemicals, (iii) the physical and health hazards of chemicals in the area; (iv) techniques to protect oneself from hazardous chemicals, and (v) details of the employer's hazard communication program.
- Written Hazard Communication Program. Employers must develop and implement comprehensive programs designed to ensure that employees are aware of hazardous chemicals in the workplace

A laboratory that ships hazardous chemicals is deemed to be either a chemical manufacturer or a distributor and must therefore comply with applicable labeling and MSDS requirements.

4. Hazardous Waste Operating and Emergency Response Standard

The Hazardous Waste Operating and Emergency Response (“HAZWOPER”) Standard is set forth at 29 C.F.R. § 1910.120 and covers, among other topics, “[e]mergency response operations for releases of, or substantial threats of releases of, hazardous substances without regard to the location of the hazard.” 29 C.F.R. § 1910.1210(a)(1)(v). ^{23/} Under the standard, employers are required to develop a

^{23/} The HAZWOPER standard also applies to operations: (1) required by a governmental body and conducted at uncontrolled hazardous waste sites; (2) corrective actions involving clean-up operations at sites covered by RCRA; (3) voluntary clean-up operations at sites recognized by governmental bodies as being uncontrolled hazardous waste sites; and (4) hazardous waste operations that are conducted at treatment, storage or disposal facilities regulated under RCRA. For the purposes of this memorandum, we discuss this standard only to the extent that it applies to, as stated above, emergency response operations conducted without regard to the location of the hazard.

written emergency response plan intended to anticipate potential emergency situations before they occur, and make that plan available to employees, their representatives and OSHA personnel. Such a plan must include:

- Pre-emergency planning and coordination with outside parties;
- Personnel roles, lines of authority, training and communication;
- Emergency recognition and prevention;
- Safe distances and places of refuge;
- Site security and control;
- Evacuation routes and procedures;
- Decontamination procedures;
- Emergency medical treatment and first aid procedures;
- Emergency alerting and response procedures;
- Critique of response and follow-up; and
- Personal protective and emergency equipment. 24/

In addition to the emergency plan requirement, among the other obligations imposed on employers by the HAZWOPER standard is the implementation of a medical surveillance program in certain circumstances, provision of employee training, and implementation of engineering controls and work practices to protect employees from exposure to hazardous substances.

5. Standards for Personal Protective Equipment

A critical element of laboratory safety is personal protective equipment ("PPE"). OSHA standards addressing various types of PPE are set forth at 29 C.F.R. §§ 1910.132-139, and cover:

- Eye and face protection;
- Respiratory protection;

24/ The plan may utilize the State or local emergency response plan, or both, to avoid duplication.

- Head protection;
- Occupational foot protection;
- Electrical protective devices;
- Hand protection; and
- Respiratory protection for M. tuberculosis.

The general requirement for PPE, set forth at 29 C.F.R. § 132(a), provides that:

Protective equipment, including personal protective equipment for eyes, face, head, and extremities, protective clothing, respiratory devices, and protective shields and barriers, shall be provided, used, and maintained in a sanitary and reliable condition wherever it is necessary by reason of hazards of processes or environment, chemical hazards, radiological hazards, or mechanical irritants encountered in a manner capable of causing injury or impairment in the function of any part of the body through absorption, inhalation, or physical contact.

For most varieties of protective equipment, employers are required to assess the potential workplace hazards and select appropriate PPE. Likewise, employers are required to provide training that addresses:

- When PPE should be used;
- What PPE is necessary;
- How to properly put PPE on, take it off and wear it;
- The limitations of the PPE; and
- The proper care, maintenance, useful life and disposal of the PPE. 25/

25/ The training and assessment requirements do not apply to respiratory protection and electrical protective devices.

6. Standards Regarding Medical Services and First Aid

The OSHA standard regarding medical services and first aid is located at 29 C.F.R. § 151 and requires that employers take the following steps:

- Ensure that medical personnel are readily available for advice and consultation;
- In the event there is not an infirmary, clinic, or hospital in close proximity to the workplace, ensure that there are personnel adequately trained in first aid procedures and that adequate first aid supplies are available; and
- When the eyes or body of an employee could be exposed to injurious or corrosive materials, ensure the immediate and emergency availability of suitable facilities for quick drenching or flushing of the eyes and/or body.

7. The Air Contaminants Standard

The Air Contaminants Standard is set forth at 29 C.F.R. § 1910.1000 and provides occupational exposure limits to a multitude of substances listed in three tables that are appended to the standard. In a very general sense, the exposure limits are based on acceptable ceiling values or concentrations and 8-hour time weighted averages.

In order to achieve compliance with this standard, an employer is required to determine and implement administrative and engineering controls "whenever feasible." If it is not feasible to achieve full compliance through such controls, other measures, such as protective equipment, must be utilized to maintain acceptable exposure limits. The use of any equipment or technical measures must be approved by a "competent" industrial hygienist or other technically qualified individual. 26/

26/ Standards for exposures to numerous other chemicals are set forth at 29 C.F.R. §§ 1910.1001-1052.

8. Standards Applicable to Specific Hazardous Materials 27/

OSHA has also promulgated, at 29 C.F.R. §§ 1910.101-111, a series of standards addressing the use and handling of hazardous materials, including:

- Acetylene;
- Hydrogen;
- Oxygen;
- Nitrous Oxide;
- Flammable and combustible liquids;
- Spray finishing using flammable and combustible liquids;
- Dip tanks containing flammable or combustible liquids;
- Explosives and blasting agents;
- Storage and handling of liquefied petroleum gases;
- Storage and handling of anhydrous ammonia; and
- General requirements regarding compressed gasses.

C. Environmental Laws 28/

1. Resource Conservation and Recovery Act

RCRA, 42 U.S.C. §§ 6901 – 6992(k), regulates the generation, storage and disposal of solid (non-hazardous) and hazardous wastes. Most laboratories generate hazardous waste and are therefore subject to hazardous waste management regulations (40 C.F.R. Parts 260 through 270). Laboratories also may be subject to liability for

27/ There are additional standards for the Process Safety Management of Highly Hazardous Chemicals. See C.F.R. § 1910.119. This standard is not, however, typically regarded as being especially relevant to laboratories, perhaps for the reason that it generally involves large quantities of chemicals.

28/ Certain specialized laboratories that use radioactive materials also may be subject to regulations promulgated by the Nuclear Regulatory Commission and codified throughout Title 10 of the Code of Federal Regulations. See, e.g., 10 C.F.R. Part 20 (Standards for Protection Against Radiation).

cleanup to the extent that their solid or hazardous wastes present an “imminent and substantial endangerment” to health or the environment.

a. Hazardous Waste Management Regulations

Hazardous waste management requirements depend on the type and volume of wastes generated at the laboratory. In general, the following requirements apply to generators of hazardous wastes:

- Determine whether wastes are hazardous. A waste is hazardous if it:
 - (1) meets the definition of solid waste at 40 C.F.R. Part 261;
 - (2) is listed as a hazardous waste at 40 C.F.R. Part 261, Subpart D, or exhibits one of the four characteristics identified by EPA (corrosivity, ignitability, reactivity or toxicity); and
 - (3) has not been exempted from regulation.

- Determine whether the laboratory qualifies as a “conditionally exempt small-quantity generator” or a “small-quantity generator” based on the amount of hazardous waste generated per calendar month at the site. Conditionally exempt small quantity generators (those that generate less than 100 kg of hazardous waste per month) are exempt from certain transport, manifesting, reporting and recordkeeping requirements. Small-quantity generators (those that generate between 100 and 1,000 kg of hazardous waste per month) are subject to more limited exemptions. Even if exempt under these provisions, if a facility generates more than 1 kg of acute hazardous waste per month, it is subject to full regulation for all quantities of that acute hazardous waste.

- Comply with waste accumulation requirements and properly prepare wastes for transport. Generators that send their hazardous waste off-site for treatment, storage or disposal must:
 - (1) obtain an EPA identification number;
 - (2) prepare a hazardous waste manifest;
 - (3) comply with packaging, labeling, marking and storage requirements; and
 - (4) obtain a permit if hazardous wastes are stored on-site for more than 90 days for (large quantity generators) or for 180 days for small-quantity generators. Small-quantity generators that

transport their hazardous waste more than 200 miles for offsite treatment, storage or disposal can accumulate hazardous waste on-site for up to 270, however.

- Select an EPA-approved transporter and an authorized disposal facility.
- Comply with “land ban” certification requirements, which restrict the disposal of certain hazardous wastes in landfills.
- Comply with applicable reporting and recordkeeping requirements.
- Comply with applicable training requirements. Laboratory staff should be trained annually on hazardous waste management and emergency procedures appropriate to the operations at the laboratory.

Many laboratories work with microorganisms, recombinant DNA (rDNA) technologies, laboratory animals, human body fluids or bloodborne pathogens. Although there are no Federal EPA standards specifically addressing management and disposal of these sorts of biological and/or medical wastes, many States regulate these waste streams. 29/

b. Imminent and Substantial Endangerment

Laboratories also should be aware that they face potential suits by EPA and citizens under RCRA’s broad citizen suit and "imminent hazard" provisions, which provide a cause of action against generators and operators of facilities that contributed to the handling or storage or disposal of solid or hazardous waste, which presents an “imminent and substantial endangerment to health or the environment.” 42 U.S.C. §§ 6972(a)(1)(B), 6973(a). 30/

29/ *Biosafety in Microbiological and Biomedical Labs*, *supra* note 3, contains guidelines that apply to laboratories involved in working with infectious microorganisms and rDNA.

30/ Recently, New York postal workers filed suit under RCRA, claiming imminent and substantial endangerment caused by the U.S. Postal Service (as the owner/operator of the anthrax contaminated building) because discarded anthrax had killed two postal workers. See *Smith v. Potter*, No. 01-9512 (S.D.N.Y. Nov. 11, 2001). While the District Court found that the anthrax contamination posed no imminent and substantial danger to the public or the environment, this case nevertheless highlights the possibility that similar suits might be brought against laboratories.

2. Toxic Substances Control Act

TSCA, 15 U.S.C. §§ 2601-92, imposes important reporting and testing obligations on persons engaged in the manufacture (including import), processing, distribution in commerce, use, or disposal of “chemical substances.” ^{31/} The key TSCA provision for research laboratories is the requirement to use Good Laboratory Practice Standards (“GLPS”) when performing health effects, environmental effects, and chemical fate testing on “existing chemicals” (those already listed on the TSCA Inventory ^{32/}) or new chemicals (those not yet listed on the Inventory) required by EPA under a TSCA Section 4 Test Rule or Enforceable Consent Agreement/ Order.^{33/} It is also EPA's policy that all data developed as a result of rules or orders under TSCA Section 5 (see discussion on Section 5 below) should be in accordance with GLPS. GLPS are found at 40 C.F.R. Part 792. These standards outline a quality system addressing the organizational process for these tests and studies and the conditions under which the tests and studies should be planned, performed, monitored, archived and reported. For example, the GLPS require the following:

- Each individual involved in the study must be appropriately trained;
- A study director must be appointed to oversee the study and a quality assurance unit must be created to monitor the study;
- Testing facilities must meet controlled indoor environment parameters (i.e. sufficient size, supply facilities, etc.);

^{31/} 15 U.S.C. § 2602(2); see also 40 C.F.R. §§ 710.2(h) & 720.3(e). Under TSCA, the term “chemical substances” does not include pesticides, tobacco, or food, drugs, cosmetics or devices when manufactured, processed, or distributed in commerce for use as such.

^{32/} The TSCA Inventory is a list of chemical substances manufactured or processed in the United States. An updated version of the Inventory is published every four years, with the most recent version published in 1998. See 63 Fed. Reg. 45,950 (Aug. 28, 1998). EPA also updates an electronic version roughly every 6 months.

^{33/} TSCA Section 4 authorizes EPA to require manufacturers and processors of chemical substances to test specified chemicals or mixtures in order to determine whether they present an unreasonable risk of injury or have potential for substantial environmental or human exposure.

- Facility requirements;
- Equipment used in the study must be appropriately located, have the proper design and capacity for the test at issue, and be properly maintained;
- The facility must create and follow standard operating procedures;
- Test, control, and/or reference samples/studies must be identified for each batch and appropriately documented;
- Each study must have an approved written protocol that indicates objectives and methods for the conduct of the study; and
- Recordkeeping and reporting requirement must be met.

Depending on the nature of the laboratory's activities, the following TSCA requirements also might apply:

- Premanufacture Notice: Under TSCA section 5, manufacturers and importers of chemical substances must notify EPA 90 days prior to manufacturing or importing a "new" chemical substance -- *i.e.*, a chemical substance that is not listed on EPA's TSCA Inventory of Existing Chemical Substances. Significantly, there are exemptions from the notice requirements for: (1) chemical substances manufactured or imported in small quantities solely for research and development and chemical substances manufactured solely for non-commercial research and development purposes. Laboratories relying on these exemptions should carefully review the regulations to be sure their operations meet the criteria for them exemptions.
- Reporting and Recordkeeping Requirements: Under TSCA section 8, manufacturers, importers and processors of certain listed chemical substances must report production and use information to EPA. Section 8 also requires all manufacturers, importers, and processors of chemical substances to maintain records of, and in some instances to report, information indicating that their chemicals pose a threat to health or the environment.
- Export and Import Requirements: Importers of chemical substances in bulk form or as part of a mixture must certify at the port of entry either that the chemical shipment is subject to TSCA and complies with all applicable rules, or that the shipment is exempt from TSCA. Exporters of must notify EPA when they export or intend to export certain chemical substances subject to regulation under the Act.

- Polychlorinated biphenyls (PCBs): EPA regulates the handling, storage, and disposal of PCBs and imposes notification, labeling, inspection and disposal requirements. PCBs can exist in laboratories in samples, microscopy fluids, standards, electrical equipment (e.g., transformers, ballast) or hydraulic systems.

3. Clean Air Act

Certain requirements under the CAA, 42 U.S.C. §§ 7401-7671(q), could impact the operations of research laboratories and other facilities that handle etiologic agents. Particularly relevant are the provisions of the CAA that address accidental releases of hazardous air pollutants and incineration of medical and infectious wastes.

a. Accidental Releases of Hazardous Air Pollutants

Section 112(r) of the CAA addresses accidental releases of hazardous air pollutants. Several common laboratory chemicals, such as formaldehyde and methylene chloride, are considered hazardous under CAA § 112. Section 112(r) has two sets of requirements: the General Duty Clause and the Risk Management Plan.

i. The General Duty Clause

Under the General Duty Clause (“GDC”) of CAA Section 112(r), owners and operators of stationary sources that produce, process, handle or store extremely hazardous substances (“EHSs”) are responsible for preventing the accidental release and minimizing the consequences of any release of such substances. EHSs are substances “known to cause or reasonably anticipated to cause death, injury or serious adverse effects to public health or the environment when accidentally released,” 42 U.S.C. § 7412(r)(3), and include, but are not limited to, all hazardous chemicals listed in 40 C.F.R. § 68.130.

Facilities subject to the GDC are responsible for:

- Identifying hazards posed by the chemicals and assessing the impacts of possible releases;
- Following codes, standards and other business practices to ensure the facility is properly constructed and maintained and that the chemical is managed safely; and

- Having a contingency planning process to minimize the consequences of any accident. 34/

ii. Risk Management Plan

Under CAA Section 112(r), facilities that use a threshold quantity of a listed substance in a “process” 35/ must develop and implement a risk management plan (“RMP”) and maintain documentation of the program at the site. A threshold quantity of a listed chemical is present at a source if the total quantity of the regulated substance contained in a process at any one time exceeds the threshold that is specified for the listed substance at 40 C.F.R. § 68.130. The “threshold quantity” varies by substance, and in many cases exceeds 10,000 pounds. In general, a research laboratory, which uses only a small amount of a chemical, will not trigger the threshold and will not be responsible for an RMP.

b. Regulations for Medical and Infectious Waste Incinerators

Pursuant to new source performance standards of the CAA, EPA has established emissions limitations and other requirements for states and tribal governments to apply to hospital, medical and infectious waste incinerators (“HMIWI”). 40 C.F.R. Part 60, Subparts Ce and Ec. 36/ Under CAA Sections 111 & 129, HMIWI are required

34/ 42 U.S.C. § 7412(r)(1); EPA Chemical and Emergency Preparedness and Prevention Office, *The General Duty Clause*, EPA 550-F-98-016 (June 1999).

35/ Under 40 C.F.R. § 68.3, “process” is defined as:

Any activity involving a regulated substance, including any use, storage, manufacturing, handling, or on-site movement of such substances, or combination of these activities. For the purposes of this definition, any group of vessels that are interconnected, or separate vessels that are located such that a regulated substance could be involved in a potential release, shall be considered a single process.

36/ The HMIWI rule applies to the incineration of medical and infectious wastes, including cultures and stocks of infectious agents, such as a virus and bacteria, from research laboratories. Environmentalists challenged the HMIWI rule, but the court upheld most of the rule and remanded the remainder to EPA for further explanation of its reasoning in determining the floors for existing and new HMIWI. See Sierra Club v. EPA, 167 F.3d 658 (D.C. Cir. 1999).

to utilize “maximum achievable control technology” to achieve emission levels reflecting the maximum degree of reduction in emissions of air pollutants, such as particulate matter and nitrogen oxides, that is achievable taking into consideration the cost of achieving such reduction. In addition to emissions limitations, requirements for regulated HMIWI include:

- Compliance monitoring and testing requirements;
- Operator training and qualification requirements;
- The development of a waste management plan; and
- Reporting and recordkeeping requirements.

Existing HMIWI, constructed on or prior to June 20, 1996, that are located in states that do not have approved air pollution plans are subject to Federal Plan requirements at 40 C.F.R. Part 62, Subpart HHH. HMIWI subject to the Federal Plan must obtain a Title V operating permit that assures compliance with all applicable requirements. See 40 C.F.R. Part 71 (establishing the requirements of a Title V operating permit). HMIWI sources subject to state air pollution plans may face requirements in addition to those listed above.

4. National Emissions Standards for Hazardous Air Pollutants

Pursuant to CAA Section 112, EPA also has promulgated stringent air pollution control requirements called the National Emissions Standards for Hazardous Air Pollutants ("NESHAP"). NESHAP provisions regulate: (1) emissions of certain types of HAPs, including mercury, beryllium and radionuclides; (2) emissions from certain types of HAP sources, such as sterilization facilities using ethyl oxides and dry cleaning facilities; and (3) emissions from certain types of equipment, e.g., oil-water and organic-water separators. Research laboratories are not directly regulated as a categorical NESHAP source. If NESHAP regulations apply to a research facility, it is mostly likely through that facility's emission of one of the HAPs listed in 40 C.F.R. § 61.01 or through the use of regulated equipment in 40 C.F.R. Part 63. NESHAP regulations include emissions standards, compliance monitoring, approval of construction or modification, and recordkeeping and reporting requirements.

5. Clean Water Act

The CWA, 33 U.S.C. §§ 1281-1387, governs discharges of pollutants into the waters of the United States. The Act imposes permitting requirements on facilities discharging pollutants directly into surface waters, such as rivers, streams, or wetlands (“direct dischargers”); pretreatment standards on facilities discharging into a municipal sewer system (“indirect dischargers”); and additional requirements on facilities

discharging oil and hazardous substances. The majority of research laboratories and other facilities that handle etiologic substances are likely to be indirect dischargers. ^{37/}

a. Indirect Discharges and Publicly Owned Treatment Works

Indirect discharges occur when pollutants – such as liquid wastes or chemicals – are poured into sinks, or discharged into drains or other structures that convey them to a Publicly Owned Treatment Works (“POTW”). Indirect dischargers are generally not required to obtain permits, although significant indirect dischargers may be subject to local permitting requirements. Instead, indirect dischargers must comply with applicable pretreatment standards. Pretreatment standards include both general and industry-specific requirements.

General pretreatment standards, or “prohibited discharges,” restrict the disposal of certain types or volumes of pollutants into POTWs and would likely apply to most research facilities that discharge to a POTW. In general, pretreatment regulations prohibit the discharge of any pollutant: (1) that may “pass through” ^{38/} the POTW processes (i.e., exit the POTW into U.S. waters) in quantities or concentrations which, alone or in conjunction with other discharges, cause environmental harm and violate any requirements of the POTW’s direct discharge permit; or (2) that will cause an “interference” ^{39/} at the POTW by inhibiting or disrupting the POTW’s operations and causing a violation of the POTW’s discharge permit. The pretreatment regulations also specifically prohibit the introduction of certain substances into a POTW. The following are among the prohibited substances:

- Pollutants that may create a fire or explosion hazard;
- Pollutants that will cause corrosive structural damage to the POTW, including those with a pH lower than 5.0, unless the POTW is specifically designed to accommodate such discharges;

^{37/} Labs that discharge wastewater directly into surface water, or that have wastewater treatment systems that discharge into surface water, will most likely require a National Pollutant Discharge Elimination System (“NPDES”) permit, from an authorized state or EPA, to conduct their treatment and discharge activities.

^{38/} 40 C.F.R. § 403.5(a)(1); see also id. § 403.3(n)(definition of pass through).

^{39/} 40 C.F.R. § 403.5(a)(1); see also id. § 403.3(i) (definition of interference).

- Solid or viscous pollutants in amounts which obstruct the flow in the POTW, resulting in an interference;
- Discharges of such volume and concentration as to cause interference;
- Petroleum oil, nonbiodegradable cutting oils, or products of mineral oil origin in amounts that will cause interference or pass through; and
- Pollutants which result in the presence of toxic gases, vapors, or fumes within the POTW in a quantity that may cause acute worker health and safety problems. 40/

Industry-specific pretreatment standards, called “categorical standards,” establish quantities or concentrations of pollutants that may be discharged into a POTW by specified industrial point sources. Most of the categorical standards apply to manufacturing facilities, and research facilities are not included as a specified point source category. One point source category, pharmaceutical manufacturing facilities, includes “discharges of process wastewater resulting from pharmaceutical research” and, therefore, may apply to pharmaceutical research facilities handling etiologic agents. In addition to the Federal POTW provisions, many local POTWs impose their own limits to which industrial users, including research facilities, may be subject.

b. Discharges of Oil or Hazardous Substances

Discharges of oil and hazardous substances into waters of the United States in excess of certain limits are prohibited by the CWA. Substances that the EPA considers hazardous include isomers and hydrates, as well as any solutions and mixtures containing these substances. A comprehensive list of such substances is set forth at 40 C.F.R. § 116.4. In addition, EPA also has set forth threshold quantities of hazardous substances that trigger Federal reporting requirements. These thresholds can be as little as one pound and as much as 5,000 pounds. In the event of a discharge of a reportable quantity of a hazardous substance within a single 24-hour period, the person in charge of the facility causing the discharge must immediately report the discharge to the appropriate Federal agency. The facility may be held liable for the costs incurred by the U.S. government in responding to (i.e., cleaning up) the unlawful discharge.

40/ See 40 C.F.R. § 403.5(b).

5. Emergency Planning and Right To Know Act and the Comprehensive Environmental Response, Compensation and Liability Act

a. Release Reporting

There are multiple Federal, state and local requirements for maintaining plans to prevent releases of hazardous substances and for responding to, and reporting, such releases when they occur. EPCRA, 42 U.S.C. §§ 1101–11050, establishes a framework for community emergency response planning at the Federal level, and CERCLA, 42 U.S.C. §§ 9601–9675, imposes an additional reporting requirement for certain releases. Reporting requirements under these statutes are outlined below. Recent attention to possible acts of eco-terrorism has heightened the importance of internal systems that assure compliance with these requirements.

- EPCRA § 302: All facilities must give one-time notice to the State Emergency Response Commission (“SERC”) if a substance on the list of Extremely Hazardous Substances (“EHSs”) is present at the facility in excess of its threshold planning quantity (“TPQ”). 41/
- EPCRA § 304: Owners/operators of any facility at which a hazardous chemical is produced, used, or stored must provide immediate notice to the Local Emergency Planning Committee (“LEPC”) and SERC if a reportable quantity (“RQ”) 42/ of an EHS or a CERCLA hazardous substance 43/ is released over a 24 hour period, with certain exceptions. 44/. Written follow-up notice is also required.

41/ The list of EHSs and their respective TPQs is published at 40 C.F.R. Part 355, Appendices A and B.

42/ The RQs for EHSs are listed at 40 C.F.R. Part 355, Appendices A and B. The list includes ammonia and chlorine.

43/ The list of CERCLA hazardous substances and their respective RQs is published at 40 C.F.R. § 302.4

44/ The following releases are exempt: (1) releases which result in exposure to persons solely within the boundaries of the facility; (2) Federally permitted releases; (3) continuous releases if they are stable in quantity and rate; and (4) certain releases of pesticide products and radionuclides. See 40 C.F.R. § 355.40.

- EPCRA § 311: Facilities that are required under OSHA's Hazardous Communication Standard to prepare or have available material safety data sheets for hazardous chemicals present on site have a one-time reporting obligation to submit a list of those chemicals to the SERC, the LEPC and the local Fire Department if the hazardous chemicals are present above a threshold amount. 45/
- EPCRA § 312: Facilities that are subject to EPCRA Section 311 also must submit an annual inventory form (the Tier I or Tier II form) to the SERC, the LEPC and the local Fire Department detailing the amount of hazardous chemicals present at the facility during the preceding year, the average daily amount of hazardous chemicals on-site and location of those chemicals. Reporting is triggered if hazardous chemicals are present on site above a threshold amount. (See EPCRA § 311). The forms are due annually on March 1.
- EPCRA § 313: Certain facilities are required to submit an annual toxic chemical release form (Form R) to EPA and to the state. The requirement only applies to facilities that are in standard industrial classification (SIC) codes 20 through 39 (manufacturing codes), that have ten or more employees, and that manufactured, processed or otherwise used a listed toxic chemical in excess of the applicable threshold quantity. Because of the SIC code restriction, this requirement may not apply to many laboratories.
- CERCLA § 103: The "person in charge" of a facility must immediately report any accidental release into the environment of hazardous substances over the RQ to the National Response Center.

b. Cleanup Liability

CERCLA also provides a comprehensive scheme for liability, compensation, cleanup, and emergency response for hazardous substances released into the environment. Under this statute, "potentially responsible parties" – including the owner or operator of any contaminated property and "generators" who send their waste offsite for disposal at a facility that ultimately requires cleanup – can be held liable for cleanup costs and natural resource damages associated with the release of the hazardous substance. 42 U.S.C. § 9607(a). It is not a defense to liability that disposal occurred in compliance with all applicable laws. In addition, liability under CERCLA is generally

45/ The threshold amounts for reporting are published at 40 C.F.R. § 370.20(b).

“joint and several,” meaning that any responsible party can be potentially liable for the entire cost of cleanup, even if other parties contributed to the damage.

IV. RECENT LEGISLATIVE INITIATIVES

Given recent events, Congress has taken an increased interest in biosafety and has already enacted one law increasing restrictions on who may have access to certain agents. Readers of this document should be mindful that legislation and regulatory action may have already or may soon be enacted that may alter the contents of this document. BIO members are encouraged to monitor the BIO website <http://www.bio.org/> for legislative activity.

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