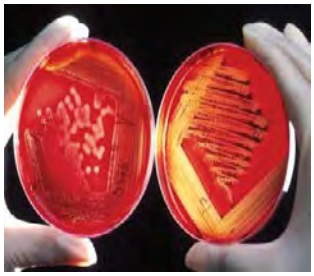

Occupational Health Program Guidance Document for Working with Tier 1 Select Agents and Toxins

7 CFR Part 331, 9 CFR Part 121, 42 CFR Part 73

05 July 2013

Centers for Disease Control and Prevention (CDC)
Division of Select Agents and Toxins
Animal and Plant Health Inspection Service (APHIS)
Agriculture Select Agent Program

Preface

Revisions: This is a living document subject to ongoing improvement. Feedback or suggestions for improvement from registered Select Agent entities or the public are welcomed. Please submit comments directly to the Federal Select Agent Program at:

CDC: LRSAT@cdc.gov
APHIS: ASAP@aphis.usda.gov

Revision History:

October 12, 2012: Initial posting
July 5, 2013 (Revision 1): The revisions are primarily changes to correct editorial errors from previous version.

Table of Contents

Introduction

The October 2012 revisions of the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121) require that individuals with access to Tier 1 biological select agents and toxins (Tier 1 BSAT) must be enrolled in an Occupational Health Program (OHP). Specifically, the amended regulations state in section 12(d): "The biosafety plan must include an occupational health program for individuals with access to Tier 1 select agents and toxins, and those individuals must be enrolled in the occupational health program."

The requirement to provide access to an OHP for all personnel having access to Tier 1 BSAT is intended to ensure the availability of professional medical evaluations and treatment. The goal of the OHP guidance is to describe how an entity in possession of Tier 1 BSAT can have a well trained workforce adequately prepared for the unique hazards presented by the Tier 1 BSAT in the workplace; with the ability to promptly detect and treat laboratory acquired infections (LAIs) to reduce any adverse impact to worker safety and public health.

Purpose of the Guidance Document

The guidance provided in this document is intended to assist entities develop and implement an OHP to protect workers with access to Tier 1 BSAT. While this information is intended to assist in this process, entities should develop and implement OHPs that address the site-specific health hazards identified by each institution's assessments. We recognize that there will be differences in the scope and complexity of OHPs developed by different entities due to the individual circumstances at each entity. Entities should also include provisions in their plans that address other recognized occupational health risks not specifically related to Tier 1 BSAT (e.g., hearing protection and chemical hygiene).

OHP Elements

An entity's written biosafety plan should include these key elements of the OHP:

- risk assessment,
- medical surveillance,
- access to clinical occupational health services and management, and
- hazard communication.

The OHP should be a living document subject to ongoing improvement over time.

The risk assessment should consider:

- the route of exposure,
- incubation period,
- infectious dose,
- agent virulence,
- environmental stability,
- communicability,
- genetic modification,
- inherent risk,
- available resources for pre- and post-exposure prophylaxis,
- available vaccine options,
- use of personal protective equipment, and

- biocontainment requirements.

The information identified in the risk assessment will provide a guide for the selection of appropriate medical preventions and countermeasures.

The risk assessment should specifically identify:

- the hazardous characteristics of a known infectious or potentially infectious agent or material,
- the activities that can result in a person's exposure to an agent,
- the likelihood that such exposure will cause an LAI, and
- the probable consequences of such an infection.

Workers who may be exposed to a Tier 1 BSAT should receive a thorough medical evaluation prior to initiation of work or contact with these agents. The healthcare provider should review any previous and ongoing medical problems, current medications, allergies, and prior immunizations in order to determine an individual's medical fitness to perform the duties of a specific position and what medical services are needed to permit the individual to safely assume the duties of the position.

Criteria of fitness for duty should be established based upon the occupational health hazards identified from the site-specific comprehensive risk assessment.

Healthcare providers should be cognizant of potential hazards via a written description of the potential health hazards present in the work environment.

Periodic medical evaluations targeted to job requirements may be appropriate for workers with substantial risk of exposure to infectious agents or other circumstances such as clearance for respirator use or work in a pressurized suit.

Medical support for occupational illnesses should also be provided for workers with access to Tier 1BSAT. Workers should be encouraged to seek medical evaluation for symptoms that they suspect may be related to infectious agents in their work area. A high index of suspicion for potential occupational exposures should be maintained during any unexplained illness among workers or visitors to worksites containing Tier 1 BSAT. The healthcare provider should have a working understanding of the biohazards present in the workplace and remain alert for evidence of infection and atypical presentations. All exposures to Tier 1 BSAT should be reported to the medical support services provider. Strategies for responding to biohazard exposures should be formulated in advance.

Proper post-exposure response is facilitated by exposure-specific protocols that define:

- appropriate first aid,
- potential post-exposure prophylaxis options,
- recommended diagnostic tests, and
- sources of expert medical evaluation.

These protocols should address how exposures or reports of potential LAIs that occur at work outside of regular work hours are handled and these protocols should be distributed to potential healthcare providers (e.g., local hospital emergency departments).

Commercial vaccines should be made available to workers to provide protection against infectious agents to which they may be occupationally exposed. Current, applicable vaccine information statements must be provided whenever a vaccine is administered. Each worker's immunization history should be evaluated for

completeness and currency at the time of employment and re-evaluated when the individual is assigned job responsibilities with a new biohazard.

At present time, the following vaccines are available for Tier 1 BSAT:

- *Francisella tularensis*,
- Variola major virus,
- Variola minor virus, and
- *Bacillus anthracis*.

The vaccines for smallpox (vaccinia vaccine) and anthrax are FDA licensed. The vaccines for tularemia are available through U.S. Food and Drug Administration (FDA) investigational new drug (IND) protocols. Immunization with IND vaccines should be optional. If indicated by risk assessment, the IND vaccines may be made available on a voluntary basis under FDA research protocols with informed consent.

The Anthrax vaccine is recommended by the U. S. Department of Health and Human Services' (HHS) Advisory Committee for Immunization Practices (ACIP) for groups at risk for repeated exposures to *B. anthracis* spores.[5] Groups at risk for repeated exposure include:

- laboratory personnel handling environmental specimens (especially powders) and performing confirmatory testing for *B. anthracis* in the U.S. Laboratory Response Network (LRN),
- workers who will be making repeated entries into known *B. anthracis*-spore-contaminated areas, and
- workers in other settings in which repeated exposure to aerosolized *B. anthracis* spores might occur.

Laboratory workers using standard Biosafety Level 2 practices in the routine processing of clinical samples or environmental swabs are not considered by ACIP to be at increased risk for exposure to *B. anthracis* spores. (For persons not at risk for repeated exposures to aerosolized *B. anthracis* spores through their occupation, pre-exposure vaccination against anthrax is not recommended).

Currently there is no vaccine available for immunization of laboratory personnel working with botulinum toxin or cultures of botulinum neurotoxin producing species of *Clostridium*. Although administered under an FDA IND since 1965, CDC discontinued distribution of the Pentavalent (ABCDE) Botulinum Toxoid vaccine in 2011 due to decline in potency and CDC observed increase in moderate local reactions. An equine-based heptavalent (A, B, C, D, E, F, and G) antitoxin is available through a CDC- sponsored FDA IND for treatment of individuals with symptoms consistent with botulism. Health-care providers for exposed laboratory personnel should consult their state health department epidemiologist to determine if use of HBAT is warranted.

When occupational exposure to highly pathogenic agents is possible and no commercial vaccine is available, it may be appropriate to immunize workers using vaccines or immune serum preparations that are investigational, or for which the specific indication constitutes an off-label use. Use of investigational products, or of licensed products for off-label indications must be accompanied by adequate informed consent outlining the limited availability of information on safety and efficacy. Use of investigational products should occur through IND protocols providing safety oversight by both the FDA and appropriate institutional human subjects research protection committees. Recommendation of investigational products, as well as commercial vaccines that are less efficacious, associated with high rates of local or systemic reactions, or that produce increasingly severe reactions with repeated use, should be considered carefully.

The healthcare provider should design medical support services in consultation with representatives from the entity's institutional environmental health and safety program and the principal investigators. Workers should be fully informed of the available medical support services and encouraged to utilize them.

An entity with Tier 1 BSAT should consider providing workers with access to Tier 1 BSAT a card that:

- lists the select agents and toxins that he/she works with,
- lists emergency phone numbers for
    - personal contacts,
    - primary care physicians,
    - occupational health physicians,
    - preferred or designated hospital, and
    - the entity's Responsible Official.

This information may be necessary when no occupational support is available (e.g., a trip to the emergency room).

Risk Assessment after Exposure

A risk assessment should be conducted after potential occupational exposures to any Tier 1 BSAT. Assessment of the potential exposure risk should cover the following circumstances:

- All breaches in the established safety practices while working with Tier 1 BSAT;
- All injuries incurred inside laboratory when handling Tier 1 BSAT;
- Unexplained acute illness or febrile disease in a Tier 1 BSAT worker;
- All incidents covered under section 19(b) of the section agent regulations including:
    - occupational exposures, or
    - release of a select agent or toxin outside of the primary containment barriers.

For additional information, please see the Federal Select Agent Program guidance for reporting incidences of theft, loss, or release, which may be found at:

http://www.selectagents.gov/TLRForm.html

The exposure risk assessment should identify all potentially exposed individuals. Factors to be considered should include:

- agent or toxin information,
- the nature of the mishap and associated circumstances,
- the specific personal protective equipment worn at the time of the incident,
- first aid procedures performed in response to the incident, or
- personal health issues that may make an individual more susceptible to infection.

Post-exposure management is necessary for:

- all potential exposures,
- suspected diseases, and
- confirmed illness.

The exposure risk assessment should be performed by qualified medical personnel on a case-by- case basis. If indicated by risk assessment and medical evaluation, post-exposure management may include:

- post-exposure immunoprophylaxis,
- post-exposure chemoprophylaxis,
- active surveillance,
- clinical intervention and treatment, or
- precautionary advisory.

Medical assessment should consider personal immunization status and personal health status.

Emergency Examinations

Prompt medical evaluation may be necessary in instances including:

- all potential exposures, including both direct exposures and proximity exposures,
- potential human disease, and
- when there is a potential impact on public health and safety.

The plan should cover contingencies during work and after hours. OHPs should contain measures for infection control.

Enhanced OHP Elements

Response Protocols - For personnel working with Ebola virus, Marburg virus, Variola major virus, and Variola minor virus and *Yersinia pestis*, isolation provisions and protocols should be considered for inclusion in the OHP.

These agents may be relatively easy to transmit from person-to-person and therefore may pose a significant public health risk. To limit the potential exposure of the general public, isolation of patients with confirmed or suspected illness caused by these agents should be considered.

Policies for Agents without Treatment Options

Since there is no pre- or post-exposure prophylaxis, nor well established treatment options at the present time available for several of the Tier 1 BSAT, entities in possession of these agents should develop plans for providing post exposure care and support for workers.

Respiratory Protection

Entities should develop and implement a respiratory protection program for workers with access to Tier 1 BSAT.

Non-Human Primate Surveillance

If non-human primates are used in work with Tier 1 BSAT, the OHP must include plans for post exposure medical surveillance and prophylaxis for Cercopithecine Herpesvirus 1 (Herpes B virus) for animal handlers.[2,3,7]

Visitor Policy

Entities should have policies and provisions in place for at-risk visitors to provide access to their occupational health service on a risk-based approach.

Hazard Communication

All personnel approved for access to Tier 1 BSAT should be provided with the following information:

- The risk and health hazards associated working with the Tier 1 BSAT;
- Typical signs and symptoms of the diseases associated with the select agent or toxin with which they work;
- The available pre- and post-exposure resources for treatment;
- Whom to contact and what to do in an emergency; and
- Policies for immediately reporting and documenting all potential occupational exposures.

The Responsible Official is required by federal regulation to immediately notify the Federal Select Agent Program regarding all occupational exposures to Tier 1 BSAT by telephone, facsimile, or e-mail (form3@cdc.gov) or (ASAP@aphis.usda.gov), and submit a completed APHIS/CDC Form 3 (Report of Theft, Loss, or Release of Select Agents and Toxins) within seven calendar days.

Reporting and Analyzing Occupational Exposure

All potential occupational exposures should be evaluated to identify factors that contributed to the incident. Corrective actions to mitigate the risk of recurrence should be identified.

Records Management and Retention

All Tier 1 BSAT personnel occupational health related documents and records must be maintained for three years.

References

1. The October 2011 revisions of the guidelines for research involving recombinant DNA molecules (NIH Guidelines). http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm.
2. Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition. HHS Publication No. (CDC) 21-1112, Revised December 2009.
3. Coppee GH. Occupational Health Services and Practice. http://www.ilo.org/safework_bookshelf/english?content&nd=857170174.
4. Vaccinia (Smallpox) Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001. MMWR. 50(RR10): 1-25, 2001.
5. CDC. Use of anthrax vaccine in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2000. 49(No. RR-15), 2000.
6. 29 C.F.R. § 1910.134 (Respiratory Protection).
7. Cohen JI, Davenport DS, Stewart JA, Deitchman S, Hilliard JK, Chapman LE, and the B virus Working Group. Recommendations for Prevention of and Therapy for Exposure to B virus (Cercopithecine Herpesvirus 1). Clinical Infectious Disease. 35: 1191-203, 2002.
8. CDC. Notice of CDC's discontinuation of investigational pentavalent (ABCDE) botulinum toxoid vaccine for workers at risk for occupational exposure to botulinum toxins. 2011. MMWR. 60 (42): 1454-1455.
9. CDC. Investigational heptavalent botulinum antitoxin (HBAT) to replace licensed botulinum antitoxin AB and investigational botulinum antitoxin E. 2010. MMWR 59 (100: 299).

Appendices

The information found in the appendices consists of information that an entity may consider in the development and implementation of OHP. The user is not required to use, or limited to, the information provided in the appendices.

Appendix I. Tier 1 List of Biological Select Agents and Toxins

Agents	Disease	Category	Recommended Biosafety Level[2]
Ebola virus	Ebola hemorrhagic fever	HHS	4
Francisella tularensis	Tularemia	HHS	2 or 3
Marburg virus	Marburg hemorrhagic fever	HHS	4
Variola major virus	Smallpox	HHS	4
Variola minor virus	Smallpox	HHS	4
Yersinia pestis	Plague	HHS	2 or 3
Botulinum neurotoxin	Botulism	HHS	2
Botulinum neurotoxin producing species of *Clostridium*	Botulism	HHS	2
Bacillus anthracis	Anthrax	Overlap	2 or 3
Burkholderia mallei	Glanders	Overlap	2 or 3
Burkholderia pseudomallei	Melioidosis	Overlap	2 or 3
Foot and Mouth Disease virus	FMDV	USDA	3
Rinderpest virus	Cattle plague	USDA	3

Appendix II. Minimum Requirements for an Occupational Health Program for Tier 1 BSAT

Agents	Minimum Requirements [1,2,6]
Ebola virus	Pre-placement Examinations Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management Isolation Protocols
Francisella tularensis	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management
Marburg virus	Pre-placement Examinations Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management Isolation Protocols
Variola major virus	Pre-placement Examinations Vaccinia immunization Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management Isolation Protocols
Variola minor virus	Pre-placement Examinations Vaccinia immunization Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management Isolation Protocols
Yersinia pestis	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management
Botulinum neurotoxin	Pre-placement Examinations Emergency Medical Evaluation Post-exposure Management
Botulinum neurotoxin producing species of *Clostridium*	Pre-placement Examinations Emergency Medical Evaluation Post-exposure Management
Bacillus anthracis	Pre-placement Examinations Risk-based anthrax vaccine Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management
Burkholderia mallei	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management

Agents	Minimum Requirements [1,2,6]
Burkholderia pseudomallei	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management
Foot and Mouth Disease virus	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management
Rinderpest virus	Pre-placement Examinations Risk-based Respiratory Protection Program Emergency Medical Evaluation Post-exposure Management

Appendix III. Vaccine Resources for Tier 1 Biological Select Agents and Toxins

Agent	Disease	Availability of vaccine	Type of vaccine	Source
Ebola virus	**Ebola hemorrhagic fever**	NA	NA	NA
Francisella tularensis	**Tularemia**	IND	Live attenuated bacteria vaccine	USAMRIID[a]
Marburg virus	**Marburg hemorrhagic fever**	NA	NA	NA
Variola major virus/ Variola minor virus	**Smallpox**	FDA licensed[4]	Live vaccine virus	CDC[b]
Yersinia pestis	**Plague**	NA	NA	NA
Botulinum neurotoxin/ Botulinum neurotoxin producing species of *Clostridium*	**Botulism**	NA	NA	NA[c]
Bacillus anthracis	**Anthrax**	FDA licensed[5]	Inactivated	Commercially available
Burkholderia mallei	**Glanders**	NA	NA	NA
Burkholderia pseudomallei	**Melioidosis**	NA	NA	NA

Notes:

- **IND** stands for the vaccine is available under an Investigational New Drug protocol and is available for limited use.
- **NA** stands for not available.
- **USAMRIID** stands for The United States Army Medical Research Institute for Infectious Diseases (USAMRIID).
- **a.** Tularemia vaccine is available through USAMRIID special immunization program.
- **b.** Smallpox Vaccine: CDC is the only source of vaccinia vaccine and VIG for civilians. Vaccine will be shipped to the responsible physician. Requests for vaccine and VIG, including the reason for the request, should be referred to:

  Centers for Disease Control and Prevention
  Drug Services, National Center for Infectious Diseases
  Mailstop D-09
  Atlanta, GA 30333
  Telephone: (404) 639-3670
  Facsimile: (404) 639-3717
- **c.** In 2011, CDC discontinued the distribution of Pentavalent (ABCDE) Botulinum Toxoid vaccine which was available under a CDC-sponsored FDA IND since 1965.