ENVIRONMENTAL HEALTH AND SAFETY
University of Nebraska-Lincoln

Safe Operating Procedure

(Revised 5/24)

SELECT AGENTS AND TOXINS – CLINICAL AND/OR DIAGNOSTIC LABORATORY ACTIVITIES

Introduction

Clinical and/or diagnostic laboratories and other entities that possess, use, or transfer biological select agents and toxins (BSAT) may be exempt from United States Departments of Agriculture (USDA) and Health and Human Services (HHS) Select Agent and Toxins regulations (42 CFR 73, 9 CFR 121, and 7 CFR 331) if certain conditions are met. The exemption is contingent upon complete and total adherence to all requirements of the exemption. A listing of select agent organisms (including genetic elements) and toxins is provided on the Federal Select Agent Program website.

Scope

This SOP describes the exemption conditions applicable to clinical and/or diagnostic laboratories and other entities that possess, use, or transfer human, animal, overlap, or plant select agents contained in specimens presented for diagnosis or verification. An exemption also exists for entities that possess, use, or transfer select human, animal, and/or overlap select agents/toxins contained in a specimen presented for proficiency testing. Possession, use, or transfer of select agents for other purposes, including but not limited to research and medical uses, are beyond the scope of this SOP. See Appendix A for definitions.

Diagnosis/Verification

Following confirmatory identification, Form 4A must be submitted to the Division of Select Agents and Toxins of CDC (for BSAT listed by CDC) or USDA (for BSAT listed by USDA) within 7 days via email or facsimile. The form has two parts – Part 1 (Section A and B) and Part 2 (Section C and D).

- The reference laboratory that provides confirmatory identification of a BSAT completes Form 4A, Part 1 (Section A and B) and submits to USDA or CDC as appropriate. They must also notify the laboratory that provided the samples, as well as other federal, state, and local authorities when required.
- The laboratory that provided the samples to the reference lab completes Form 4A, Part 2 and is submited to CDC or USDA as appropriate.

- Identification of specific BSAT must be reported immediately to CDC or USDA as appropriate, followed by submission of Form 4A. BSAT that have an immediate notification requirement include:
    - Bacillus anthracis (CDC or USDA)
    - Bacillus cereus Biovar anthracis (CDC)
    - Botulinum neurotoxins (CDC)
    - Botulinum neurotoxin producing species of Clostridium (CDC)
    - Burkholderia mallei (CDC or USDA)
    - Burkholderia pseudomallei (CDC or USDA)
    - Ebola virus (CDC)
    - Foot-and-mouth disease virus (USDA)
    - Francisella tularensis (CDC)
    - Marburg virus (CDC)
    - Rinderpest virus (USDA)
    - Variola major virus (Smallpox virus) (CDC)
    - Variola minor virus (Alastrim) (CDC)
    - Yersinia pestis (CDC)
- The select agent or toxin and associated specimens must be ***transferred*** to a registered facility or ***destroyed*** within seven (7) calendar days of definitive identification. Transfer prior to definitive identification is not subject to any special requirements, other than compliance with transport rules (e.g., DOT or IATA). Transfer after definitive identification requires prior approval from CDC or APHIS, as appropriate, using Form 2.
- The select agent or toxin and associated specimens must be ***secured*** against theft, loss, or release during the period between positive identification and transfer or destruction.
- Identification of select agents must be ***reported to other federal, state, and local authorities*** as required by other laws. This generally pertains to disease surveillance reporting.

Proficiency Testing

Laboratories in possession of BSAT affecting humans and/or animals that are contained in specimens presented for proficiency testing are also exempt and must follow the same general rules for reporting, transfer/destruction, and security. However, in the case of proficiency testing, the period for transfer or destruction and reporting is established at 90-days from the

time of receipt. There are no exemption provisions for proficiency testing for select agents affecting plants.

Submission of an APHIS/CDC Form 4B is required for labs that conduct proficiency testing on samples that contain select agents or toxins. Records must be retained for 3 years.

Identification

"Identification" occurs at that point and time that a definitive test confirms the presence of a select agent in or from a specimen. Presumptive or suspect identification based on clinical signs or symptoms and non-confirmatory tests do not trigger regulatory requirements, including exemption conditions, for select agents. All associated specimens, samples, and isolates (including regulated genetic elements, nucleic acids, and recombinant organisms – See EHS SOP, ***Select Agents and Toxins***) are subject to the requirements established for the diagnostic/clinical lab exemption once the identification of a select agent is confirmed, regardless of whether the confirmation is made by the same or another laboratory. The clock and regulatory obligations begin on the day of confirmatory identification.

Transfer or Destruction

As a condition of the clinical/diagnostic laboratory exemption, all specimens, samples, and isolates (including regulated genetic elements, recombinant organisms, etc.) must be destroyed, inactivated/rendered incapable of replication, or transferred to a ***registered*** facility within seven (7) calendar days following confirmatory identification. If a secondary laboratory is utilized for confirmatory testing, EHS recommends complete and total transfer of all associated specimens, samples, and isolates at the time that confirmatory testing is requested, or destruction of unneeded specimens, samples, and isolates at the same time. This eliminates the need for later transfer permission from the CDC or APHIS or destruction, as well as adherence to specific timeframes and security measures.

Destruction of all suspect and/or confirmed specimens, samples and isolates must happen on-site by a recognized sterilization or inactivation process.

A biological indicator **must** be used for all suspect and/or confirmed specimens, samples and isolates that are destroyed by autoclaving. The results of the indicator testing and details of the autoclave cycle run must be maintained for 3 years following the destruction. Refer to the EHS SOP, **Autoclave Performance Testing** for instructions on biological indicator testing.

Recordkeeping

Copies of forms, sample destruction logs, and documented reports must be maintained for a minimum of three (3) years.

Suspected or Known Exposures

Suspected or known occupational exposures to a select agent, even in the context of a diagnostic/clinical laboratory, may be considered a “release” and therefore reportable to APHIS/CDC. All such situations must be reported to EHS immediately.

Appendix A - Definitions

Diagnosis means the analysis of specimens for the purpose of identifying or confirming the presence or characteristics of a select agent or toxin provided that such analysis is directly related to protecting the public health or safety, animal health or animal products, or plant health or plant products.

Proficiency testing means the process of determining the competency of an individual or laboratory to perform a specified test or procedure.

Specimen means samples of material from humans, animals, plants, or the environment or isolates or cultures from such samples for the diagnosis, verification, or proficiency testing.

Verification means the demonstration of obtaining established performance (e.g., accuracy, precision, and analytical sensitivity and specificity) specifications for any procedure used for diagnosis.