ENVIRONMENTAL HEALTH AND SAFETY
University of Nebraska-Lincoln

Safe Operating Procedure

(Revised 3/26)

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

Introduction

During clinical or diagnostic laboratory work a select agent or toxin may be identified or found to be contained in specimens presented for diagnosis, proficiency testing or verification. If this is the case, the laboratory will need to complete what the Federal Select Agent Program calls a "CDC/ APHIS Form 4A". The APHIS/CDC Form 4, Report of the Identification of a Select Agent or Toxin, is used by clinical or diagnostic laboratories and other entities to notify the Federal Select Agent Program of identification and final disposition of agents or toxins and specimens containing agents and toxins. See https://www.selectagents.gov/sat/list.htm for the complete Select Agents and Toxins list.

Note: The select agents and toxins listed below must be **immediately** reported (**within 24 hours**) to the Federal Select Agent Program (**Email:** DASAT@usda.gov or **Email:** CDCForm4@cdc.gov). An APHIS/CDC Form 4A must be submitted within 7 calendar days of identification and within 90 days of receipt of a proficiency sample. Email the Form 4 to:

- **Animal and Plant Health Inspection Service (APHIS)**
  Division of Agricultural Select Agents and Toxins
  5601 Sunnyside Ave #AP-780-003
  Beltsville, MD 20705

  Fax: 301-734-3652
  Email: DASAT@usda.gov

- **Centers for Disease Control and Prevention (CDC)**
  Division of Regulatory Science and Compliance
  1600 Clifton Road, NE, Mailstop H21-5
  Atlanta, GA 30329

  Fax: 404-471-8375
  Email: CDCForm4@cdc.gov

HHS (CDC) Agents and Toxins Requiring Immediate (within 24 hours) Notification to CDC

- *Bacillus cereus* Biovar *anthracis*
- Botulinum neurotoxins
- Botulinum neurotoxin producing species of *Clostridium*
- *Ebolavirus*
- *Francisella tularensis*
- Marburg virus
- Variola major virus (Smallpox virus)
- Variola minor virus (Alastrim)
- *Yersinia pestis*

Overlap Agents Requiring Immediate (within 24 hours) Notification to CDC or APHIS

- *Bacillus anthracis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*

USDA Agents Requiring Immediate (within 24 hours) Notification to APHIS

- African swine fever virus
- Avian influenza virus (highly pathogenic) (H5Nx is currently exempt from 9 CFR Part 121)
- Classical swine fever virus
- Foot-And-Mouth disease virus
- Virulent Newcastle disease virus
- Rinderpest virus
- Swine vesicular disease virus

Scope

The Form 4A has two parts – Part 1 Form 4A-AB (Section A and B) and Part 2 Form 4A-CD (Section C and D).

PART 1 Form A-AB: Reference Lab Information

- The reference laboratory, or the laboratory that confirms the presence of Biological Select Agent or Toxin (BSAT), completes Form 4 Section A, 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, if applicable, that a select agent or select toxin was confirmed. See https://www.selectagents.gov/forms/docs/APHIS-CDC_Form-4A-AB_Guidance_508.pdf

  NOTE: if you are a diagnostic laboratory or have samples that were taken directly from the environment and identified by PCR or another method as containing a select agent or select toxin, and are NOT using a reference laboratory, **complete Part 1 section A and B and email it to:** DASAT@usda.gov OR CDCForm4@cdc.gov.

- The reference laboratory (or the clinical/ diagnostic laboratory where the select agent or toxin was identified) completes Section B as well.

PART 2: Form A-CD: Report of Identification (Sample Provider)

- The sample provider completes Section C, the sample provider information, and Section D.
- Section D covers the information regarding the agent identified, the date that it was confirmed by the reference lab, the number of samples produced and tested, the date the samples were shipped to the reference lab, as applicable, the name of the reference lab and the disposition of the samples. It also covers potential exposures, source of the samples, and notifications

Identification

"Identification" occurs at that point and time that a test confirms the presence of a select agent in or from a specimen. 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 BSAT identification once the identification of a select agent is confirmed, regardless of whether the confirmation is made by the same lab or another laboratory. The clock and regulatory obligations begin on the day of identification.

For example, if a lab identifies through PCR that an arthropod or specimen is PCR positive for a select agent, the person responsible for the laboratory (e.g., Principal Investigator, Laboratory Director, etc.) needs to file a Form 4A. Immediate notification, followed by submission of Form 4, as described above, must be observed.

Diagnosis/Verification

Regardless of the amount identified, clinical and diagnostic laboratories that identify a select toxin contained in a sample presented for diagnosis or verification must report the identification of the toxin using APHIS/CDC Form 4.

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 DOT/ IATA transport rules. Transfer **after** definitive identification requires prior approval from CDC or APHIS, as appropriate, using The Federal Select Agent Program 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

Proficiency testing is an external quality assessment process in which a laboratory analyzes unknown specimens—simulating patient, donor, or environmental samples—provided by an outside, authorized agency. Laboratories in possession of BSAT affecting humans and/or animals that are contained in specimens presented for proficiency testing also must follow the same general rules for reporting, transfer/destruction, and security as diagnostic and clinical laboratories.

Form 2: The entity sending the sample for proficiency testing is not required to submit a Form 2 to authorize the transfer, but they must notify the Federal Select Agent Program at least seven (7) calendar days prior to the transfer of the name and address of the recipient.

Form 4B: Reporting the identification of a select agent or toxin: Proficiency testing needs to be completed within ninety (90) days of receipt. Identification of a toxin in a proficiency sample must be reported.

Transfer or Destruction

All specimens, samples, and isolates (including regulated genetic elements, recombinant organisms, etc.) identified to contain a select agent or select toxin 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.

If destruction of suspect and/or confirmed specimens, samples and isolates must happen on-site, it has to be performed 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 (within 24 hours).

Appendix A - Definitions

Specimen means samples of material from humans, animals, arthropods, plants, or the environment or isolates or cultures from such samples for 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.