

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

Introduction

Clinical and/or diagnostic laboratories and other entities that possess, use, or transfer select agents and toxins 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 in the EHS SOP titled, **Select Agents and Toxins**.

This document provides an overview and general guidance for clinical and/or diagnostic laboratories and other entities that possess, use, or transfer select agents and toxins. If you need more specific information/guidance, the Federal Select Agent Program has a list of frequently asked questions on their website at <https://www.selectagents.gov/faq-reporting.html>.

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 I for definitions.

Diagnosis/Verification

Following confirmatory identification, a clinical and/or diagnostic laboratory possessing a select agent in or from a specimen or sample presented for diagnosis, verification, or proficiency testing is subject to certain regulatory requirements established by the United States Departments of Agriculture (USDA) and/or Health and Human Services (HSS). In summary:



- The reference laboratory (the laboratory providing the confirmatory/definitive identification) must file a formal report with the Federal Select Agent Program. The Responsible Official (RO) or Facility Director (FD) is responsible to file the official report using the appropriate forms.
- The notification to CDC or APHIS must be made within the specified reporting **period** for the specific select agent/toxin. With the exceptions noted below, written reports, using the most current CDC/APHIS Form 4A, must be filed by the RO or FD within seven (7) calendar days of confirmed identification.
 - All select agents/toxins affecting plants require immediate notification to the Federal Select Agent Program via email, telephone, or facsimile, followed by submission of Form 4A within 7 calendar days.
 - Select agents/toxins that require **immediate notification** (followed by submission of Form 4A within 7 calendar days) include:
 - Bacillus anthracis
 - Bacillus cereus Biovar anthracis
 - Botulinum neurotoxins
 - Botulinum neurotoxin producing species of Clostridium
 - Burkholderia mallei
 - Burkholderia pseudomallei
 - Ebola virus
 - Foot-and-mouth disease virus
 - Francisella tularensis
 - Marburg virus
 - Rinderpest virus
 - Variola major virus (Smallpox virus)
 - Variola minor virus (Alastrim)
 - Yersinia pestis
- 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.



- 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 select agents affecting humans and/or animals that are contained in specimens presented for diagnosis or verification 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.

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 does 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.

Reporting

For internal tracking purposes only, UNL laboratories are required to notify EHS of suspect specimens and/or presumptive identification of select agents and toxins. Notification should be made before confirmation testing is initiated and include laboratory contact name, phone number, and e-mail address; suspect agent identification; and a description of all associated specimens, samples, and isolates retained on-site pending confirmatory analysis. Initial reporting to EHS can be accomplished by e-mail (bosthus1@unl.edu or

manderson11@unl.edu), fax (402.472.9650), or telephone (402.472.4927, 402.472.4925, or 402.472.9554).

Upon confirmatory identification of a select agent or toxin, UNL laboratories must notify EHS immediately of the results. If any associated specimens, samples, and isolates were retained on-site pending confirmatory analysis they must be destroyed or transferred to a registered facility within 7 days of confirmed identification of a select agent. Transfer must be preceded by transfer approval from CDC or APHIS (CDC/APHIS Form 2), as arranged by the RO or FD.

The RO or FD of the reference laboratory (laboratory providing confirmatory/definitive identification) must complete and submit CDC/APHIS Form 4A to the appropriate agency within seven (7) calendar days of confirmatory identification, even when an immediate report was filed by telephone, fax, or e-mail. Form 4A is available on the CDC and APHIS web sites. If UNL provided the specimen for confirmatory testing, UNL's RO or FD will also be required to sign the form.

Reporting of select agents affecting humans (including overlap agents) to other federal, state, or local authorities for purposes other than compliance with the select agent regulations (i.e., disease surveillance reporting) is the responsibility of the laboratory, and is a condition of the exemption. The RO does not conduct this type of reporting.

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.



The RO or FD must secure approval from CDC or APHIS prior to transferring any specimen, sample, or isolate after confirmatory identification of a select agent. With the exceptions noted below, transfers must be conducted as follows:

- Must be authorized by CDC or APHIS. The RO or FD must apply for approval by filing APHIS/CDC form 2.
- Receiver must be registered.
- Sender must adhere to the exemption conditions or be registered.
- Exceptions: (1) A select agent or toxin that is contained in a specimen for proficiency testing may be transferred without prior authorization from CDC or APHIS provided that, within seven (7) calendar days prior to the transfer the sender reports to CDC or APHIS the select agents or toxin to be transferred and the name and address of the recipient for the tracking of select agents or toxins including those contained in a specimen presented for proficiency testing; (2) special circumstance by HHS.
- In accordance with all applicable packaging/shipping/transport laws (e.g., IATA or DOT, as applicable).
- In some cases, additional CDC or APHIS import/export/interstate permits may be required.

Recordkeeping

Copies of forms, sample destruction logs, and documented reports must be maintained for a minimum of three (3) years. Both the RO and FD are responsible to maintain documentation/records as discussed above.

Security

Immediately following confirmatory identification, specimens, isolates, and all regulated genetic materials associated with the select agent must be secured against theft, loss, or release until the materials have been transferred to a registered facility, inactivated/rendered incapable of replication, or destroyed. Suspected or known theft, loss, or release (including known or suspected occupational exposures) of a specimen or associated materials must be reported immediately to the RO and UNL Police Department.

Secured means that individuals not associated with the laboratory diagnostic process do not have access (able to carry, use, or manipulate) at any point in time to specimens, isolates, or other regulated materials. The standard of security is generally met if all of the following are met:



- All select agents and toxins have been secured in locked cabinets, rooms, or other containers;
- The containers cannot be forced open without tools and without visible signs of damage;
- Rooms are secure against entry by unauthorized personnel;
- Keys, combinations, etc., are controlled; and
- Access to the area is limited to employees of the entity.

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 I - 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 the analytical sensitivity and specificity) specifications for any procedure used for diagnosis.