



Select Agents and Toxins Theft, Loss or Release Information Document

7 CFR Part 331.19, 9 CFR Part 121.19, 42 CFR Part 73.19

Prepared by

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Theft, Loss, or Release of Select Agents or Toxins

Purpose

This document describes practices and procedures for submitting an APHIS/CDC Form 3 (Report of Theft, Loss, or Release of Select Agents and Toxins). These practices and procedures are for general information purposes only and do not constitute or establish minimum acceptable standards that would automatically meet the requirements of title 7 of the *Code of Federal Regulations* (7 CFR) 331.11 and 331.19, 9 CFR 121.11 and 121.19, or 42 CFR 73.11 and 73.19. On March 4, 2010, six additional TLR scenarios were added to this document.

In general, we view the following terms as:

Contaminated: The presence of blood, infectious materials, potentially infected materials, toxins, or prions on an item or surface.

Decontamination: A process that consists of cleaning combined with disinfection or sterilization.

Loss: A failure to account for select agent or toxin.

Occupational exposure: Any event which results in any person in a registered entity facility or lab not being appropriately protected in the presence of an agent or toxin. This may include reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potential infectious materials that may result from the performance of a person's duties. For example, a sharps injury from a needle being used in select agent or toxin work would be considered an occupational exposure.

Primary containment barriers: Specialized items designed or engineered for the capture or containment of hazardous biological agents. Examples include biological safety cabinets, trunnion centrifuge cups, and aerosol-containing blenders. For the purposes of assessing a potential select agent release, the laboratory room may be considered a primary containment barrier in facilities meeting the requirements of biosafety level-4 (BSL-4) or BSL-3Ag as described in the 5th edition of the Centers for Disease Control and Prevention/National Institutes of Health (CDC/NIH) Biosafety in Microbiological or Biomedical Laboratories manual.

Release: A discharge of a select agent or toxin outside the primary containment barrier due to a failure in the containment system, an accidental spill, occupational exposure, or a theft. Any incident that results in the activation of a post exposure medical surveillance/prophylaxis protocol should be reported as a release.

Theft: Unauthorized removal of select agent or toxin.

Security, Biosafety, and Incident Response Plans

All registered entities must develop and implement security, biosafety, and incident response plans in accordance with Security, Biosafety, and Incident Response Sections outlined in 7 CFR 331, 9 CFR 121, and 42 CFR 73.

Reporting Incidents

Upon discovery of the theft, loss, or release of a select agent or toxin, entities must report all incidents as specified below.

- First, an individual or entity must immediately notify the lead Agency; i.e., the Animal and Plant Health Inspection Service (APHIS) or the CDC by telephone, fax, or e-mail. (The contact information is provided below.)
 - If the entity is not registered with either APHIS or CDC (such as an unregistered clinical or diagnostic facility), then it may notify either Agency.
 - If a responsible official (RO) has a reasonable suspicion that a theft, loss, or release has occurred, the RO should notify APHIS or CDC to make APHIS or CDC aware of a potential incident. This will help the Agency respond quickly if the incident is confirmed.
 - If the entity is unsure whether a report is required, then it should contact the lead Agency immediately.
- The individual or entity must also notify the appropriate Federal, State, or local law enforcement agencies for the theft or loss of a select agent or toxin. For the release of a select agent or toxin, the entity should notify the appropriate local, state, and federal health agencies.
- Individuals or entities must report thefts or losses even if the select agent or toxin is subsequently recovered and/or the responsible parties are identified.
- The initial report should include as much information as possible about the incident. As required by the regulations, the entity must report the following:
 - Type of incident
 - Date and time
 - Agent and quantity
 - Summary of events that include the location of the incident and list of other agencies notified. If a release occurred, the entity must provide the number of individuals potentially exposed, actions taken to respond to the release such as medical intervention and biocontainment, and hazards posed by the release such as estimate of the severity of the event and the proposed impact to public or agricultural health.
- Information should be submitted as it becomes known, but no later than 24 hours.
- Within seven (7) days, the entity must submit a complete APHIS/CDC Form 3, Report of Theft, Loss or Release to the lead Agency or to either APHIS or CDC if the entity is not registered with either agency. All appropriate data fields should be completed. Supporting documentation, such as access logs, standard operating procedures, and the follow up investigation, should be provided regarding the reported incident. The form and supporting documentation may be submitted by either fax or mail.
- Contact information:

APHIS

Agricultural Select Agent Program
4700 River Road, Unit 2, Mailstop 22, Cubicle 1A07
Riverdale, MD 20737
Telephone: 301-734-5960
Fax: 301-734-3652
Agricultural.Select.Agent.Program@aphis.usda.gov

CDC

Division of Select Agents and Toxins
1600 Clifton Road NE, Mailstop A-46
Atlanta, GA 30333
Telephone: 404-718-2000
Fax: 404-718-2096
Irsat@cdc.gov

Biosafety Release Scenarios

These scenarios represent examples for which a Form 3 report may be required. This list is not all inclusive and should not be used in place of an incident-specific risk assessment.

Scenario 1: In a BSL-2 laboratory, a laboratorian is working with a culture from an anthrax patient inside a biological safety cabinet. The laboratorian's chair unexpectedly shifts causing the glass vial containing the anthrax to slip out of the laboratorian's hand and break on the floor. Is this considered a release?

Yes. The primary containment barrier for this specimen (the biological safety cabinet) was breached and the splash potential could cause a wider area of contamination. The entire area surrounding the spill would require disinfection of the affected area and follow up evaluation. Medical surveillance and prophylaxis may be necessary.

Scenario 2: A specimen containing *Yersinia pestis* is undergoing centrifugation in a BSL-3 laboratory. The centrifuge safety cup malfunctions, and the specimen is released within the centrifuge. Staff members are wearing proper personal protection equipment (PPE), including a powered, air-purifying respirator (PAPR), during all operations associated with this material. Is this reportable as a release?

Yes. Although proper PPE was being worn, the specimen container broke, and the specimen was no longer under containment.

Scenario 3: An animal caretaker in an animal BSL-3 facility opens the door to a cage to remove what was mistakenly thought to be a dead mouse. During the removal process, the mouse bit the caretaker on the finger penetrating the protective gloves being worn. The mouse was confirmed to be infected with *Y. pestis*. Is this reportable?

Yes. An occupational exposure has occurred with a mouse infected with *Y. pestis*. Medical intervention and follow-up will be required.

Scenario 4: On completion of a study, a haemorrhagic fever virus suspension is securely wrapped in a leak-proof container and passed out of a BSL-4 laboratory through a dunk tank for transport to a gamma cell irradiator for inactivation. Although specific written procedures for biosafety and security are followed, a slip occurs during transport, and the leak-proof outer container breaks exposing a broken vial containing the virus. Is this reportable?

Yes. The area between the laboratory and gamma cell irradiator would provide inadequate containment and would be subject to decontamination. Follow up evaluation and medical surveillance of the exposed workers would be indicated.

Scenario 5: A worker is manipulating a haemorrhagic fever virus suspension in a BSL-4 suit laboratory. During transport of the suspension from a biological safety cabinet to an incubator, the suspension is dropped and spills on the floor. The worker reports the incident to the supervisor, and the spill is cleaned up following established protocols. All building containment systems were operating within normal limits, and no breaches of containment suits were reported during the incident and resulting cleanup. Is this reportable?

No. The BSL-4 engineering controls in place prevented the release of the agent to the environment and exposure to the workers. However any event that results in a breach of the positive pressure suit or secondary containment barrier should be reported to DSAT.

Scenario 6: A diagnostic laboratory has received a suspected sample of *Coccidioides immitis*, an overlap select agent. Further testing confirms the original diagnosis, and an APHIS/CDC Form 4 has been completed and submitted to the appropriate Agency. Before the confirmed sample is destroyed, the diagnostician discovers the confirmed sample is missing and may have been stolen. Is this a reportable incident?

Yes. Diagnostic laboratories are required to report the theft, loss, or release of a confirmed select agent.

Scenario 7: During a quarterly inventory review, the RO discovers a discrepancy of one vial of a select agent. The RO immediately verifies the most recent inventory records to validate the missing vial and contacts the principal investigator to determine if the vial was incorrectly removed from the storage freezer. After 6 hours of investigating the problem, the RO has not located the missing vial, but has not completed the investigation. Is this a reportable incident?

Yes. A loss should be reported to the lead Agency even if the investigation has not been completed. Further, appropriate law enforcement officials should be made aware of the situation. Should the vial be subsequently recovered, the lead Agency and law enforcement officials should be informed. Regardless of recovery, a Form 3 is still required within 7 days of the incident.

Scenario 8: A flood occurs at a laboratory causing significant destruction. During the flood, emergency responders enter the laboratory. After the flood, it is noticed that several vials are damaged or compromised, such that inventory reconciliation is not possible. Is this a reportable incident?

Yes. The entity should immediately report the incident. If there is reasonable suspicion that containment was breached, resulting in occupational exposure to responders or the public, the incident should be reported to the lead Agency as a release. Appropriate public health officials should be notified.

Scenario 9: ABC Corporation, a registered entity working with select agents, conducts monthly tests on all autoclaves used to sterilize select agent waste. During a routine test, it is discovered that the autoclave is not reaching the threshold temperatures needed to achieve sterilization. The logbook indicates a load with select agent waste was autoclaved 3 days before and put in the dumpster for removal. Is this a reportable incident?

Yes. The RO should report a release because the autoclave did not reach appropriate temperatures and the select agents may not have been inactivated by the decontamination process. Therefore, there is reason to conclude that an environmental release of the select agent has occurred. Notification should also be made to the waste disposal firm, appropriate law enforcement officials, and appropriate public health officials.

Scenario 10: A vaccine production company has a rupture in a high volume production tank of Botulinum neurotoxin. Is this a reportable incident?

Yes. The primary containment vessel has been compromised.

Scenario 11: A laboratory is doing research with high pathogenicity avian influenza (H5N1) in poultry inside an approved space with negative air pressure. While in the laboratory, the heating, ventilating, and air conditioning system fails, causing a potential backflow of air outside of containment. The redundant system reestablishes directional airflow. Is this a reportable incident?

Possibly. If all select agent materials were maintained in primary containment devices and there was no evidence of a device failure during the ventilation malfunction, then the incident would not be reportable. However, if primary containment devices were not in use and the laboratory became positively pressured during this time, then the incident would be reportable.

Scenario 12: A laboratory is doing research with 54 mice infected with *Bacillus anthracis*. On Monday morning, the animal technician discovers that one cage is missing two mice. Is this a reportable incident?

Possibly. If there are no indications of the fate of the mice, then the incident is reportable as a loss. However, if there is indication of cannibalization, such as a tail or skeletal remains, the incident is not reportable.

Scenario 13: A researcher is working with chickens infected with the velogenic strain of Newcastle disease. The animal technician contracts conjunctivitis, a condition caused by exposure to Newcastle disease. Is this a reportable incident?

Yes. A release should be reported to the lead Agency.

Scenario 14: A laboratorian receives a self-inflicted cut with a scalpel during a necropsy of an animal infected with a select agent. The glove and skin were penetrated. The necropsy took place on a downdraft table that pulled air away from the laboratorian, and there was no contact between the laboratorian's hand and any tissue or fluid from the carcass. Is this a reportable incident?

Possibly. If the scalpel was not sterile and the possibility exists that it was contaminated with tissue or fluids from the animal, then the incident is reportable. However, if the scalpel was sterile at the time of the cut (i.e., prior to use in the necropsy) and there was no likelihood of an occupational exposure, the incident would not be reportable.

Scenario 15: In a BSL-3, a laboratorian spills an agent on the floor. The agent's route of infection is only via the mucous membrane. The laboratorian, who is wearing PAPR protection, bends over to clean up the spill and notices a rip in the personal protective clothing he or she is wearing. Is this a reportable incident?

Yes. Although the risk of exposure to the laboratorian may be minimal, the incident still resulted in a release of select agent materials from primary containment.

Scenario 16: A laboratorian is working with *Brucella abortus* and has a needle stick from a used syringe. The outside of the needle had been sterilized with alcohol, but the laboratorian thinks there may have been a few drops inside the needle. Is this a reportable incident?

Yes. If there is any possibility that a needle stick might result in infection, the incident must be reported as a release.

Scenario 17: Power to a biosafety cabinet goes down for 30 seconds during a manipulation. The laboratorian, who was not wearing any respiratory protection, was working with an aerosol- transmitted agent. Although the manipulation did not appear to generate an aerosol, the laboratorian was placed on a fever watch as a precaution. Is this a reportable incident?

Yes. The activation of the post exposure medical surveillance protocol is evidence of a significant probability of release of the agent outside of containment.

Scenario 18: A non-registered BSL-2 clinical laboratory performs multiple manipulations with a fastidious gram-negative bacterial isolate from the blood of a febrile patient. The work is performed outside of a biological safety cabinet. The laboratory is unable to identify the isolate and sends it to a reference laboratory for further studies. The reference laboratory identifies the isolate as *Francisella tularensis*. Is this a reportable incident?

Yes. The manipulation of this material outside of a biological safety cabinet in the clinical laboratory represents a non-contained condition.

Scenario 19: A set of 10 “trap” or sentinel plants is located 18 feet outside of a containment greenhouse and within the perimeter of the security fence. Visual monitoring reveals that one plant is showing disease symptoms. Diagnosis tests confirm that the symptomatic plant is infected with a select agent that is being studied in the greenhouse and is not known to be present within the United States. Is this a reportable incident?

Yes. The RO should report this as a release. The only source of the select agent was from the greenhouse through transmission means (e.g., insect vector or mechanical transmission) possible for the select agent. The RO should investigate the event to determine the source and means of pathogen transmission to prevent future incidents.

Scenario 20: Routine serological testing of a worker in a Q-Fever laboratory shows an elevated antibody titer (above the established positive threshold for the assay). Is this reportable as an occupational exposure?

Possibly. The entity must perform a follow-up investigation to determine if the elevated titer is the result of: 1) previous exposure to the organism prior to work at the entity; 2) possible exposure to the organism while doing non-work related activities; or 3) exposure at the workplace. If the investigation shows that the exposure most likely occurred at the workplace, then the incident is reportable.

Additional Theft, Loss, Release Scenarios added June 8, 2010

The following six additional TLR Scenarios have been developed by CDC’s Division of Select Agents and Toxins and USDA’s Animal and Plant Health Inspection Service to assist the Regulated Community in better understanding the circumstances and events that lead to the reporting of a select agent theft, loss or release. These scenarios are based on real events that have been reported on Theft, Loss, or Release Form (CDC/APHIS Form 3).

Scenario 21: A state veterinarian reports that small numbers of bison are dying in a Midwest state; Anthrax is suspected. However, as animals expire, no specimens are collected or tissue samples taken.

The carcasses are sprayed with antibacterial foam and buried. In addition, all equipment used to move the carcasses are disinfected with antibacterial foam. Is this a reportable incident?

No. Since no tissue samples or body fluids were collected in the field and taken to a laboratory for analysis, the agents are considered to be in their “naturally occurring state.” This event is, therefore, not reportable to CDC or APHIS as a release of select agents under 42 CFR 73.4 (d)(1) or 9 CFR 121.4(d)(1).

However, if specimens had been collected or extracted for laboratory analysis, the laboratory receiving these samples would be required under 42 CFR 73.5 (a) (1-3) or 9 CFR 121.5 (a)(1-3) to properly transfer the specimens (**once the samples are confirmed positive**). If not registered with CDC or APHIS to possess these materials, secure the materials against theft, loss or release and report the identification of a select agent to CDC or APHIS and to other appropriate authorities when required by Federal, state, or local law.

Scenario 22: A state health department reports that a deer was observed ramming its head against wood deck railings at a private residence. The deer continues to ram the railings until state wildlife officials arrive to remove the animal. The animal is euthanized, removed from the residential community and taken to a state lab for post mortem examination. Based on the observed erratic behavior, chronic wasting disease (Transmissible spongiform encephalopathy) is suspected. Bone saws are used during necropsy to obtain brain specimens for TSE testing without the use of respiratory protection for laboratory staff involved in the procedure. Samples collected during this necropsy are then sent to another laboratory for testing. Results from these tests indicate that the deer was infected with the Eastern Equine Encephalitis virus. The veterinary laboratory where the necropsy was performed is not registered for possession and use of select agents. Is this a reportable event?

Yes. In this incident, the use of aerosol producing equipment outside of primary containment and without respiratory protection has resulted in a potential exposure to laboratory workers during the necropsy. The state agency that conducted the necropsy is responsible for submitting the CDC/APHIS Form 3 report immediately after receiving confirmation that the necropsy materials contained the select agent. As part of the follow up process, DSAT (since this involves an HHS-only agent) will review work practices that led to this exposure, make recommendations for improvements in containment practices, and confirm that all exposed laboratory workers have been evaluated and are receiving appropriate medical surveillance. The state laboratory that identified the select agent is required to complete a CDC/APHIS Form 4 reporting the identification of a select agent.

Scenario 23: A stray, domestic cat is discovered outside of a veterinary clinic. The cat is friendly but has heavy purulent drainage from its respiratory passages. During the initial workup and examination by veterinary staff, no PPE was worn other than gloves. Samples from the cat are taken and sent to the state veterinary diagnostic laboratory. The cat was treated with antibiotics and housed in a cage where it expired the next day. The state veterinary laboratory confirms the samples to be positive for *Yersinia pestis*. Is this reportable?

Yes. Although the select agent is considered to be in a “naturally occurring state” until it was brought into the clinic (i.e. in a stray cat not experimentally infected with the agent), collection of the samples from this animal, represents an event that meets the requirement given in 42 CFR 73.3(d)(1) as select agents, i.e., “*intentionally introduced, cultivated, collected, or otherwise extracted from its natural source*”. In this incident, all veterinary assistants who worked with the cat were potentially exposed by these activities.

Although, the veterinary clinic treating the cat is not registered with the Select Agent Program, the clinic is still required to submit the CDC/APHIS Form 3. As noted above in Scenario 22, DSAT (since this is an HHS-only agent) conducts follow up activities to ensure worker and public health issues are addressed after events such as these. The laboratory that identified the select agent is required to complete a CDC/APHIS Form 4.

Scenario 24: A patient reports to a local hospital (hospital # 1) after working with imported drum skins. The patient is evaluated in the emergency room and attending physicians suspect a possible anthrax infection. Since this hospital does not have the laboratory capability to confirm the diagnosis, the patient is transferred to another hospital (hospital # 2) with better diagnostic and therapeutic capabilities for this type of infection. However, the second hospital also cannot conclusively identify the agent(s) responsible for the infection. Specimens collected from both hospitals are then forwarded to the state laboratory where they are confirmed to be *Bacillus anthracis*. Only the state laboratory is registered with the select agent program. It had been determined that laboratory workers at both hospitals worked with the specimens outside primary containment. Is this reportable?

Yes. Since laboratory staff at both hospitals worked with the specimens outside primary containment, these activities meet the requirements given in 42 CFR 73.19 (b) as a “*release of a select agent or toxin outside of the primary barriers of the biocontainment area*”. A CDC/APHIS Form 3 report must be submitted by both hospitals as separate incidents. The state laboratory that identified the select agent would also be required to complete a CDC/APHIS Form 4 report. In addition, a CDC/APHIS Form 2 report would also be required each time specimens were transferred to a new location after identification of the microorganism as a select agent.

Scenario 25: During a DSAT inspection at a registered select agent entity, inspectors discovered that an environmental sample tested positive for *Francisella tularensis* two years ago but this information was not reported to either CDC or APHIS at the time. Is the event still reportable?

Yes. Although the regulatory requirement given in 42 CFR 73.19 that “*Upon discovery of a release of an agent or toxin causing occupational exposure or release of a select agent or toxin outside of the primary barriers of the biocontainment area, an individual or entity must immediately notify CDC or APHIS*” was not met, DSAT does require that theft, loss and release events discovered under such circumstances be reported as soon as these events are recognized. The rationale for belated event reporting is based on the need to ensure tracking of such events by DSAT, and to ensure entity compliance with regulatory requirements under 42 CFR 73. Although delays in reporting releases of select agents can result from misunderstandings of the regulatory requirements, repeated instances of such tardiness can result in compliance actions against the entity.

Scenario 26: Rhesus macaques are housed in a colony solely for genealogy studies and do not involve any experimental work with select agents. During a routine animal husbandry activity, one of the animal caretakers is accidentally bitten by a monkey. Knowing that Old World monkeys are the enzootic host of Herpes B virus, which is a select agent, is this a reportable event?

No. Since there was no attempt to intentionally introduce, cultivate, collect, or otherwise extract the agent from its natural source (42 CFR 73.3(d)(1)), no CDC/APHIS Form 3 is required. However, if wound swabs collected from the injured worker as part of medical surveillance activities recommended for B virus exposures are positive for this agent, the diagnostic laboratory must report this identification immediately to

CDC or APHIS using a Form 4 report. Unless approved for manipulation of B virus (at BSL4) by CDC or APHIS, the laboratory making the diagnosis should destroy the B virus cultures or transfer these materials to a registered laboratory capable of safely handling this agent. Transfers of select agents require a CDC/APHIS Form 2.

References

For biosafety and containment procedures, please refer to standard biosafety references. Registered entities should reference and be familiar with the following:

- Principles and Practices of Disinfection, Preservation and Sterilization, 3rd ed. Russell, Hugo, and Ayliffe, 1999.
- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition, located at <http://www.cdc.gov/od/ohs/biosfty/bmb15/bmb15toc.htm>.
- NIH Guidelines for Research Involving Recombinant DNA Molecules, located at <http://www4.od.nih.gov/oba/rac/guidelines/guideline.html>.
- Material Safety Data Sheets on HHS and Overlap Select Agents, located at <http://www.phac-aspc.gc.ca/msds-ftss/index.html>.
- APHIS/CDC Form 3, Report of Theft, Loss or Release.

For further information, contact the CDC Select Agent Program at LRSAT@CDC.gov or the APHIS Agricultural Select Agent Program at Agricultural.Select.Agent.Program@aphis.usda.gov.