




APHIS/CDC Form 4
Request to Transfer Select Agents and Toxins

Form 4 Team
Federal Select Agent Program

Multi-Agency Informational Meeting to Discuss Select Agent and Toxin Reporting Requirements

September 23, 2020

APHIS/CDC Form 4A – Reporting the Identification of a Select Agent or Toxin from a Clinical/Diagnostic Specimen

- APHIS/CDC Form 4 Purpose
- Statistics
- APHIS/CDC Form 4A Overview
- Reporting Requirements
- International sample providers
- Communication
- Disposition
- Common Concerns
- Scenarios, Questions and Answers

Purpose of the APHIS/CDC Form 4

The purpose of this form is to report select agents or toxins contained in specimens presented for diagnosis, verification, or proficiency testing and seizure of select agents or toxins by federal law enforcement agencies.

- Diagnostic/Verification (4A)
- Proficiency Testing (4B)
- Law Enforcement (4C)

Select Agent Regulations
Exemptions (Sections 5 and 6)

- Diagnostic, verification, or proficiency testing
- Cleared, approved, licensed, or registered products
- Investigational product
- Domestic or foreign public health or agricultural emergency

APHIS/CDC Form 4A Overview – Regulatory Requirements

- Report within 7 calendar days
- Report Tier 1 select agents/toxins immediately
- Transfer per Section 16 or destroy on site by a recognized sterilization or inactivation process
- Secure agents against theft, loss, or release between identification and final disposition
- Proper reporting to appropriate authorities when required
- Maintain form for 3 years

NOTE: Reporting requirements may be made less stringent in times of extraordinary circumstances (i.e., outbreak)

APHIS/CDC Form 4A Overview – Immediate Notification of Tier 1 Select Agents

HHS select agents and toxins:

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

Overlap select agents:

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

USDA select agents:

- Foot-and-mouth disease virus
- Rinderpest virus

APHIS/CDC Form 4A – Total Form 4A Sections A and B Reported

APHIS/CDC Form 4A – Total Form 4A Sections C and D Reported

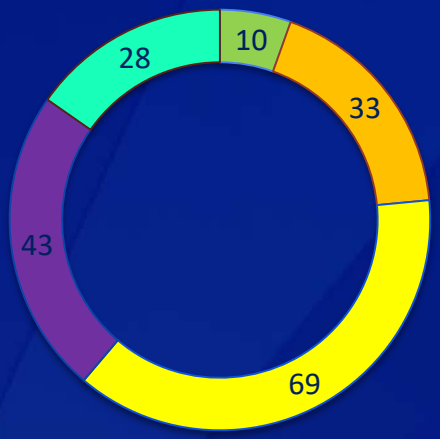
APHIS/CDC Form 4A – Sample Types Reported

Sample Types	2018	2019
Animal clinical/diagnostic/isolate	385*	621
Human clinical/diagnostic/isolate	570*	592
Environmental	41*	64
Food	10*	25
Plant clinical/diagnostic	0*	2

***DSAT only**

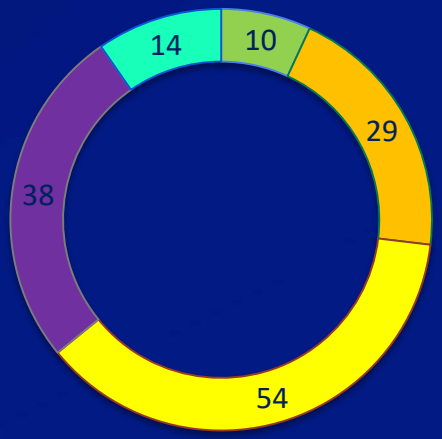
APHIS/CDC Form 4A – Top 5 Select Agents Reported by NREs on Form 4A A/B

2018



- Bacillus anthracis
- Botulinum neurotoxin producing species of Clostridium
- Coxiella burnetii
- Eastern Equine Encephalitis virus
- Francisella tularensis

2019



- Bacillus anthracis
- Botulinum neurotoxin producing species of Clostridium
- Coxiella burnetii
- Eastern Equine Encephalitis virus
- Francisella tularensis

APHIS/CDC Form 4A – Top 3 States Reporting Select Agents on Form 4A A/B for NREs in 2018

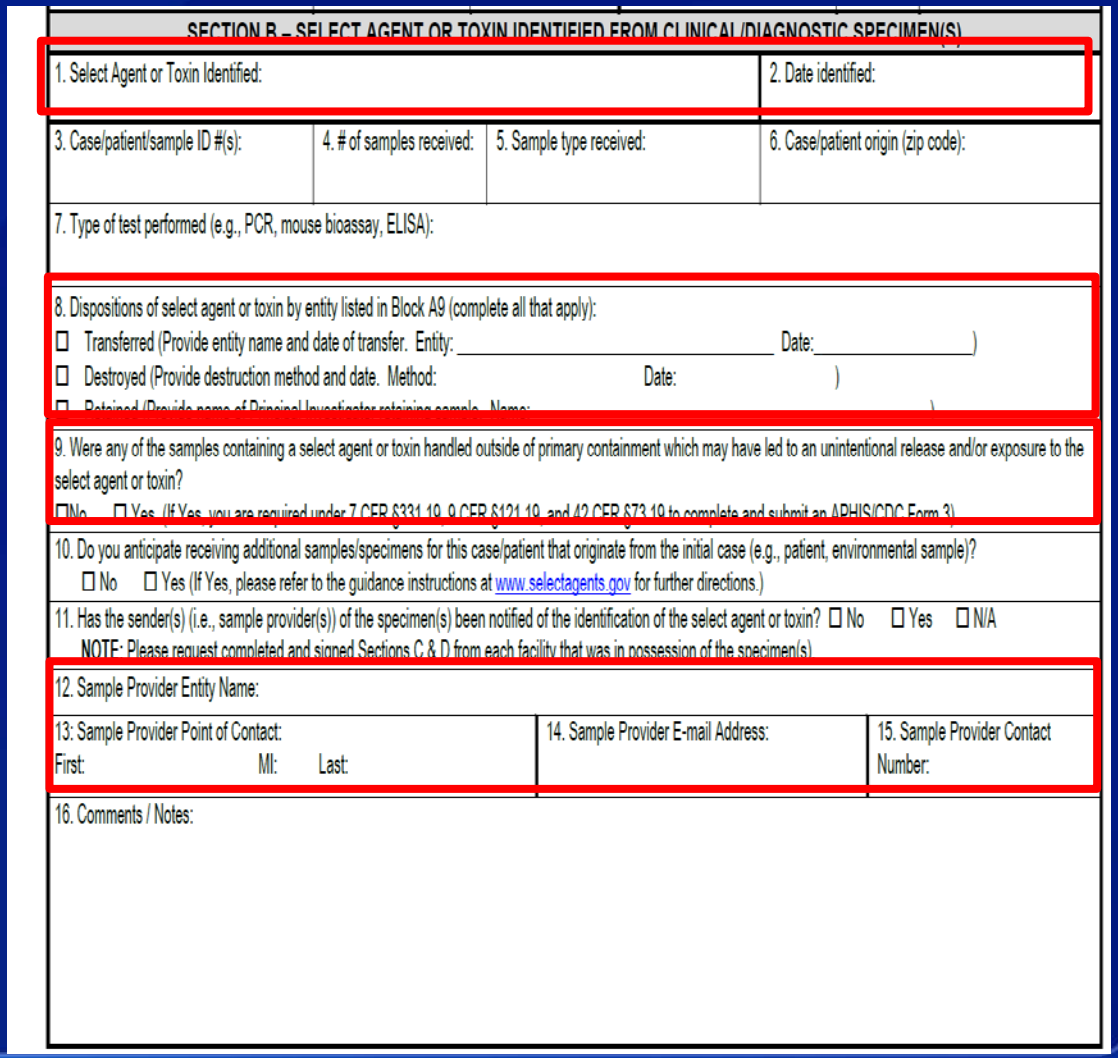
Highest reported #	*Coxiella burnetii*	Eastern Equine Encephalitis virus	Francisella tularensis	*Botulinum neurotoxin* producing species of *Clostridium*	*Bacillus anthracis*
#1	Texas	New Jersey	Wyoming	Pennsylvania	South Dakota
#2	Wisconsin	Louisiana	California/ Washington	Michigan	Texas
#3	Wyoming/ New York	North Carolina	Kansas	North Carolina/ Florida	Wyoming/ Wisconsin

APHIS/CDC Form 4A – Top 3 States Reporting Select Agents on Form 4A A/B for NREs in 2019

Highest reported #	*Coxiella burnetii*	Eastern Equine Encephalitis virus	*Botulinum neurotoxin producing species of Clostridium*	*Francisella tularensis*	*Bacillus anthracis*
#1	Wisconsin	Louisiana	Pennsylvania	California	Texas
#2	Texas	Michigan	Michigan	Wyoming/ Illinois/ South Dakota	North Dakota
#3	Indiana	Wisconsin	N/A	North Dakota/ New Mexico/ Delaware/ Washington	N/A

APHIS/CDC Form 4A Overview – Sections A and B – Reference Laboratory

- Reference laboratory information
- Identification
- Final disposition
- Exposures
- Provide any sample provider information



SECTION B – SELECT AGENT OR TOXIN IDENTIFIED FROM CLINICAL/DIAGNOSTIC SPECIMEN(S)

1. Select Agent or Toxin Identified:			2. Date identified:
3. Case/patient/sample ID #(s):	4. # of samples received:	5. Sample type received:	6. Case/patient origin (zip code):
7. Type of test performed (e.g., PCR, mouse bioassay, ELISA):			

8. Dispositions of select agent or toxin by entity listed in Block A9 (complete all that apply):
☐ Transferred (Provide entity name and date of transfer. Entity: _____ Date: _____)
☐ Destroyed (Provide destruction method and date. Method: Date:)
☐ Retained (Provide name of Principal Investigator retaining sample. Name:)

9. Were any of the samples containing a select agent or toxin handled outside of primary containment which may have led to an unintentional release and/or exposure to the select agent or toxin?
☐ No ☐ Yes (If Yes, you are required under 7 CFR §331.19, 9 CFR §121.19, and 42 CFR §73.19 to complete and submit an APHIS/CDC Form 3)

10. Do you anticipate receiving additional samples/specimens for this case/patient that originate from the initial case (e.g., patient, environmental sample)?
☐ No ☐ Yes (If Yes, please refer to the guidance instructions at www.selectagents.gov for further directions.)

11. Has the sender(s) (i.e., sample provider(s)) of the specimen(s) been notified of the identification of the select agent or toxin? ☐ No ☐ Yes ☐ N/A
NOTE: Please request completed and signed Sections C & D from each facility that was in possession of the specimen(s).

12. Sample Provider Entity Name:		
13: Sample Provider Point of Contact: First: MI: Last:	14. Sample Provider E-mail Address:	15. Sample Provider Contact Number:

16. Comments / Notes:

APHIS/CDC Form 4A Overview – Section C – Sample Provider

- Sample Provider Information

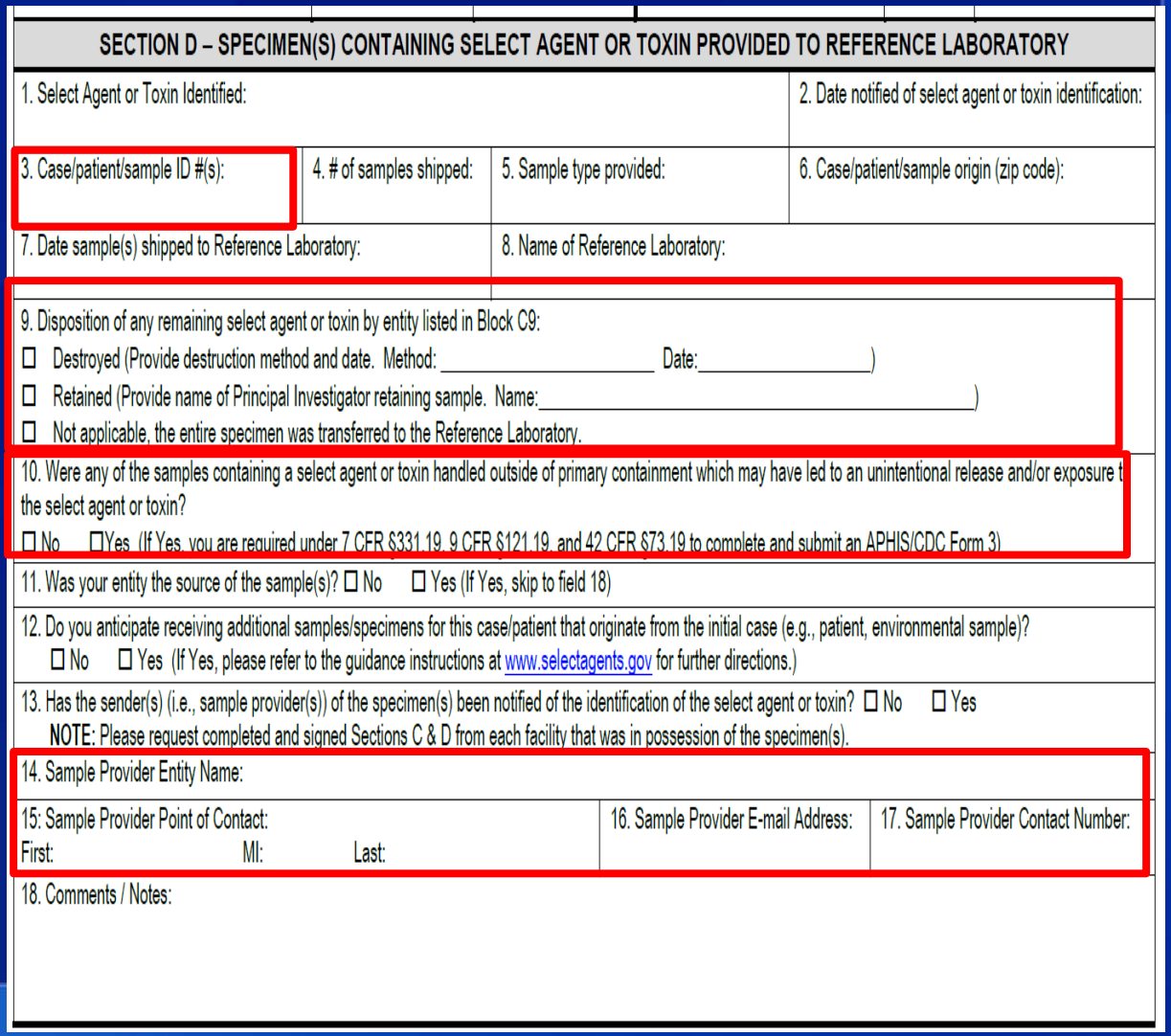
Submit completed form only once by either e-mail, fax, or mail

SECTION C – SAMPLE PROVIDER INFORMATION

1. Name of individual completing Sections C and D: First: MI: Last:			2. E-mail address:		3. Telephone #:
4. ☐ Registered Entity (APHIS or CDC Registration #: _____) ☐ Clinical or Diagnostic Laboratory [non-registered entity (NRE)] (NRE # (provided by APHIS or CDC): _____)			9. Entity name:		
5. Responsible Official or Laboratory Supervisor name (if same as field 1 then skip to field 9): First: MI: Last:			10. Address (NOT a post office address):		
6. E-mail address:	7. Telephone #:	8. Fax #:	11. City:	12. State:	13. Zip Code:

APHIS/CDC Form 4A Overview – Section D – Sample Provider

- Case-specific information
- Final disposition
- Exposures
- Additional sample provider information



SECTION D – SPECIMEN(S) CONTAINING SELECT AGENT OR TOXIN PROVIDED TO REFERENCE LABORATORY

1. Select Agent or Toxin Identified:			2. Date notified of select agent or toxin identification:
3. Case/patient/sample ID #(s):	4. # of samples shipped:	5. Sample type provided:	6. Case/patient/sample origin (zip code):
7. Date sample(s) shipped to Reference Laboratory:		8. Name of Reference Laboratory:	

9. Disposition of any remaining select agent or toxin by entity listed in Block C9:
- ☐ Destroyed (Provide destruction method and date. Method: _____ Date: _____)
- ☐ Retained (Provide name of Principal Investigator retaining sample. Name: _____)
- ☐ Not applicable, the entire specimen was transferred to the Reference Laboratory.

10. Were any of the samples containing a select agent or toxin handled outside of primary containment which may have led to an unintentional release and/or exposure t the select agent or toxin?
☐ No ☐ Yes (If Yes, you are required under 7 CFR §331.19, 9 CFR §121.19, and 42 CFR §73.19 to complete and submit an APHIS/CDC Form 3)

11. Was your entity the source of the sample(s)? ☐ No ☐ Yes (If Yes, skip to field 18)

12. Do you anticipate receiving additional samples/specimens for this case/patient that originate from the initial case (e.g., patient, environmental sample)?
☐ No ☐ Yes (If Yes, please refer to the guidance instructions at www.selectagents.gov for further directions.)

13. Has the sender(s) (i.e., sample provider(s)) of the specimen(s) been notified of the identification of the select agent or toxin? ☐ No ☐ Yes
NOTE: Please request completed and signed Sections C & D from each facility that was in possession of the specimen(s).

14. Sample Provider Entity Name:

15: Sample Provider Point of Contact: First: MI: Last:	16. Sample Provider E-mail Address:	17. Sample Provider Contact Number:

18. Comments / Notes:

APHIS/CDC Form 4A – Reporting Requirements

- **APHIS/CDC Form 4A**
  - Immediate notification (Tier 1 agents)
  - Report identification within 7 days
  - Non-registered entities (NRE)
    - Fillable form and email
  - Registered entities (RE)
    - eFSAP

- **Who completes and when are Sections A/B and C/D completed?**
  - Sections A/B – Reference Laboratory
  - Sections C/D – Sample Provider(s)

APHIS/CDC Form 4A – Reporting Requirements

- **International sample providers**
  - International entities do NOT need to report
  - Reference laboratory completes sample provider questions (#B12-16)

NOTE: Please request completed and signed Sections C & D from each facility that was in possession of the specimen(s).
12. Sample Provider Entity Name:
13: Sample Provider Point of Contact: First: MI: Last: / 14. Sample Provider E-mail Address: / 15. Sample Provider Contact Number:
16. Comments / Notes:

APHIS/CDC Form 4A – Communication

- **Use general discussion box (if registered)**
  - eFSAP
- **Use email (if not registered)**
  - cdcform4@cdc.gov
  - AgSAS@usda.gov
- **Use case/patient/ID number – NOT the CID-F4**
  - Numbers are used when following up about cases
- **Split samples**
  - List all laboratories that were in possession of the samples
  - All laboratories must submit Sections C/D

APHIS/CDC Form 4A – Disposition

- **Destruction methods**
  - Destroy onsite – Autoclave, incinerator, chemical, etc.
  - Proper disposal can be found in *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), Material Safety Data Sheets (MSDS), and Safety Office
- **Transfer**
  - Select if part of sample was forwarded to reference laboratory
  - After identification has been made
- **Not applicable (Form 4A C/D only)**
  - Select if entire sample was forwarded to reference laboratory
  - No work performed on sample
- **Retaining samples**
  - Samples only retained if registered with FSAP
    - Must be registered for that BSAT

APHIS/CDC Form 4A – Most Common Concerns

- **Missing information**
  - Difficult to process forms
- **Reporting discrepancies**
  - Between reference lab and sample provider
  - Zip code is for patient location, not laboratory location (B6)
- **Exposure reporting**
  - Form 3 team needs to follow up
- **Entity sample retention**
  - Cannot retain samples more than 7 days once notified

APHIS/CDC Form 4A – Most Common Concerns

- **Field collection samples**
  - Reference laboratory lists the sample provider
    - Veterinary clinic/hospital
    - Veterinary laboratory
    - Farm/wildlife center with veterinary staff
  - Sample provider reporting
    - Necropsy versus carcass
    - Field collection (soil, water, insects)
    - Mosquito testing

APHIS/CDC Form 4A – Scenario 1

- **Scenario – Split Sample**

  A hospital laboratory sends a patient sample to two regional laboratories for testing. The regional laboratories are unable to identify the isolate. Regional laboratory A sends the isolate to the state laboratory while Regional laboratory B sends the isolate to the Centers for Disease Control and Prevention (CDC) for identification. The state laboratory and CDC identify a select agent and notify the sending regional laboratories. The notification of the select agent identification was sent to all sample providers. Both the CDC and the state laboratory submitted a Form 4A Sections A/B.

- **Which laboratory is required to submit APHIS/CDC Form 4A Sections C/D?**

  A) Hospital laboratory only

  B) The two regional laboratories that received the sample

  C) All of the above

  D) No one – nothing else to submit

APHIS/CDC Form 4A – Scenario 1

- Scenario - Split Sample
- Which laboratory is required to submit APHIS/CDC Form 4A Sections C/D?

  C) All of the above – account for each location that is in possession of the sample containing the select agent/toxin upon identification

APHIS/CDC Form 4A – Scenario 2

- **Scenario – Multiple Sample Locations**

  A Principal Investigator is conducting a regional project testing for a select agent. Multiple samples types are collected from multiple locations and tested in batches.

- **How are these samples reported to FSAP?**

  A) One APHIS/CDC Form 4A report for all samples

  B) Multiple APHIS/CDC Form 4A reports for each sample type

  C) Multiple APHIS/CDC Form 4A reports by location

  D) Samples are not reported

Polls are open…Submit your answer now!

APHIS/CDC Form 4A – Scenario 2

- Scenario – Multiple Sample Locations
- How are these samples reported to FSAP?

  C) Multiple APHIS/CDC Form 4A reports by location

APHIS/CDC Form 4A – Scenario 3

- **Scenario – Clostridium botulinum reporting**

  Reference laboratory receives a sample from a patient suspected as having Botulism. They run a mouse bioassay and report to FSAP that they have identified Botulinum neurotoxins. They continue testing and later identify Botulinum neurotoxins producing species of *Clostridium*. The sample provider reports Botulinum neurotoxins producing species of *Clostridium*.

- **How should this identification have been reported?**

  A) Botulinum neurotoxins

  B) Botulinum neurotoxins producing species of *Clostridium*

  C) Both

  D) Neither

Polls are open…Submit your answer now!

APHIS/CDC Form 4A – Scenario 3

- **Scenario – *Clostridium botulinum* reporting**
- **How should this identification be reported?**

  C) Both

APHIS/CDC Form 4A – Scenario 4

- **Scenario**

  A non-registered entity (NRE) has a tissue sample and culture isolates that were identified as containing *Brucella melitensis*. The reference laboratory that identified the select agent later requests that the tissue sample be sent to them for further testing.

- **How should the NRE indicate the sample disposition on the APHIS/CDC Form 4A Sections C/D?**

  A) No need to indicate on the APHIS/CDC Form 4A

  B) Transferred and provide the reference laboratory name and date of the transfer

  C) Not applicable because the entire sample was sent

  D) Transferred and destroyed because the tissue sample will be sent but the culture isolates were destroyed

Polls are open…Submit your answer now!

APHIS/CDC Form 4A – Scenario 4

- **How should the NRE indicate the sample disposition on the APHIS/CDC Form 4A?**

  D) Transferred and destroyed because the tissue sample will be sent but the culture isolates were destroyed