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
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

- Total Form 4A Sections A and B Reported
- Non-registered entities
- Registered entities

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-registered entities</th>
<th>Registered entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>199</td>
<td>1062</td>
</tr>
<tr>
<td>2019</td>
<td>89</td>
<td>1227</td>
</tr>
<tr>
<td>Total</td>
<td>288</td>
<td>2289</td>
</tr>
</tbody>
</table>
APHIS/CDC Form 4A – Total Form 4A Sections C and D Reported

- 2018:
  - Non Registered Entities: 626
  - Registered Entities: 284

- 2019:
  - Non Registered Entities: 491
  - Registered Entities: 134

- Total:
  - Non Registered Entities: 1117
  - Registered Entities: 518
APHIS/CDC Form 4A – Sample Types Reported

<table>
<thead>
<tr>
<th>Sample Types</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal clinical/diagnostic/isolate</td>
<td>385*</td>
<td>621</td>
</tr>
<tr>
<td>Human clinical/diagnostic/isolate</td>
<td>570*</td>
<td>592</td>
</tr>
<tr>
<td>Environmental</td>
<td>41*</td>
<td>64</td>
</tr>
<tr>
<td>Food</td>
<td>10*</td>
<td>25</td>
</tr>
<tr>
<td>Plant clinical/diagnostic</td>
<td>0*</td>
<td>2</td>
</tr>
</tbody>
</table>

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

2018
- Bacillus anthracis: 43
- Botulinum neurotoxin producing species of Clostridium: 69
- Coxiella burnetii: 33
- Eastern Equine Encephalitis virus: 10
- Francisella tularensis: 28

2019
- Bacillus anthracis: 54
- Botulinum neurotoxin producing species of Clostridium: 38
- Coxiella burnetii: 14
- Eastern Equine Encephalitis virus: 10
- Francisella tularensis: 29
### APHIS/CDC Form 4A – Top 3 States Reporting Select Agents on Form 4A A/B for NREs in 2018

<table>
<thead>
<tr>
<th>Highest reported #</th>
<th><em>Coxiella burnetii</em></th>
<th>Eastern Equine Encephalitis virus</th>
<th><em>Francisella tularensis</em></th>
<th><em>Botulinum neurotoxin producing species of Clostridium</em></th>
<th><em>Bacillus anthracis</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#1</strong></td>
<td>Texas</td>
<td>New Jersey</td>
<td>Wyoming</td>
<td>Pennsylvania</td>
<td>South Dakota</td>
</tr>
<tr>
<td><strong>#2</strong></td>
<td>Wisconsin</td>
<td>Louisiana</td>
<td>California/Washington</td>
<td>Michigan</td>
<td>Texas</td>
</tr>
<tr>
<td><strong>#3</strong></td>
<td>Wyoming/New York</td>
<td>North Carolina</td>
<td>Kansas</td>
<td>North Carolina/Florida</td>
<td>Wyoming/Wisconsin</td>
</tr>
</tbody>
</table>
### APHIS/CDC Form 4A – Top 3 States Reporting Select Agents on Form 4A A/B for NREs in 2019

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<thead>
<tr>
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<th><em>Botulinum neurotoxin producing species of Clostridium</em></th>
<th><em>Francisella tularensis</em></th>
<th><em>Bacillus anthracis</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#1</strong></td>
<td>Wisconsin</td>
<td>Louisiana</td>
<td>Pennsylvania</td>
<td>California</td>
<td>Texas</td>
</tr>
<tr>
<td><strong>#2</strong></td>
<td>Texas</td>
<td>Michigan</td>
<td>Michigan</td>
<td>Wyoming/ Illinois/ South Dakota</td>
<td>North Dakota</td>
</tr>
<tr>
<td><strong>#3</strong></td>
<td>Indiana</td>
<td>Wisconsin</td>
<td>N/A</td>
<td>North Dakota/ New Mexico/ Delaware/ Washington</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### APHIS/CDC Form 4A Overview – Sections A and B – Reference Laboratory

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

<table>
<thead>
<tr>
<th>Section B – Select Agent or Toxin Identified from Clinical/Diagnostic Specimen(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Select Agent or Toxin Identified:</td>
</tr>
<tr>
<td>3. Case/patient/sample ID(s):</td>
</tr>
<tr>
<td>6. Case/patient origin (zip code):</td>
</tr>
<tr>
<td>7. Type of test performed (e.g., PCR, mouse bioassay, ELISA):</td>
</tr>
<tr>
<td>8. Dispositions of select agent or toxin by entity listed in Block A9 (complete all that apply):</td>
</tr>
<tr>
<td>- Transferred (Provide entity name and date of transfer. Entity: __________________________ Date: ____________):</td>
</tr>
<tr>
<td>- Destroyed (Provide destruction method and date. Method: __________________________ Date: ____________):</td>
</tr>
<tr>
<td>- Retained (Provide name of Clinical Investigator retaining sample. Name: __________________________):</td>
</tr>
<tr>
<td>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?</td>
</tr>
<tr>
<td>- No</td>
</tr>
<tr>
<td>10. Do you anticipate receiving additional sample/specimens for this case/patient that originate from the initial case (e.g., patient, environmental sample)?</td>
</tr>
<tr>
<td>- No</td>
</tr>
<tr>
<td>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?</td>
</tr>
<tr>
<td>- No</td>
</tr>
<tr>
<td>12. Sample Provider Entity Name:</td>
</tr>
<tr>
<td>13. Sample Provider Point of Contact: First: __________________________ Last: __________________________</td>
</tr>
<tr>
<td>14. Sample Provider E-mail Address:</td>
</tr>
<tr>
<td>15. Sample Provider Contact Number:</td>
</tr>
<tr>
<td>16. Comments / Notes:</td>
</tr>
</tbody>
</table>
### APHIS/CDC Form 4A Overview – Section C – Sample Provider Information

- **Sample Provider Information**

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

**SECTION C – SAMPLE PROVIDER INFORMATION**

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

<table>
<thead>
<tr>
<th>1. Select Agent or Toxin Identified:</th>
<th>2. Date notified of select agent or toxin identification:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Case/patient/sample ID #(#s):</td>
<td>4. # of samples shipped:</td>
</tr>
<tr>
<td>5. Sample type provided:</td>
<td>6. Case/patient/sample origin (zip code):</td>
</tr>
<tr>
<td>7. Date sample(s) shipped to Reference Laboratory:</td>
<td>8. Name of Reference Laboratory:</td>
</tr>
<tr>
<td>9. Disposition of any remaining select agent or toxin by entity listed in Block C9:</td>
<td></td>
</tr>
<tr>
<td>□ Destroyed (Provide destruction method and date. Method: __________________ Date: ____________)</td>
<td></td>
</tr>
<tr>
<td>□ Retained (Provide name of Principal Investigator retaining sample. Name: __________________)</td>
<td></td>
</tr>
<tr>
<td>□ Not applicable, the entire specimen was transferred to the Reference Laboratory.</td>
<td></td>
</tr>
<tr>
<td>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 to the select agent or toxin?</td>
<td></td>
</tr>
<tr>
<td>□ No  □ Yes. (If Yes, are you required under 7 CFR §331.19, 9 CFR §121.18, and 42 CFR §73.19 to complete and submit an APHIS/CDC Form 3)</td>
<td></td>
</tr>
<tr>
<td>11. Was your entity the source of the sample(s)? □ No □ Yes (If Yes, skip to field 18)</td>
<td></td>
</tr>
<tr>
<td>12. Do you anticipate receiving additional samples/specimens for this case/patient that originate from the initial case (e.g., patient, environmental sample)?</td>
<td></td>
</tr>
<tr>
<td>□ No □ Yes (If Yes, please refer to the guidance instructions at <a href="http://www.selectagents.gov">www.selectagents.gov</a> for further directions.)</td>
<td></td>
</tr>
<tr>
<td>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</td>
<td></td>
</tr>
<tr>
<td>NOTE: Please request completed and signed Sections C &amp; D from each facility that was in possession of the specimen(s).</td>
<td></td>
</tr>
<tr>
<td>14. Sample Provider Entity Name:</td>
<td></td>
</tr>
<tr>
<td>15. Sample Provider Point of Contact:</td>
<td>16. Sample Provider E-mail Address:</td>
</tr>
<tr>
<td>First:</td>
<td>Last:</td>
</tr>
<tr>
<td>18. Comments / Notes:</td>
<td></td>
</tr>
</tbody>
</table>
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)
International sample providers

- International entities do NOT need to report
- Reference laboratory completes sample provider questions (#B12-16)
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
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
**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
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
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!
Scenario – Multiple Sample Locations

How are these samples reported to FSAP?

C) Multiple APHIS/CDC Form 4A reports by location
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!*
Scenario – *Clostridium botulinum* reporting

How should this identification be reported?

C) Both
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!*
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