Reporting the Identification of a Select Agent or Toxin in a Clinical or Diagnostic Laboratory:
Revised APHIS/CDC Form 4

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The Animal and Plant Health Inspection Service (APHIS) and the Centers for Disease Control and Prevention (CDC) recently revised the form for reporting the identification of a select agent or toxin from clinical specimens [Form 4, Reporting of the Identification of a Select Agent or Toxin, Exp 12/13/2008]. Major changes were made to simplify the reporting process. Guidance is given below to help laboratories fill out and submit this new form.

Section 1A (To be completed by all)

1. **Legal name of entity**. The legal entity refers to the reporting laboratory's official name.
2. **Entity registration number**. This number is recorded by the Nebraska Public Health Laboratory (NPHL), while all other laboratories record "Not applicable".

3-7. **Address.** This is self explanatory.

7-11. **Responsible official (RO) or facility director, title, telephone, fax, and e-mail.** This is generally the Laboratory Director but it may also be another responsible person such as the Medical Director or Biosafety Officer.

12-15. **Address of RO or facility director.** This is self explanatory.

Section 1B (Leave Blank)

16-24. **Name of federal law enforcement agent.** To be completed by a federal law enforcement agency when appropriate.

Section 2 (To be completed by all)

25. **Select agent or toxin being reported.** Include a scientific name.
26. **Date(s) agent was identified.** This can be recorded as the "date for notification of final result" for those laboratories submitting a clinical specimen or isolate to a reference lab for testing, or the date of identification for those laboratories doing confirmation testing.
27. **Agent ID number.** Record the specimen accession number or whichever number is used to identify the specimen/agent.
28. **Total quantity of select agent or toxin identified.** Record quantity if an environmental sample is tested otherwise record as, "Not applicable".
29. C**haracterization of select agent or toxin.** For laboratories submitting a specimen to a reference laboratory without testing, indicate the following: "Specimen submitted to [list the laboratory] for isolation and/or confirmation". For laboratories submitting an isolate to a reference laboratory for confirmation testing, indicate the following: "Isolate presumptively identified as [give presumptive ID] using the following characteristics [list the methods used] was submitted to [list the laboratory] for confirmation testing". For laboratories performing confirmation testing indicate the following: "Confirmation of species identification performed using the following criteria: [list the criteria used]". Attach additional sheets if necessary.
30. **Type of specimen.** For all laboratories handling the original specimen, check "Clinical/diagnostic sample". Check "Environmental sample" if from the environment or "Isolate" if the laboratory received an isolate for confirmation testing. Indicate "Other" for situations that do not meet criteria for the other categories and specify the sample type.
31. **Specimen type.** For laboratories handling the original specimen, indicate whether the sample is a "Fluid" or "Tissue" and specify sample type. Check "Isolate" if applicable or "Other" for situations not listed and then specify the specimen type.
32. **Source of sample.** In most cases the sample will be "Human", but it may also represent other sources as described.
33. **Is the source expected to provide additional specimens?** Usually check "No" or "Unknown". If additional specimens are expected, check "Yes" and give anticipated quantity and end date.
34. **Location where laboratory testing was conducted.** If no testing was done, list as "Not applicable", otherwise list the building and room where testing was performed.
35. **Biosafety level of laboratory.** For laboratories sending a specimen to a reference laboratory without testing, record as "Not applicable". For laboratories performing tests on the specimen and/or the isolate, list either BSL-2 or BSL-3 depending on the containment of the laboratory used.

36. **Was select agent or toxin isolated under conditions prescribed by the BMBL?** Generally answer as "Yes". Specimens can be handled under BSL-2 conditions while an identified isolate may require BSL-3 conditions where appropriate. In unusual circumstances where exposure to a select agent in culture may have occurred, indicate "No" and describe whether the appropriate medical surveillance has been instituted according to laboratory protocol.

37. **Has the sender of the sample been notified of the identification of the select agent or toxin?** Indicate "Yes". Laboratories performing confirmation testing should routinely notify the submitting laboratory of the identification of a select agent or toxin.

38-43. **Name of the entity that sent sample.** For laboratories who received the original specimen, indicate, "Not applicable". For reference laboratories who received the specimen or isolate from another facility, indicate the sending facility legal name and record the sender's telephone number and address.

44-48. **Name of RO or facility director for the sending entity.** Only fill out this section if different than Section 1. This could be the supervisor or medical director of the laboratory handling the original specimen.

49-50. **Name of treating physician, veterinarian, botanist, or person most familiar with the case and telephone number.** Normally this is the primary care physician of the patient from whom the specimen was obtained.

51. **If more than one case.** Generally this will be listed as "Not applicable" however, when multiple cases are involved, describe the date of the index case, the number of cases, and the inclusive reporting dates if known.

Section 3 (Leave blank)

52-58. This section is completed for select agents or toxins identified from proficiency testing. Contact personnel at the NPHL for advice on filling out this information when needed.

Section 4 (To be completed by all)

59. **Deposition of select agent or toxin.** The laboratory that receives the specimen for culture and subsequently sends an isolate for confirmation testing to a laboratory other than the NPHL or the laboratory that has done in-house confirmation testing should check "Transferred" and then call the NPHL personnel to make arrangements for transfer of the identified isolate [an APHIS/CDC Form 2 will need to be processed in consultation with personnel at NPHL]. **NOTE: NO TRANSFER IS TO OCCUR UNTIL FORM 2 HAS BEEN PROCESSED AND AN AUTHORIZATION NUMBER HAS BEEN ISSUED BY THE CDC.** The laboratory that receives a specimen for culture and subsequently sends a suspicious isolate for confirmation testing to the NPHL should check, "Destroyed on site" and indicate date specimen and culture material are destroyed and the method of destruction. A laboratory that receives an isolate for confirmation testing that is subsequently retained after confirmation should check, "Retained" and then give the name of the Principal Investigator and the date the select agent or toxin was transferred [only registered laboratories such as the NPHL can retain these isolates]. The laboratory that submits a specimen to a reference laboratory for testing should indicate "Other, Specimen submitted to reference laboratory for culture and confirmation testing".

60. **Signature**. The Laboratory Director or other individual as indicated in Section 1 of the form if generally the individual who signs the form however, it may be another person who can certify that the information provided is true and correct to the best of their knowledge.

When questions occur, please do not hesitate to contact personnel at the NPHL or Dr. Iwen at 402-559-7774 for additional information.

Table 1. Which laboratories must complete and submit the APHIS/CDC Form 4?[a,b]

Laboratories who:

- Handle the original specimen that contained a viable select agent or toxin prior to submission to a reference laboratory for testing.
- Conduct the initial plating of the specimen but submit the suspect isolate to reference laboratory for confirmation testing.
- Conduct the initial plating of the specimen and perform confirmation testing.[c,d]
- Confirm the identification following isolate submission[c,d,e](Select agent confirmation is performed at the NPHL in most circumstances)

[a]In many instances, multiple laboratories may handled a specimen or isolate containing a select agent or toxin which thus requires multiple submissions of Form 4.

[b]The laboratory handling serum from a patient who ultimately is confirmed as positive for a select agent-caused disease by serological testing does not need to file Form 4. However, they are still responsible for reporting immediately the result to the county or State Health Department.

[c]The laboratory performing confirmation testing is responsible to contact the CDC for those agents that require immediate reporting (telephone 404-498-2255, facsimile 404-498-2265, or e-mail [Irsat@cdc.gov]).

[d]Agents that require immediate reporting to the CDC are listed in the instructions for Form 4.

[e]The UNMC/NPHL Special Pathogens Laboratory has the reagents and protocols available to confirm the identification of a

Table 2. Checklist to report a select agent or toxin after diagnosis and verification.

- Report immediately to the CDC by telephone, facsimile, or e-mail when required.[a] **Note:** Only for laboratories performing confirmation testing.
- Report immediately to the county or to the Nebraska State Health Department.
- Dispose of the select agent or toxin to include specimen and cultured material[b,c] **Note:** Either by transfer to the NPHL or by onsite destruction.
- Obtain a copy of the APHIS/CDC Form 4 from the CDC web site.[d]
- Complete Sections 1A, 2, and 4 and sign/date form.
- Make 3 copies of the completed form.
- Send the original Form 4 to the CDC, one copy to the NPHL, and one copy is retained by the laboratory for three years.[e]

[a]The instructions to the APHIS/CDC Form 4 lists those agents that require immediate reporting to the CDC (telephone, 404-498-2255; facsimile, 404-498-2265; or e-mail at Irasat@cdc.gov)

[b]Only laboratories registered by the Select Agent Program may retain materials containing a known select agent or toxin.

[c]A subculture of a select agent identified by a reference laboratory other than the NPHL should be sent to the NPHL for banking. **Transfer of a known select agent or toxin will require additional paperwork. Personnel at the NPHL will coordinate this transfer.**

[d]Refer to the CDC website at http://www.selectagents.gov/cdForm.htm to obtain Form 4.

[e]Send the completed form to the CDC at the Centers for Disease Control and Prevention, Division of Select Agents and Toxins, 1600 Clifton Road NE, Mailstop E-79, Atlanta, GA 30333.