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Memorandum

Date: August 25, 2014

From: Deputy Chief Research and Development Officer
VHA Office of Research and Development (ORD), (10R), Washington, DC

Executive Director
VHA Office of Research Oversight (ORO), (10R), Washington, DC

Subj: Research Safety Stand-Down

To: Network Directors
Facility Directors
Associate Chiefs of Staff for Research and Development

1. The White House issued a memorandum on August 18, 2014, directing a governmentwide "safety stand-down" in response to several recent biosafety and biosecurity incidents involving federal research laboratories. The VA is a partner in this effort, and will be conducting a research safety stand-down that includes two components: (1) verification there are no unregistered biological select agents or toxins (BSATs) in VA research areas, and (2) a review of current VA policies related to research safety and laboratory security to ensure they reflect current best practices.

2. To meet these objectives, the Office of Research and Development (ORD) and the Office of Research Oversight (ORO) have developed a plan to conduct a survey of all VA research areas to verify that there are no previously unidentified or unregistered BSATs. Instructions and forms to guide VA research program staff in conducting these surveys are attached. The Associate Chief of Staff for Research and Development (ACOS/R&D) must submit an institutional attestation verifying completion of the research survey to AskORO@va.gov by September 24, 2014.

3. We have also initiated dialogue with representatives from several VA research programs to discuss current VHA policies related to research safety and laboratory security and to identify areas for improvement. All VA research programs are encouraged to contribute ideas and suggestions to guide this process, and may submit comments or questions by email to AskORO@va.gov .

4. We understand that launching this initiative will require time, patience, and creative thinking from many individuals, and thank you for your cooperation and contributions to this effort. We also look forward to sharing more information and updates on the progress that is being made in the coming weeks and months.

holly.birdsall@va.gov
Digitally signed by holly.birdsall@va.gov
DN: cn=holly.birdsall@va.gov
Date: 2014.08.25 11:25:19 -04'00'

Holly Birdsall, MD, PhD
ORD Deputy Chief Research and Development Officer

John T. Puglisi 104858
Digitally signed by John T. Puglisi 104858
DN: dc=gov, dc=va, o=internal, ou=people, 0.9.2342.19200300.100.1.1=tom.puglisi@va.gov, cn=John T. Puglisi 104858
Date: 2014.08.25 11:27:56 -04'00'

Tom Puglisi, PhD
ORO Executive Director

BSAT Survey Instructions

Instructions for Surveying VA Research Areas for Unidentified Biological Select Agents and Toxins

1. Recent biosafety and biosecurity lapses in research laboratories at the CDC, NIH, and FDA have prompted an inter-agency initiative to verify that all regulated biological select agents and toxins (BSATs) in federal research laboratories are appropriately registered and securely maintained.

2. The VA is a partner in this effort, and all VA research programs are required to conduct an assessment of the research laboratories and associated storage areas[1] at their institution to verify there are no unidentified and/or unsecured BSATs present.

3. The process will involve individual Principal Investigators (PI) and/or Laboratory Directors (LD) surveying the areas under their responsibility, and signing an attestation that no BSATs have been found or that all BSATs are properly identified, registered, and secured. The scope of this survey includes all regulated BSATs (Attachment 1 and also found at List of Select Agents and Toxins). **Exempt quantities of select toxins are excluded.**

   a. A risk-based approach can be used to determine the survey methods used.

   b. Some laboratories are at higher risk and will require a complete, comprehensive assessment of all biological materials that are present. These include:

      (1) Laboratories that have been used for research involving BSATs, including research that was initiated prior to implementation of the Select Agent regulations in October 2001.

      (2) Laboratories and/or storage areas that were transferred to the PI/LD without being properly cleaned out and/or decommissioned by the previous occupants.

      (3) Laboratories that include biological materials that are not clearly identified or for which responsibility cannot be traced to a specific individual still associated with the research program at your institution.

      (4) Laboratories and storage areas that are used by multiple researchers, and are not under the responsibility of a specific individual.

   c. At the discretion of the ACOS/R&D, targeted or abbreviated surveys may be considered for laboratories which have been continuously occupied by the same PIs/LDs since the BSAT regulations were implemented or for laboratories that have implemented an inventory system for biological materials that are used and/or stored. In these situations, a random survey may be substituted for a comprehensive (100%) survey.

4. Any individual that discovers any previously unidentified BSATs during this process is required to notify the ACOS/R&D, or equivalent individual, at their institution the same day.

   a. The institution must register, transfer, or dispose of the materials within 7 days of discovery. The process must be documented.

   b. BSATs can only be transferred to institutions that are authorized to possess, transfer, and/or use BSATs and registered with CDC and/or USDA. Prior approval must be obtained from the CRADO for VA research programs to be registered.

   c. Disposal of BSATs must be coordinated with the facility safety staff, through the ACOS/R&D, and witnessed. BSATs will be transferred to facility safety staff for disposal as medical pathological waste using Lab Packs. All transfers and disposal will be recorded on a manifest

[1] Storage areas include cabinets, shelves, drawers, incubators, freezers (all types), refrigerators, and/or cold rooms.

that documents the materials' chain of custody from identification through incineration. Associated records are considered research records, and must be retained accordingly.

d. The ACOS/R&D will notify the Office of Research Oversight, Research Safety and Animal Welfare Team (oroask@va.gov) within 24 hours of discovery if previously unidentified BSATs are found during local surveys. An optional reporting template is provided (Attachment 2).

5. While conducting this survey, PIs/LDs should also verify that biological materials maintained in all research areas are appropriately identified and labeled. Unidentified samples include those without labels and/or labeled samples that do not have sufficient information to clearly identify the contents. Samples that cannot be accurately identified and/or have no intended use can be significant liabilities to the institution, and researchers should be encouraged to use the "sweep" as an opportunity to collect and appropriately dispose of these materials.

6. An attestation must be completed for every laboratory, equipment room, and storage area used for research activities, including any space that is leased to an outside entity. The ACOS/R&D must assign qualified individual(s) to take responsibility for surveying all shared laboratories, equipment rooms, and storage areas and/or space that is leased to outside entities.

7. Upon completion of the laboratory survey, each PI/LD must sign an attestation to document that no BSATs were found, or that any previously unidentified BSATs have been properly reported (Attachment 3). The completed survey must be provided to the ACOS/R&D at each institution as directed.

8. The ACOS/R&D is responsible for collecting attestations and ensuring all research areas have been surveyed at their institution. The ACOS/R&D may include the local research safety oversight subcommittee in the verification process. A signed attestation on their institution's behalf must be submitted to the Office of Research Oversight – Research Safety and Animal Welfare Team (oroask@va.gov), with copies provided to the Facility Director and the VISN Director by **September 24, 2014** (Attachment 4).

9. Laboratories may be subject to random checks to independently verify the accuracy of the attestation that is provided. Any individual signing an attestation is accountable for the accuracy of the information provided, and can be subject to disciplinary and/or criminal action if the information provided is determined to be intentionally false or misleading.

10. Questions regarding this survey should be directed to Office of Research Oversight, Research Safety and Animal Welfare Team (oroask@va.gov).

Attachment 1: Select Agents and Toxins List

HHS AND USDA SELECT AGENTS AND TOXINS
7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73

HHS SELECT AGENTS AND TOXINS

Abrin
Botulinum neurotoxins*
Botulinum neurotoxin producing species of *Clostridium**
Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$)[1]
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus[3]
Ebola virus*
*Francisella tularensis**
Lassa fever virus
Lujo virus
Marburg virus*
Monkeypox virus[3]
Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)
Ricin
Rickettsia prowazekii
SARS-associated coronavirus (SARS-CoV)
Saxitoxin
South American Haemorrhagic Fever viruses:
- Chapare
- Guanarito
- Junin
- Machupo
- Sabia

Staphylococcal enterotoxins A,B,C,D,E subtypes
T-2 toxin
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses:
- Far Eastern subtype
- Siberian subtype

Kyasanur Forest disease virus
Omsk hemorrhagic fever virus
Variola major virus (Smallpox virus)*
Variola minor virus (Alastrim)*
*Yersinia pestis**

OVERLAP SELECT AGENTS AND TOXINS

Bacillus anthracis *
Bacillus anthracis Pasteur strain
Brucella abortus
Brucella melitensis
Brucella suis
*Burkholderia mallei**
*Burkholderia pseudomallei**
Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan equine encephalitis virus[3]

USDA SELECT AGENTS AND TOXINS

African horse sickness virus
African swine fever virus
Avian influenza virus[3]
Classical swine fever virus
Foot-and-mouth disease virus*
Goat pox virus
Lumpy skin disease virus
Mycoplasma capricolum[3]
Mycoplasma mycoides[3]
Newcastle disease virus[2,3]
Peste des petits ruminants virus
Rinderpest virus*
Sheep pox virus
Swine vesicular disease virus

USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS

Peronosclerospora philippinensis (Peronosclerospora sacchari)
Phoma glycinicola (formerly Pyrenochaeta glycines)
Ralstonia solanacearum
Rathayibacter toxicus
Sclerophthora rayssiae
Synchytrium endobioticum
Xanthomonas oryzae

*Denotes Tier 1 Agent

[1] C = Cysteine residues are all present as disulfides, with the 1st and 3rd Cysteine, and the 2nd and 4th Cysteine forming specific disulfide bridges; The consensus sequence includes known toxins α-MI and α-GI (shown above) as well as α-GIA, Ac1.1a, α-CnIA, α-CnIB; X1 = any amino acid(s) or Des-X; X2 = Asparagine or Histidine; P = Proline; A = Alanine; G = Glycine; X3 = Arginine or Lysine; X4 = Asparagine, Histidine, Lysine, Arginine, Tyrosine, Phenylalanine or Tryptophan; X5 = Tyrosine, Phenylalanine, or Tryptophan; X6 = Serine, Threonine, Glutamate, Aspartate, Glutamine, or Asparagine; X7 = Any amino acid(s) or Des X and; "Des X" = "an amino acid does not have to be present at this position." For example if a peptide sequence were XCCHPA then the related peptide CCHPA would be designated as Des-X.

[2] A virulent Newcastle disease virus (avian paramyxovirus serotype 2) has an intracerebral pathogenicity index in day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

[3] Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus , west African clade of Monkeypox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies Mycoplasma capricolum except subspecies capripneumoniae (contagious caprine pleuropneumonia), all subspecies Mycoplasma mycoides except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, and Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3, provided that the individual or entity can verify that the agent is within the exclusion category.

Attachment 2: BSAT Reporting Template

Report of Discovery of Previously Unidentified Biological Select Agent and/or Toxin (BSAT)

Facility Name:	
City, State:	
Date of Report:	
Reported by:	
Name of BSAT:	
Quantity:	
Date Found:	
Date SRS Notified:	
Date ACOS/R&D Notified:	
Give the location that the BSAT was found. Include the building identification, room number, and specific storage area (i.e., cabinet, shelf, drawer, incubator, freezer, refrigerator, or cold room).	
Describe the condition of the primary container and storage area used to store the BSAT.	
Provide the name(s) of individual(s) responsible for the location where the BSAT was found.	
Provide the name(s) of the individual(s) who possessed, used, or transferred the BSAT.	
When was the BSAT last used, and for what purpose?	
What was the disposition of the BSAT (include relevant dates)?	

The completed form must be submitted electronically as a PDF file to the Office of Research Oversight – Research Safety and Animal Welfare Team (oroask@va.gov) within 24 hours of the BSAT discovery. The Facility Director and VISN Director must be copied on the submission.

Attachment 3: VA PI or Laboratory Director Attestation Form

BIOLOGICAL MATERIAL SURVEY ATTESTATION

For all VA Principal Investigators, Laboratory Directors, and other Individuals
Assigned to Survey Specific Research Areas

This form must be completed by every Principal Investigator and/or Laboratory Director conducting VA research. VA research includes research conducted by VA investigators [serving on compensated, work without compensation (WOC), or Intergovernmental Personnel Agreement (IPA) appointments] while on VA time, utilizing VA resources (e.g. equipment), or on VA property including space leased to, or used by VA. The research may be funded by VA, by other sponsors, or be unfunded.

1. I currently possess or previously have possessed, used, and/or transferred Biological Select Agents and Toxins (BSATs) that are listed on the attached document:

   ☐ YES ☐ NO

2. If I answered "Yes" to Question No. 1, all the BSATs that I possess, use, and/or transfer have been registered with the appropriate oversight entities:

   ☐ YES ☐ NO ☐ None Possessed, Used, or Transferred

   If you answered "NO," please attach a supplemental sheet explaining your response.

3. I have surveyed my research laboratory, its contents and all associated freezers (including those used for off-site storage), refrigerators, cold rooms, and storage areas for BSATs:

   ☐ YES ☐ NO Date of Survey:

   A list of the rooms and/or storage areas that I have surveyed is attached to this attestation.

4. I attest that I did not find, and do not have, any unregistered and/or improperly secured BSATs.

   ☐ YES ☐ NO

   If you answered "NO," please attach a supplemental sheet explaining your response.

5. Any unregistered BSATs and/or BSATs stored in non-registered areas, which were found during the survey of my research laboratory and its contents, were immediately reported to the ACOS/R&D and research safety and/or biosafety subcommittee at my institution and properly registered, transferred, and/or disposed.

   ☐ YES ☐ NO ☐ None Found

By signing this document, I understand that my inventory or survey will be subject to independent verification, and that I am personally accountable for the accuracy of the information on this attestation. Criminal prosecution could result if the information submitted is intentionally false or misleading.

Please print your name legibly in the space below, then sign (digitally or manually) and date the form.

Signature _____ Date _____

The completed form must be submitted electronically as a PDF file, or as a hard copy, to the Associate Chief of Staff for Research and Development at your Institution as directed.

Attachment 4: VA ACOS or Research Leader Attestation Form

BIOLOGICAL MATERIAL SURVEY ATTESTATION

For all VA Associate Chiefs of Staff for Research and Development or Their Equivalents

This form must be completed by every Associate Chief of Staff for Research and Development (ACOS/R&D) or other individual(s) with equivalent responsibility for the management and administration of a VA research program. VA research includes research conducted by VA investigators [serving on compensated, work without compensation (WOC), or Intergovernmental Personnel Agreement (IPA) appointments] while on VA time, utilizing VA resources (e.g. equipment), or on VA property including space leased to, or used by VA. The research may be funded by VA, by other sponsors, or be unfunded.

1. My institution has research activities that involve possession, use, and/or transfer of Biological Select Agents and Toxins (BSATs) that are listed on the attached document:

   ☐ YES ☐ NO

2. If I answered "Yes" to Question No. 1, all the BSATs that are possessed, used, and/or transferred for research purposes have been registered with the appropriate oversight entities:

   ☐ YES ☐ NO ☐ None Possessed, Used, or Transferred

   If you answered "NO," please attach a supplemental sheet explaining your response.

3. I attest that all research laboratories, contents and all associated freezers, refrigerators, cold rooms, and storage areas have been surveyed for BSATs:

   ☐ YES ☐ NO

4. I attest that the institution's research program does not have any unregistered BSATs.

   ☐ YES ☐ NO

   If you answered "NO," please attach a supplemental sheet explaining your response.

5. Any unregistered BSATs and/or BSATs stored in non-registered areas, which were found during the survey of my institution's research laboratories and contents, were immediately reported and properly transferred and/or disposed.

   ☐ YES ☐ NO ☐ None Found

By signing this document, I understand that the inventories and surveys at my institution will be subject to independent verification, and that I am accountable for the accuracy of the information on this attestation. Criminal prosecution could result if the information submitted is intentionally false or misleading.

Please print your name legibly in the space below, then sign (digitally or manually) and date the form.

Signature _____ Date _____

The completed form must be submitted electronically as a PDF file to the Office of Research Oversight – Research Safety and Animal Welfare Team (oroask@va.gov) by **September 24, 2014**.
The Facility Director and VISN Director must be copied on the submission.