Doc 13

USDA

United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

National Import Export Services

Agriculture Select Agent Services

4700 River Road, Mailstop 22, Unit 2, Room 1A-07
Riverdale, MD 20737

(301) 851-3300, opt. 3
FAX (301) 734-3652
www.selectagents.gov

May 5, 2014

[redacted]
Responsible Official
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mail Stop A-22
Atlanta, Georgia 30333

Dear [redacted]

The Animal and Plant Health Inspection Service (APHIS), Agricultural Select Agent Services (AgSAS) and the Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT) conducted an APHIS-Led CDC joint renewal inspection March 3, 2014 to March 12, 2014 at the Centers for Disease Control and Prevention. DSAT has completed the review of the inspection and requires additional information from you. Please see the attached DSAT letter and provide a response to DSAT no later than 14 calendar days from receipt of this letter.

If there are any questions or concerns in reference to this correspondence please contact [redacted] at [redacted] with the Centers for Disease Control and Prevention, Division of Select Agents and Toxins.

Sincerely,

[redacted]
Staff Veterinary Medical Officer
Agricultural Select Agent Services

Department of Health and Human Services
Centers for Disease Control and Prevention
Division of Select Agents and Toxins
Atlanta, Georgia

U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Agriculture Select Agent Services
Riverdale, Maryland

May 05, 2014

[redacted] (Responsible Official)
Centers for Disease Control and Prevention
1600 Clifton Road, NE, Mailstop A-22
Atlanta, GA 30333
FAX: (404) 639-0437

RE: Entity Inspection Report: Centers for Disease Control and Prevention

Pursuant to the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) have established regulatory requirements for the possession, use, and transfer of biological agents and toxins that have the potential to pose a severe threat to public health and safety, animal and plant health, and animal and plant products. These requirements can be found at 42 CFR Part 73 (HHS), 7 CFR Part 331 (USDA-PPQ), and 9 CFR Part 121 (USDA-VS). The Centers for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins (DSAT) inspects entities to evaluate whether they meet the regulatory requirements set forth in 42 CFR Part 73, and the Animal and Plant Health Inspection Service (APHIS) Agriculture Select Agent Services (AgSAS) inspects entities to evaluate whether they meet the regulatory requirements set forth in 7 CFR Part 331 and 9 CFR Part 121. The above referenced regulations and supporting guidance information may be found at http://www.selectagents.gov/.

AgSAS and DSAT inspectors visited your facility located at 1600 Clifton Road, NE, Mailstop A-22 Atlanta, GA 30333 from March 03, 2014 to March 12, 2014. A list of laboratories inspected on these dates is on file with this letter at APHIS.

The following personnel from the APHIS Agriculture Select Agent Services inspected the facility:

[redacted] Lead Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector
[redacted] Inspector

Individuals from Centers for Disease Control and Prevention present during the inspection included:

[redacted] Technician, Animal Resources Branch
[redacted] Microbiologist
[redacted] Branch Chief, SMB
[redacted] Team Lead TSO
[redacted] Veterinary Medical Officer
[redacted] Microbiologist
[redacted] Biologist
[redacted] System Engineer
[redacted] ARO
[redacted] Biologist

[redacted] Biologist
[redacted] Animal Health Technician
[redacted] Team Lead
[redacted] Supervisory Microbiologist
[redacted] Technician, Animal Resources Branch
[redacted] Team Lead, BRRAT Lab
[redacted] Deputy Project Manager, Goodwill
[redacted] Branch Chief, LPRB
[redacted] Biosafety Team Lead
[redacted] Associate, LPRB
[redacted] Supply Management Specialist
[redacted] Biosafety Officer
[redacted] RO
[redacted] Microbiologist
[redacted] Associate Service Fellow
[redacted] Branch Chief
[redacted] ESHCO
[redacted] Chief, Pathogen Biology and Ecology
[redacted] Microbiologist
[redacted] Biologist
[redacted] Assistant to Director, EMOSO
[redacted] Team Lead
[redacted] PI Viral Special Pathogens Branch
[redacted] Microbiologist
[redacted] ASM Fellow
[redacted] Team Lead, Viral Special Pathogens Branch
[redacted] Research Biologist
[redacted] Team Leader, SEA
[redacted] Microbiologist
[redacted] Controls Engineer
[redacted] ARO

During the inspection, departures from regulatory requirements cited above were noted. Please address each of the items described in Attachment 1 (List of Entity Departures) and include in your response the specific actions or changes to be adopted to correct these departures. A detailed response should be received by this office not later than 14 calendar days from receipt of this letter. An electronic copy of your response should be sent to the lead inspector. Failure to fully respond may result in the initiation of proceedings for the withdrawal of your facility registration to possess, use, or transfer select agents and toxins.

If you have any questions concerning this correspondence please contact APHIS Representative at [redacted] option 3.

Sincerely,

[redacted]
Director, Division of Select Agents and Toxins
Department of Health and Human Services
Centers for Disease Control and Prevention

[redacted]
National Director, Agriculture Select Agent Services
United States Department of Agriculture
Animal and Plant Health Inspection Service

Attachment: 1:
List of Entity Departures

Attachment 1: Entity Departures

Departures noted from March 03, 2014 to March 12, 2014 at Centers for Disease Control and Prevention (citations from 42 CFR Part 73 specifying each requirement are given in brackets).

1 **Requirement:** The security plan must be designed according to a site-specific risk assessment and must provide graded protection in accordance with the risk of the select agent or toxin, given its intended use. [Section 11(b)]

Observation: Principal Investigator (PI) [redacted] provided a current security plan dated April 2013; however, areas designated for laboratory-specific information were left blank. Please provide a completed copy of the security plan that applies to PI [redacted] laboratory and contains laboratory specific security information.

2 **Requirement:** An individual or entity must adhere to the following security requirements or implement measures to achieve an equivalent or greater level of security: allow access only to individuals with access approval from the HHS Secretary or Administrator. [Section 11(d)(1)]

Observation: Manual visitor access records for the [redacted] Suite registered for [redacted] and [redacted] and kept in the anteroom, indicate entry by [redacted] and [redacted] representing JCI, on 8/15/2011. No escort was indicated on the access record, and the purpose of entry was recorded as "access control." According to the Responsible Official (RO), [redacted] is [redacted] who was SRA approved on 5/6/2008, removed with Amendment 114388 (approved 12/30/2008), and reactivated with Amendment 211560 (SRA approved 8/2/2013). There is no record of [redacted] being SRA approved on your entity's registration. At the time of entry in 2011, neither of these individuals was SRA approved. Please describe the measures implemented to ensure that only individuals with access approval from the HHS Secretary or Administrator are allowed access to select agents and toxins.

3 **Requirement:** In addition to the requirements contained in paragraphs (c) and (d) of this section, the security plan for an individual or entity possessing a Tier 1 select agent or toxin must also: describe procedures for conducting a pre-access suitability assessment of persons who will have access to a Tier 1 select agent or toxin. [Section 11(f)(1)]

Observation: The Suitability Assessment Guidance for CDC Tier 1 Biological Select Agents and Toxins, under Pre-Access Suitability of Contractors (p. 10) states "in progress". Inspectors were informed that contract personnel, provided initial access to Tier 1 select agents and toxins after the date this requirement became effective, will now undergo an assessment for pre-access suitability. Please provide the updated section of the Suitability Assessment Guidance for CDC Tier 1 Biological Select Agents and Toxins that reflects this change.

4 **Requirement:** In addition to the requirements contained in paragraphs (c) and (d) of this section, the security plan for an individual or entity possessing a Tier 1 select agent or toxin must also: describe procedures for the ongoing assessment of the suitability of personnel with access to a Tier 1 select agent or toxin. The procedures must include: the ongoing suitability monitoring of individuals with access to Tier 1 select agents and toxins. [Section 11(f)(3)(iii)]

Observation: The Suitability Assessment Guidance for CDC Tier 1 Biological Select Agents and Toxins, page 11, states that self-evaluations using the CDC Tier 1 BSAT On-Going Suitability Self Assessment Questionnaire will be completed by individuals with access to Tier 1 BSAT initially and every six months thereafter. From interviews with the RO and Alternate Responsible Officials (AROs), inspectors understood that this procedure will be changed to require completion of the questionnaire annually. Please provide an updated section of the Suitability Assessment Guidance for CDC Tier 1 Biological Select Agents and Toxins that reflects this change.

Attachment 1: Entity Departures

5 **Requirement:** The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures for the select agent or toxin, including any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent. [Section 12(a)]

Observation: Please provide a risk assessment for use of the following equipment located in [redacted] registered for PI [redacted] and to include biocontainment measures, personal protective equipment (PPE) worn at time of use, any training required prior to use, and inactivation of the select agent prior to use, if applicable: 1) VirTis Advantage Wizard 2.1 Lyophilizer located in [redacted] 2) [redacted] flow cytometer in [redacted] and 3) SPEX Sample Prep Geno/Grinder 2010 homogenizer in [redacted] Alternatively, if a piece of equipment will not be used with select agents, please provide documentation that it has been labeled as not for select agent use.

Also, an Accuri C6 flow cytometer was present in [redacted] solation room registered for [redacted] and [redacted] Please provide a risk assessment for use of the flow cytometer to include biocontainment measures, PPE worn at time of use, any training required prior to use, and inactivation of the select agent prior to use, if applicable.

6 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]

Observation: Entry into PI [redacted] laboratory during active work requires a solid front gown and gloves. When the laboratory is inactive, no PPE is required. Please provide the risk assessment used to determine the level of PPE required for both active work and entry when the laboratory is inactive, including respiratory protection and the criteria used to determine when the laboratory is inactive.

7 **Requirement:** The plan must be reviewed annually and revised as necessary. Drills or exercises must be conducted at least annually to test and evaluate the effectiveness of the plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident. [Section 12(e)]

Observation: The signature page for the Chemical Hygiene Plan for PIs [redacted] and [redacted] states that the PI, Chemical Hygiene Officer, and the RO must review and sign the plan annually. However, there was no signature indicating RO review in 2011. Please describe the measures implemented to ensure that entity plans are reviewed annually, and documented with signatures consistent with entity policy.

The signature page for PI [redacted] biosafety plan states that the Biosafety Officer (BSO) is to review and sign the plan annually. However, there was no signature indicating BSO review in 2012. Please describe the measures implemented to ensure that entity plans are reviewed annually, and documented with signatures, consistent with entity policy.

There was no evidence that the biosafety plan for PIs [redacted] and [redacted] was reviewed in 2013. Please describe the measures implemented to ensure that entity plans are reviewed annually, and documented with signatures, consistent with entity policy.

A PI signature page was generally used to document that plans were reviewed and revised, as necessary, after any drill or exercise and after any incident. This PI signature page was not included in the biosafety plan documentation for PIs [redacted] and [redacted] Please describe the measures implemented to ensure that the biosafety plan for PIs Rollin and Nichol is reviewed and revised, as necessary, after any drill or exercise and after any incident.

8 **Requirement:** The incident response plan must also contain the following information: a list of personal protective and emergency equipment, and their locations. [Section 14(d)(9)]

Attachment 1: Entity Departures

Observation: A list of emergency equipment and their locations was included in the 2011 incident response plan for PIs [redacted] and [redacted] but was not included in the 2012 and 2013 versions. Please provide an updated section of the incident response plan for PIs [redacted] and [redacted] that contains a list of emergency equipment and their locations. Note that this observation was previously cited in the report resulting from the October 12-22, 2010 inspection of your facility.

9 **Requirement:** The plan must be reviewed annually and revised as necessary. Drills or exercises must be conducted at least annually to test and evaluate the effectiveness of the plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident. [Section 14(f)]

Observation: Documentation was provided that the incident response plan for PIs [redacted] and [redacted] was reviewed in November 2011, December 2012, and February 2014; however, no documentation of plan review for 2013 was provided. Please provide evidence that the incident response plan for PIs [redacted] and [redacted] was reviewed in 2013, or describe the measures implemented to ensure that a plan review will be performed annually, or as necessary after any drill or exercise and after any incident.

10 **Requirement:** The Responsible Official must ensure a record of the training provided to each individual with access to select agents and toxins and each escorted individual (e.g., laboratory workers, visitors, etc.) is maintained. The record must include the name of the individual, the date of the training, a description of the training provided, and the means used to verify that the employee understood the training. [Section 15(d)]

Observation: Interviews revealed new laboratorians [redacted] (SRA approved 9/4/2013), [redacted] (SRA approved 6/3/2013), and [redacted] (SRA approved 4/3/2013), and working under PIs [redacted] and [redacted], had received initial BSL3 training; however, no record of this training was made available. Please describe the measures implemented to ensure that a record of initial BSL3 training is maintained for all personnel approved for access to select agents and toxins.

11 **Requirement:** An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: Accurate, current inventory for each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and recombinant and/or synthetic organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials), including: [Section 17(a)(1)]

Observation: The version of the inventory record provided to inspectors and used to check the physical inventory for PIs [redacted] and [redacted] did not contain information for all select agents held in long-term storage. Box 4 containing 42 vials of [redacted] was present in long-term storage; however, no information for box 4 was included in the current inventory record. A laboratorian searched through electronic versions of the inventory record and located information for these vials of select agents in a previous version of the record, but it is not clear why this information was not present in the current inventory.

A box of [redacted] samples for PIs [redacted] and [redacted] ("MSI box #3") was labeled as containing 43 vials (Numbered 99-141); however, MSI box #3 actually contained 49 vials (numbered 99-147).

Please provide corrected copies of the inventory records described in the above observations, and describe the measures implemented to ensure inventory records are kept accurate and current in the future.

Attachment 1: Entity Departures

12 **Requirement:** An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: accurate, current inventory for each select agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials), including: The select agent used and purpose of use. [Section 17(a)(1)(v)]

Observation: Use of [redacted] was documented on the biological safety cabinet (BSC) usage log in [redacted] and also stated in an email from [redacted] to PI [redacted] sent on 12/16/2013. However, the inventory record for PIs [redacted] and [redacted] did not indicate access to, nor use of, [redacted] in December 2013. Please describe the measures implemented and the methods used to record when a select agent is moved from or returned to storage and by whom, as well as the purpose of use, and that the methods implemented are consistently followed by personnel with access to inventory.

PI [redacted] stated that all vials of select agent are single-use and not returned to storage. During the inventory audit, inspectors observed that three vials of [redacted] identified as 811855, 811856, and 811857) held in long term storage in [redacted] Suite had colored markings on the lid of each vial. The escort explained that an individual removing the select agent places a colored "dot" on the vial lid to record the number of times the vial was accessed. At the time of inspection, there was no record of vials 811855, 811856, and 811857 being returned to storage, nor was it clear where this information would be captured in the inventory record. Additionally, for these vials indicated as being accessed multiple times, there was no record of when they were moved from storage and by whom and purpose of use beyond the initial time they were accessed. Please describe the measures implemented to ensure compliance with the requirement to record when a select agent is moved from storage and by whom, returned from storage and by whom, and the purpose of use.

13 **Requirement:** An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: Accurate, current inventory for each toxin held, including: [Section 17(a)(3)]

Observation: The current version of the inventory record provided and used to check physical inventory for PIs [redacted] and [redacted] did not contain information for all select toxins held in long-term storage. Box 4 contained 4 vials of [redacted] however, no information for box 4 was included in the current inventory record. A laboratorian searched through past, electronic versions of the inventory record and located information for these vials in a previous version of the record, but it is not clear why this information was not present in the current inventory. Please describe the measures implemented to ensure inventory records are kept accurate and current.

14 **Requirement:** An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: Information about all entries into areas containing select agents or toxins, including the name of the individual, name of the escort (if applicable), and date and time of entry. [Section 17(a)(5)]

Observation: A manual visitor log is used to record entry of visitors into [redacted] Suite registered for PIs [redacted] and [redacted] For some entries, the escort's initials rather than name was recorded. Please describe the measures implemented to ensure that, when applicable, the name of the escort is recorded. If initials are to be used, please provide documentation that the visitor log contains a key that associates the escort's initials with a full name.

15 **Requirement:** An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: A written explanation of any discrepancies. [Section 17 (a)(7)]

Attachment 1: Entity Departures

Observation: Please provide documentation that you have included a written explanation of discrepancies in the inventory records for the following items noted in this report: 1) the deletion of inventory records for box 4 containing [redacted] and [redacted] for PIs [redacted] and [redacted] 2) the number of vials of [redacted] present in MSI box #3 for PIs [redacted] and [redacted] and 3) lack of record of access for [redacted] vials 811855, 811856, and 811857 for PIs [redacted] and [redacted]

16 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. The risk of infectious aerosols from infected animals or their bedding also can be reduced if animals are housed in containment caging systems (such as solid wall and bottom cages covered with filter bonnets, open cages placed in inward flow ventilated enclosures, HEPA-filter isolators and caging systems, or other equivalent primary containment systems). [BMBL: (ABSL-3) B3]

Observation: An environmental chamber [redacted] housed in non-containment caging in [redacted] for [redacted] and [redacted] is used to hold ferrets infected with [redacted] Records of service performed October 2012 and 2013 were provided, but did not indicate testing of a HEPA filter. If this environmental chamber provides biocontainment, please describe the method of such containment, where exhaust air from this chamber is discharged (e.g., into room), and if the exhaust air is HEPA filtered. If exhaust air is HEPA filtered, please provide annual replacement documentation or certifications for the chamber's exhaust HEPA filter performed in 2011, 2012, and 2013. If exhaust air is not HEPA filtered, please provide a risk assessment for the chamber's use with infected animals.

17 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. BSCs should be certified at least annually to assure correct performance. [BMBL: (ABSL-3) D11]

Observation: During the inspection, a certification document dated 4/13/2012 was provided for the exhaust HEPA filter (AF1153R) servicing [redacted] 1, registered space for PIs [redacted] and [redacted] This certification did not indicate if the exhaust HEPA passed or failed overall certification. Also test results for HEPA filter leak test were indicated as "N/A." A second copy of this certification document was provided on 3/26/2014, manually indicating that the cabinet passed overall certification; yet test results for HEPA filter leak test were still indicated as "N/A." Please explain how the documents provided adequately certify the proper functioning of this exhaust HEPA filter. Alternatively, please describe the measures implemented to ensure that adequate documentation of exhaust HEPA certification is obtained and maintained in accordance with this safety standard.

18 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. When a procedure cannot be performed within a BSC, a combination of personal protective equipment and other containment devices, such as a centrifuge safety cup or sealed rotor, must be used. [BMBL: (BSL-3) B10]

Observation: A fixed angle rotor present in [redacted] registered for PIs [redacted] and [redacted] and to be used in an [redacted] high speed centrifuge did not have a gasket between the lid and body of the rotor. If this rotor is not used for select agent work, please provide documentation that it has been labeled as such or removed from the suite if appropriate. If this rotor is or will be used for select agent work, please provide documentation that the rotor now contains a gasket to provide a seal between the rotor lid and body.

19 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. [BMBL: (BSL-3) C3]

Attachment 1: Entity Departures

Observation: At the time of the inspection, the biosafety plan for PIs [redacted] and [redacted] did not state that eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. Please provide the updated or section(s) of the plan addressing this safety standard.

20 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. In addition, BSL-3 laboratory workers should: Change gloves when contaminated, integrity has been compromised, or when otherwise necessary. [BMBL: (BSL-3) C4-a]

Observation: While conducting an audit of the PI [redacted] and [redacted] select agent and toxin inventory, the escort handling the vials wore double gloves. However, one of the outer gloves contained a large tear across the palm. Please describe how you will ensure that gloves worn in the BSL-3 laboratory will be changed when their integrity has been compromised.

21 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. Hand washing protocols must be rigorously followed. [BMBL: (BSL-3) C4-c]

Observation: During an inspection of [redacted], registered space for PI [redacted], neither inspectors nor escorts washed hands upon exiting the laboratory, and inspectors were not instructed to wash hands when exiting the laboratory. Also, when exiting [redacted] neither inspectors nor escorts washed hands or used an alternative method such as hand sanitizer upon exiting. Please describe the measures implemented to ensure individuals wash hands after working with potentially hazardous materials and before leaving the laboratory.

22 **Requirement:** An individual or entity required to register under this part must develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use. The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures for the select agent or toxin, including any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent. [Section 12(a)]. Decontamination of the entire laboratory should be considered when there has been gross contamination of the space, significant changes in laboratory usage, for major renovations, or maintenance shut downs. [BMBL: (BSL-3) D3]

Observation: The biosafety plan for PIs [redacted] and [redacted] did not contain procedures for decontamination of the entire laboratory in the event of gross decontamination. Please update the biosafety plan to add these procedures including the method and means used, and provide a copy of the updated pages or section of the biosafety plan.

23 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. HEPA filtered exhaust air from a Class II BSC can be safely re-circulated into the laboratory environment if the cabinet is tested and certified at least annually and operated according to manufacturer's recommendations. BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or a direct (hard) connection. [BMBL: (BSL-3) D10]

Observation: BSCs in Buildings [redacted] and [redacted] laboratories registered for PIs [redacted] and [redacted] had items such as mechanical pipetting devices and pens obstructing the front grill. Please describe the measures implemented to ensure that BSCs are operated according to manufacturer's recommendations and that the grills are kept clear to allow for proper air flow.

Attachment 1: Entity Departures

24 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. Provisions to assure proper safety cabinet performance and air system operation must be verified. [BMBL: (BSL-3) D10]

Observation: Inspectors smoke tested the thimble connections on the BSCs in rooms [redacted] and [redacted] registered space for for PIs [redacted] and [redacted], and observed air flowing out of the thimble and into the laboratory. A work order dated 3/12/2014 was provided, stating that the exhaust valve was opened further to increase exhaust flow, and upon re-testing the thimbles were found to be operating as designed. No further action is required.

25 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. BSCs should be certified at least annually to assure correct performance. [BMBL: (BSL-3) D10]

Observation: Certifications were provided for a Class III BSC (SN 83318) located in [redacted], registered space for PIs [redacted] and [redacted] Please verify the following information for this BSC and, as applicable, provide documentation of test results:

Has the interlock between the exhaust monitor safety alarm and cabinet's blowers (as noted by [redacted] in an email dated 3/26/2013) been tested to ensure it is functioning as designed?

Are there any other interlocks present on this BSC (such as between the door into the antechamber and the door from the antechamber to the working area preventing these doors from being opened simultaneously), and, if so, have these been tested to ensure they are working as designed?

Reviewing the BSC test reports for certification performed on 9/8/2011, 11/9/2012, and 11/25/2013, it is not clear if the negative pressure/ventilation rate was verified. Please provide documentation that the magnehelic gauges indicate a negative air pressure of at least 0.5 inches water column once the cabinet is balanced and the system is operational. Alternatively, please explain how negative pressure/ventilation rate is verified on the provided test report.

26 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. A method for decontaminating all laboratory wastes should be available in the facility, preferably within the laboratory (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method). [BMBL: (BSL-3) D11]

Observation: The pass-through autoclave located in [redacted] Suite, registered space for PIs [redacted] and [redacted] was not operational at the time of inspection. Waste was being stored within the secured suite while the autoclave was awaiting repair. Please provide documentation (e.g., completed work order) that the autoclave has been repaired and is now operational.

27 **Requirement:** An individual or entity required to register under this part must develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use. The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures for the select agent or toxin, including any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent. The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(a)(b)]. Equipment that may produce infectious aerosols must be contained in primary barrier devices that exhaust air through HEPA filtration or other equivalent technology before being discharged into the laboratory. These HEPA filters should be tested and/or replaced at least annually. [BMBL: (BSL-3) D12]

Attachment 1: Entity Departures

Observation: A [redacted] ultracentrifuge was present in [redacted] registered space for PI [redacted] The log book showed it was last used in 2010, and the PI stated it is needed for purification of select agent. It was not clear whether the ultracentrifuge has a HEPA filter. Please confirm whether or not a HEPA filter is present on this ultracentrifuge. If it does not have a HEPA filter, please provide a risk assessment for use with select agent. If it does have a HEPA filter, please provide service records for the last 3 years showing that the HEPA filter has been tested or replaced annually. If it has a HEPA filter that has not been tested or replaced at least annually, please describe how you will ensure this is performed annually.

28 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. The BSL-3 facility design, operational parameters, and procedures must be verified and documented prior to operation. Facilities must be re-verified and documented at least annually. [BMBL: (BSL-3) D15]

Observation: The [redacted] side of the [redacted] area registered for PIs [redacted] and [redacted] has 2 autoclaves. Prior to August 2013, both autoclaves were validated monthly using a biological indicator. Since August 2013, only one of these autoclaves has been tested. Per PI [redacted] one autoclave is currently used for waste and the other is used exclusively for sterilizing non-select agent items such as media. Please confirm that A-009 is the autoclave used for waste. In addition, please provide documentation that the "sterilizing" autoclave has been labeled "not for select agent waste." Alternatively, if another method is used to verify the "sterilizing" autoclave annually, please describe how this is performed.

29 **Requirement:** The biosafety and containment procedures must be sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). [Section 12(b)]. When toxins are in use, the room should be clearly posted: "Toxins in Use—Authorized Personnel Only." [BMBL: Appendix I Training and Laboratory Planning]

Observation: "Toxin Working Area" was posted on the door to [redacted] to denote that this room had been designated as the location for any work with toxins. No work with toxins was occurring at the time of inspection. A "Toxin in Use" sign was not present. Please provide documentation that a "Toxin in Use" sign is available in [redacted] Suite and that, in the event of work with toxin, this sign will be posted at the appropriate room within the suite.