Policy Statement for BSL-4 and ABSL-4 Laboratory Verification

May 18, 2023

Policy Statement Details

- The draft policy statement was published for public comment in January 2022.
- The comments were reviewed and the policy revised.
- The final policy statement on BSL-4/ABSL-4 Laboratory Verification was released in February 2023
  - https://www.selectagents.gov/regulations/policy/BSL4ABSL4.htm

Rationale for Policy

- Currently, the BSL-3/ABSL-3 verification policy sets Federal Select Agent Program (FSAP) expectations for entities with BSL-3/ABSL-3 laboratories.
- The FSAP saw a need to develop a similar policy for BSL-4/ABSL-4 laboratories that clearly outlines facility verification, preventative maintenance and documentation requirements for the regulated community.
- Links the FSAP's expectations with facility and verification requirements for BSL-4/ABSL-4 laboratories described in Biosafety in Microbiological and Biomedical Laboratories 6th Ed.

References for Policy

- Federal Regulations
  - 42 CFR 73.12(b), 9 CFR 121.12(b)
    - Biosafety and containment procedures must be sufficient to contain the select agent or toxin.
  - 42 CFR 73.12(a), 9 CFR 121.12(a)
    - Must develop and implement a written biosafety plan that is commensurate with the risk of the agent or toxin, given its intended use.
- Biosafety in Microbiological and Biomedical Laboratories 6th Edition
  - BSL-4 D16(a)
  - ABSL-4 D16(a)
  - BSL-4 (Cabinet laboratory D17; Suit laboratory D20)
  - ABSL-4 (Cabinet facility D18; Suit facility D21)

Heating, Ventilation, and Air Conditioning (HVAC) Operational Verification

HVAC Operational Verification

HVAC operational verification is conducted **initially, annually,** and after any **major changes** or after resolving **major problems**.

- HVAC operational verification must be performed and **documented.**

- HVAC design verification process must provide evidence that secondary containment will be maintained during both normal operating conditions as well as **failure** conditions in order to prevent air-flow reversals into non-containment areas or positive pressurization events (e.g., outside the containment boundary, hallways).

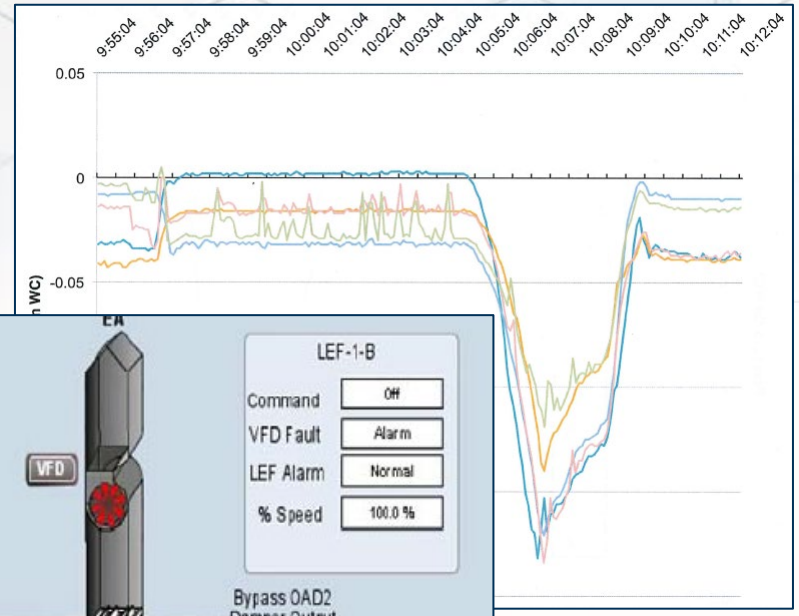
Failure Conditions

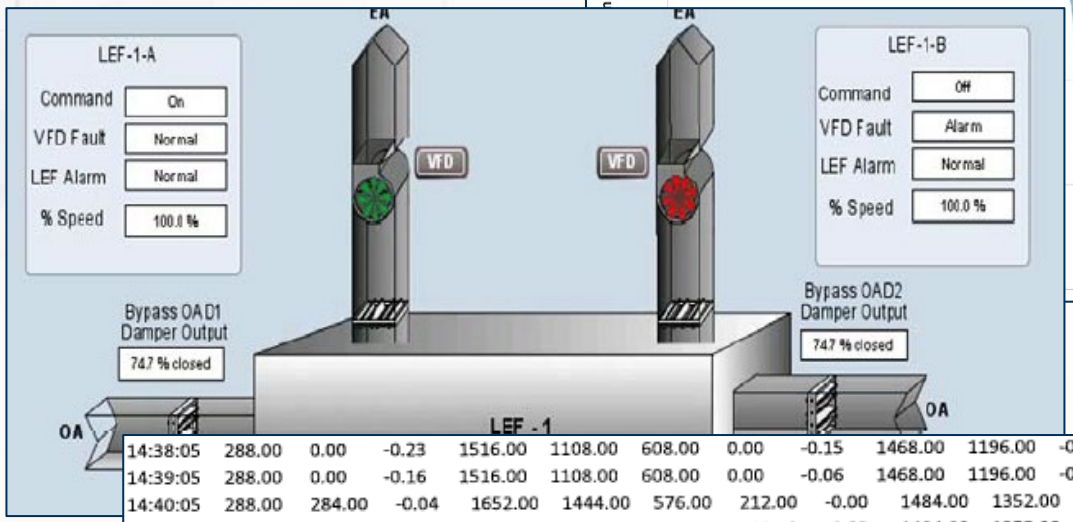
Three Failure Conditions

- Mechanical failure of the supply and exhaust fans or their components.
  - Ability to transition to the redundant fan.
- Transfer to an uninterrupted power supply.
  - Ability to transition to automatically activated backup power supply.
- Return from emergency power to normal power status.
  - Ability to transition from backup power supply to normal power.

Failure test results

- Results of failure tests must demonstrate that there is no airflow reversal that originates within the BSL-4/ABSL-4 containment areas that escape the containment boundary.





14:38:05	288.00	0.00	-0.23	1516.00	1108.00	608.00	0.00	-0.15	1468.00	1196.00	-0.03	256.00	168.00	0.00
14:39:05	288.00	0.00	-0.16	1516.00	1108.00	608.00	0.00	-0.06	1468.00	1196.00	-0.01	256.00	168.00	0.01
14:40:05	288.00	284.00	-0.04	1652.00	1444.00	576.00	212.00	-0.00	1484.00	1352.00	-0.01	264.00	232.00	-0.02
14:41:05	288.00	284.00	-0.00	1652.00	1444.00	576.00	212.00	-0.02	1484.00	1352.00	-0.02	264.00	232.00	-0.05
14:42:05	288.00	284.00	-0.05	1652.00	1444.00	576.00	212.00	-0.05	1484.00	1352.00	-0.03	264.00	232.00	-0.04
14:43:05	288.00	284.00	-0.04	1652.00	1444.00	576.00	212.00	-0.05	1484.00	1352.00	-0.04	264.00	232.00	-0.06
14:44:05	288.00	284.00	-0.05	1652.00	1444.00	576.00	212.00	-0.05	1484.00	1352.00	-0.04	264.00	232.00	-0.08
14:45:05	288.00	276.00	-0.05	1604.00	1368.00	576.00	192.00	-0.04	1480.00	1316.00	-0.04	252.00	220.00	-0.05
14:46:05	288.00	276.00	-0.04	1604.00	1368.00	576.00	192.00	-0.05	1480.00	1316.00	-0.05	252.00	220.00	-0.05
14:47:05	288.00	276.00	-0.07	1604.00	1368.00	576.00	192.00	-0.06	1480.00	1316.00	-0.05	252.00	220.00	-0.06
14:48:05	288.00	276.00	-0.05	1604.00	1368.00	576.00	192.00	-0.05	1480.00	1316.00	-0.05	252.00	220.00	-0.07
14:49:05	288.00	276.00	-0.06	1604.00	1368.00	576.00	192.00	-0.04	1480.00	1316.00	-0.04	252.00	220.00	-0.05

Major Changes

Major Changes to the HVAC System

- Replacement or repairs of exhaust and supply fans serving the BSL-4/ABSL-4 containment areas.
- Replacement, repairs, or modifications of ductwork valves or dampers that serve BSL-4/ABSL-4 containment areas.
- Replacement, repairs, or modifications of HVAC control system components that serve BSL-4/ABSL-4 containment areas.
- Building automation system (BAS) logic programming changes.
- Structural changes to the BSL-4/ABSL-4 containment areas.
- Addition or removal of hard-ducted biological safety cabinets (BSCs), Class III cabinets, or decontamination systems.
- Events that compromise the containment envelope.

Major Problems

Major Problems with the HVAC System

- Recurring failures of the HVAC system.
- Observation or evidence that HVAC alarms are not working properly.
- Observation or evidence that BSCs with an HVAC connection (hard duct or thimble) are not working properly.
- Supply or exhaust interlocking system failures.

BSL-4/ABSL-4 Facility Verification

Conducting BSL-4/ABSL-4 Facility Verification

BSL-4/ ABSL-4 facility verification is conducted initially, annually, and after any major changes or after resolving major problems.

- Minimum verification requirements performed and documented.
- Eight required items.

Minimum Verification Requirements (1-2)

1. Recalibration of components that monitor containment parameters (e.g., differential pressure gauges, pressure transducers, BAS).

2. Verification of BAS-programmed alarm communication.

Minimum Verification Requirements (3A)

3. Confirmation that decontamination systems are operating as designed (e.g., autoclave, room decontamination systems, tissue digesters, liquid effluent systems)
    A. Effluent, tissue, and autoclave decontamination systems:
        i. Annual verification of system operational components to ensure biologically validated set point parameters are maintained (e.g., volumetric, pressure, temperature components);
        ii. Biological validation is performed at least annually or more often, if required by institutional policy and/or risk assessment;
        iii. Annual certification testing of associated high-efficiency particulate air (HEPA) filters, if applicable (e.g., operating vent, pressure relief vent, chamber effluent/vent);

Minimum Verification Requirements (3A) Continued

3. Confirmation that decontamination systems are operating as designed (e.g., autoclave, room decontamination systems, tissue digesters, liquid effluent systems)
    A. Effluent, tissue, and autoclave decontamination systems:
        iv. Annual verification that system failure communication systems are operating as designed (e.g., alarms, leak detection);
        v. Verify appropriate filter media is selected and maintained annually (e.g., HEPA, polytetrafluoroethylene [PTFE]); and
        vi. Implementation of a risk-based preventative maintenance for other equipment that is critical to containment components, but is not specifically included above (e.g., cook tanks, etc.);

Minimum Verification Requirements continued (3B,C)

3. Confirmation that decontamination systems are operating as designed (e.g., autoclave, room decontamination systems, tissue digesters, liquid effluent systems)
    B. Annual verification that chemical shower delivery systems are operating as designed (e.g., system delivery components and conductivity and alarm monitoring);
    C. Annual verification that room decontamination systems are operating as designed and tested using biological indicators (e.g., biological indicator strips);

Minimum Verification Requirements (4-8)

4. Certification of laboratory HVAC, plumbing vent line, and decontamination system filters by appropriate means and appropriate acceptance criteria to ensure integrity (e.g., HEPA, PTFE).
5. Assessment of breathing air quality for both main and backup air breathing air supply.
6. Certification of BSCs.
7. Verification of primary containment integrity (e.g., centrifuges, Class III cabinets, animal caging) with component replacement if defective.
8. Confirmation that all alarms (e.g., air supply, exhaust, life support, BAS alarms, fire, airflow, security, access systems, water supply backflow prevention devices) have been checked and are functioning according to approved design specifications.

BSL-4/ABSL-4 Ongoing Facility Verification

Four items that the entity must perform and document on an ongoing, routine basis.

BSL-4/ABSL-4 Ongoing Facility Verification (1,2)

1. Surveillance and implementation of routine maintenance programs for HVAC supply and exhaust fans, main and backup breathing air systems, and decontamination systems.
2. Surveillance of containment envelope for penetrations, cracks, breaks, and performance of related repairs. Identifying and confirming proper operation of various BSL-4/ABSL-4 containment boundary points of failure (such as penetrations, cracks, breaks, etc.) may be successfully tested through proper pressure decay testing.

BSL-4/ABSL-4 Ongoing Facility Verification (3,4)

3. Surveillance and verification of secondary containment envelop integrity (e.g., Air Pressure Resistant (APR) door gaskets, HVAC dampers).
4. Confirmation and testing of critical interlocks and manual overrides (e.g., between exhaust fans and air handling units, between laboratory exhaust fan airflows and supply airflows, and between mechanical and electronic door interlocks).

Note: Entities may need to perform additional facility verification in addition to these and other systems due to the entity's facility design, operation, work objectives, etc., to ensure containment of select agents and toxins.

Questions

www.selectagents.gov

CDC Contact Information
Division of Select Agents and Toxins
LRSAT@cdc.gov
404-718-2000

APHIS Contact Information
Division of Agricultural
Select Agents and Toxins
DASAT@usda.gov
301-851-2070

DEPARTMENT OF HEALTH & HUMAN SERVICES·USA

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION

USDA