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GUIDELINES FOR WORKING WITH *BACILLUS ANTHRACIS*

Scope

Bacillus anthracis, the causative agent of anthrax, is a spore-forming bacterium capable of causing cutaneous, gastric, and respiratory infections. Cases of laboratory associated infections with *B. anthracis* (primarily cutaneous) have been reported (1, 2). Disease is moderate to severe, even fatal, in animals and humans depending upon the route of exposure. Due to the ability of *B. anthracis* spores to persist in the environment, and the potential for infection and accompanying high mortality resulting from respiratory exposure to aerosolized spores, *B. anthracis* is classified as an overlap Select Agent by the Centers for Disease Control and Prevention (CDC) and the U. S. Department of Agriculture (USDA). An effective anthrax vaccination is available (3) and is offered free of charge to employees who are determined to have an elevated risk of exposure to *B. anthracis* through duties of employment with the University of Pittsburgh. This SOP was designed to establish a system of information and safeguards that should be followed at the University of Pittsburgh when working with *Bacillus anthracis*.

Definitions

Select Agent - The U.S. Department of Health and Human Services (DHHS)/CDC and the USDA regulate the possession, use, and transfer of select biological agents and toxins that could pose a severe threat to human, animal or plant health, or to the safety of plant or animal products. Possession, use, storage, and/or transfer of *B. anthracis* requires registration with the CDC through the University of Pittsburgh's Select Agent Program.

Attenuated strains of *B. anthracis* – The DHHS and USDA, under the auspices of the National Select Agent Registry have determined that certain attenuated strains of *B. anthracis* are excluded from the Select Agent Program (4). *B. anthracis* contains two plasmids that encode virulence factors, pXO1 and pXO2. Plasmid pXO1 encodes three protein toxins while plasmid pXO2 encodes the bacterium's anti-phagocytic capsule. *Bacillus anthracis* strains devoid of both plasmids pXO1 and pXO2 are attenuated and are excluded from the Select Agent Program. *Bacillus anthracis* strains that do not carry plasmid pXO2 (e.g. Sterne strain, pXO1⁺ and pXO2⁻) are also excluded from the Select Agent Program.

Virulent strains of *B. anthracis* – All *B. anthracis* strains that are not specifically cited by the CDC/USDA Select Agent Program as being excluded from the regulation (3).

1. Procedure

1.1 **Agent** - *Bacillus anthracis*, causative agent of anthrax

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1.2 **Employees at risk** - Naturally or experimentally infected animals are a potential source of infection via bite or scratch to non-vaccinated individuals. The organism may be present in blood, skin lesion exudates, cerebrospinal fluid, and sputum. Risk is also posed to laboratory and animal workers that handle pure bacterial cultures of *B. anthracis*. Potential exposures to aerosolized *B. anthracis* spores further increase risk to workers. To delineate employees at risk, categories of exposure and risk have been developed.

1.2.1 High Risk Category – Personnel with potential exposure due to manipulation of virulent *B. anthracis* cultures or spore preparations. This category includes research staff who routinely work with pure cultures of *B. anthracis*, prepare batches of concentrated spores and/or perform aerosol producing procedures, as well as veterinary and research staff who handle animals that have been infected with *B. anthracis* or unfixed specimens from infected animals.

1.2.2 Low Risk Category – Personnel with potential exposure due to naturally occurring infection in large research animals (sheep, goats, and cattle) or *B. anthracis* contamination in environmental samples. This category includes veterinary and research staff who enter rooms where *B. anthracis* work is performed but do not manipulate cultures or infected animals, or who are exposed to research animals with negligible endemic anthrax rates. Research staff who work with environmental samples, and personnel who handle diagnostic specimens are included in this category.

1.3 **Laboratory Hazards** - there are three modes of transmission for anthrax: inhalational, cutaneous, and gastrointestinal

1.3.1 Respiratory exposures to aerosolized *B. anthracis* cultures or spore preparations pose the most significant hazards to laboratory and animal care personnel. Of particular concern are aerobiology protocols where animals are exposed to concentrated, aerosolized spore preparations, as well as the protocols related to production of concentrated spore preparations.

1.3.2 Percutaneous exposures to cultures, spore preparations, and/or specimens from infected animals, such as blood, skin lesion exudates, cerebrospinal fluid, and sputum may result in cutaneous anthrax.

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1.3.3 Gastrointestinal exposures can be avoided through proper use of personal protective equipment and safe work practices as described in the most recent edition of the CDC publication *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) (1).

1.3.4 Different strains of *B. anthracis* used in the laboratory present different levels of risks to laboratory and animal care personnel. Virulent strains of *B. anthracis* present a greater risk due to the presence of virulence factors and the potential for serious and/or lethal disease. The recommendations for anthrax vaccination differ depending upon the strain and setting in which the agent will be used in the laboratory or animal holding facility.

1.4 Required Procedures

1.4.1 Attenuated strains of *B. anthracis*:

1.4.1.1 All Principal Investigators (PIs) using attenuated strains of *B. anthracis* as defined above must be registered with the Biosafety Officer/EH&S. A registration document may be obtained from the web site www.ehs.pitt.edu or by contacting the Biosafety Officer (412-624-8919).

1.4.1.2 Biosafety Level 2 practices, containment equipment, and facilities are required for all activities involving the use or manipulation of attenuated strains of *B. anthracis*.

1.4.2 Virulent strains of *B. anthracis*:

1.4.2.1 Virulent strains of *B. anthracis* are designated as Select Agents. Only individuals who have been registered and approved through the Select Agent Program may work with virulent strains of *B. anthracis*. All work with virulent strains of *B. anthracis* must be pre-approved by EH&S and must occur in laboratories that have been registered with the Select Agent Program. For more information regarding the University of Pittsburgh Select Agent Program, contact the University Responsible Official for Select Agents (412-624-9505).

1.4.2.2 It shall be the responsibility of the Principal Investigator and/or any individuals responsible for control or access to

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a facility where work with virulent strains of *B. anthracis* is being performed to assure that individuals with potential for *B. anthracis* exposure are enrolled in the medical screening component of this Guideline and are vaccinated prior to any work handling virulent strains of *B. anthracis*.

1.4.2.3 Visitors to areas approved for Select Agent use must be escorted at all times by an individual who has been registered and approved through the Select Agent Program. Visitors are not allowed to handle Select Agents or infected animals. Visitors and other authorized personnel who do not handle virulent *B. anthracis* cultures or infected animals are exempt from the vaccination requirements.

1.4.2.4 Individuals who work in Biosafety Level 3 or Animal Biosafety Level 3 facilities must participate in both the BSL-3 Worker Health Screening Program and the Respiratory Protection Program. Enrollment documents and additional information pertaining to each of these programs can be found on the EH&S website (www.ehs.pitt.edu).

1.4.2.5 Biosafety Level 3 practices, containment equipment, facilities, and personal protective equipment in accordance with current CDC/NIH guidelines published in the most recent edition of *Biosafety in Microbiological and Biomedical Laboratories* (1) and the *NIH Guidelines for Research Involving Recombinant DNA Molecules*(5) are required for all activities involving the use or manipulation of virulent strains of *B. anthracis*.

2. Pre-exposure Prophylaxis

2.1 High Risk Category – After completing the BSL-3 Health Screening administered by Employee Health Services, these individuals are required to undergo pre-exposure vaccination (2). Vaccination shall be five doses of the Anthrax Vaccine Adsorbed (AVA) given intramuscularly. Vaccine is given in 0.5 mL doses at 0 and 4 weeks, and 6, 12, and 18 months. After the primary course of vaccination, booster doses are given annually to maintain immunity.

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2.1.1 Vaccination is not recommended for pregnant or breastfeeding women, persons with any active infection or acute illness, or undergoing treatment with immune-suppressing drugs such as corticosteroids (2). Medical contraindications for AVA will be assessed by Employee Health Services during the BSL-3 Health Screening.

2.2 Low Risk Category – For this group of individuals the vaccination is available but not recommended.

3. **Pre- exposure Prophylaxis**

3.1 **Attenuated strains of *B. anthracis*:**

3.1.1 Post exposure prophylaxis is not recommended for exposures to attenuated strains of *B. anthracis*.

3.2 **Virulent strains of *B. anthracis*:**

3.2.1 Cutaneous exposure: If exposure is due to a bite, scratch, or percutaneous exposure, the exposed individual should immediately cleanse the wound with soap and water and a disinfectant such as a povidone-iodine solution. If the mucous membranes are exposed, the site should be irrigated with potable water for 15 minutes.

3.2.1.1 The individual must immediately report the exposure to their supervisor and to Employee Health Services. A 7 – to 14 – day course of appropriate antimicrobials shall be offered and strongly recommended.

3.2.1.2 Employee Health Services (*MyHealth@Work*) is located at Medical Arts Building, Fifth floor, Suite 500.59, 3708 Fifth Avenue, Pittsburgh, PA 15213, Monday through Friday 7 AM – 3:30 PM. For *B. anthracis* exposures occurring outside these times personnel should proceed to the UPMC Presbyterian Emergency Department for clinical evaluation and treatment.

3.2.1.3 The exposure must also be promptly reported to the University Responsible Official for the Select Agent Program (412-624-9505).

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3.2.2 Respiratory exposure: A respiratory exposure is considered to have occurred after any type of disruption of respiratory protection or engineering control failure.

3.2.2.1 The individual must immediately report the exposure to their supervisor, Employee Health Services, and the University Responsible Official for the Select Agent Program as above. The circumstances surrounding the potential exposure will be evaluated by Employee Health Services in conjunction with the Department of Environmental Health and Safety, and treatment will be determined according to the risk assessment.

3.2.2.2 Previously vaccinated individuals should receive at least 30 days of appropriate antimicrobial treatment. In addition, previously vaccinated individuals should continue with annual boosters.

3.2.2.3 Partially vaccinated individuals have either received <5 intramuscular doses of AVA or have not received all annual boosters as indicated by the licensed vaccination schedule. Partially vaccinated individuals should receive at least 30 days of antimicrobial treatment as outlined above, and should continue with the licensed vaccination schedule.

3.2.2.4 Unvaccinated individuals should receive 60 days of appropriate antimicrobial treatment. Further consultation with Employee Health Services on the risks and possible benefits of supplementing antimicrobials with the anthrax vaccine under an Investigational New Drug (IND) application as part of post-exposure prophylaxis may be advisable. If the individual chooses to receive the vaccine under an IND protocol and is to continue to work with *B. anthracis* the licensed vaccination schedule should be resumed at 6 months.

4. Implementation

4.1 Vaccination is required for all individuals who routinely handle pure cultures of virulent strains of *B. anthracis*, who routinely handle animals infected with virulent *B. anthracis*, or who perform aerosol producing procedures including

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veterinary, animal care, and research staff directly involved in aerosol infection studies with virulent strains of *B. anthracis*.

4.2 Individuals may begin to work with virulent strains of *B. anthracis* three weeks after the third dose of the vaccine has been administered (6, 7). Individuals refusing or having a medical contraindication to the AVA as determined by the Employee Health Services will be prohibited from directly handling virulent *B. anthracis* cultures, spore preparations, or infected animals at the University of Pittsburgh. The determination of all prohibited tasks will be made by the employee's supervisor in consultation with the Department of Environmental Health and Safety.

4.2.1 Staff members refusing or having a medical contraindication to the AVA shall be referred to their supervisor. The supervisor, in consultation with the Office of Human Resources (and if necessary EH&S and Employee Health Services), will examine the feasibility of other duties for the employee that do not involve handling of virulent *B. anthracis*.

4.2.2 Faculty members refusing or having a medical contraindication to the AVA shall be referred to the respective department chair or dean. The supervisor, in consultation with the Office of Human Resources and the Office of the Provost (and as necessary EH&S and Employee Health Services), shall determine other duties for the faculty member that do not involve handling of virulent *B. anthracis*.

5. References

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