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TUBERCULOSIS PROTECTION IN RESEARCH ENVIRONMENTS

1. Scope

Tuberculosis is a zoonotic disease, which is difficult to detect in nonhuman primates and spreads rapidly in nonhuman primate colonies. Due to the devastating consequences of tuberculosis for old world and new world nonhuman primates and associated research projects, special precautions are taken to reduce the risk that workers involved in the use and care of animals will infect non-human primates with *M. tuberculosis*.

University of Pittsburgh research facilities, which utilize *M. tuberculosis* organisms, or specimens **known to** contain *M. tuberculosis*, operate at Biosafety Level 3 (BSL-3) in accordance with current CDC/NIH guidelines published in the latest edition of *Biosafety in Microbiological and Biomedical Laboratories and Recombinant DNA Guidelines*.

2. Procedure

2.1. Agent - Mycobacterium tuberculosis

2.2. Individuals at risk- All individuals (including visitors) entering areas where non-human primates are housed or utilized are at risk of acquiring *M. tuberculosis* infection and pose a risk of transmitting *M. tuberculosis* to a non-human primate. All individuals utilizing non-fixed primary tissue from non-human primates and all individuals authorized to enter research facilities that utilize *M. tuberculosis* or specimens that potentially contain *M. tuberculosis* are at potential risk for *M. tuberculosis* infection.

2.3. All individuals at risk, as defined above, shall undergo baseline screening for M. tuberculosis exposure upon hire or upon enrollment in the University Animal Exposure Surveillance Program. During normal business hours (7 AM – 3:30 PM), screening may be obtained at Employee Health Services (*MyHealth@Work*), Suite 500.59, Medical Arts Building, 3708 Fifth Avenue, Pittsburgh, PA 15213, 412-647-4949

2.4. TWO STEP TUBERCULIN SKIN TEST: Participants who do not have a history of a prior positive reaction to a tuberculin skin test (TST, nomenclature replaces Purified Protein Derivative, PPD test) will receive a” two-step” tuberculin skin test on enrollment in the Animal Exposure Surveillance Program.

2.4.1. If the first TST is negative, the second tuberculin test should be given 1-3 weeks after the first. If the participant has documented negative TST tests within the previous 12 months, only a single tuberculin skin test is administered. The second TST is also not required for visitors to the facility.

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- 2.4.2. If the first tuberculin skin test is positive, a medical history is obtained for symptoms suggestive of active pulmonary tuberculosis and a chest radiograph is obtained.). Such individuals undergo evaluation as indicated in these guidelines for “History of positive TST”.The participant may also be referred to the Allegheny County Health Department for follow-up, per the discretion of the University Employee Medical Director.
- 2.4.2.1. If the individual did not have a documented negative TST in the preceding 24 months (e.g. the test result does not represent a tuberculin skin test conversion) and there is no clinical or radiographic evidence of active pulmonary disease, the employee is medically cleared with re-evaluations every six months.
- 2.4.2.2. If the worker had a documented negative TST in the preceding 24 months and is now TST reactive (i.e. a converter), and there is no clinical or radiographic evidence of active pulmonary disease, the employee is restricted from contact with live nonhuman primates until appropriate medical treatment has been received for at least three days prior to returning to work.
- 2.4.2.3. If there is clinical or radiographic evidence of active pulmonary tuberculosis, the employee is medically restricted. This restriction is not removed until the individual provides documentation establishing that the clinical or radiographic findings can reasonably be attributed to a condition other than active pulmonary tuberculosis, or appropriate medical treatment has been initiated. While on treatment, the individual will be monitored by Employee Health for adherence to the treatment regimen. These individuals will not be allowed to enter non-human primate areas until cleared by the Employee Medical Director. The worker is not cleared to return to any University work place until the University Employee Medical Director is reasonably convinced that the individual does not represent a health risk.
- 2.4.2.4. If the medical recommendation is that the employee be prohibited from entry to areas with live nonhuman primates or not return to work at the University, the employee, supervisor, and Human Resources are notified the day the decision is reached.
- 2.4.3. If the initial tuberculin skin test is negative and the second test is positive during the 2-step procedure, the response is indicative of a prior infection (booster phenomenon). Such individuals undergo evaluation as indicated in these guidelines for “History of positive TST”.
- 2.4.4. If the tuberculin skin tests are both negative and there are no other medical contraindications, the employee is medically cleared for work.

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2.5. SEMI-ANNUAL EVALUATION: All participants shall undergo tuberculin skin testing or medical screening for active tuberculosis infection every six months.

2.5.1. If the prior tuberculin skin test was negative, but the current test indicates positive, this is considered a recent conversion and the individual will undergo medical evaluation and a chest radiograph is obtained.

2.5.1.1. If the chest radiograph is positive, medical treatment in consultation with the Allegheny County Health Department is initiated. The individual will be medically restricted as outlined in this document.

2.5.1.2. If the chest radiograph is negative, the individual will undergo further medical evaluation including but not limited to Interferon-Gamma Release Assays, (i.e. Quantiferon or T-spot).

2.5.2. If the prior tuberculin skin test was positive, the employee will not be subjected to a TST but will be sent a Tuberculosis Health Questionnaire that asks the worker to self-identify any symptoms suggestive of active tuberculosis. The form must be completed and signed by the participant and submitted to Employee Health Services every six months. At the discretion of the University Employee Medical Director, Interferon-Gamma Release Assay may be utilized to conduct on-going semi-annual surveillance for exposure of the employee to tuberculosis.

2.6. HISTORY OF POSITIVE TST: If the participant has documentation of a previous positive reaction to a tuberculin skin test, further skin testing is not performed. At the discretion of the University Employee Medical Director, Interferon-Gamma Release Assay may be utilized to conduct current and/or on-going semi-annual surveillance for exposure of the employee to tuberculosis. If the individual has no knowledge of ever receiving Bacillus Calmette-Guerin immunization (BCG), the following occurs:

2.6.1. A Tuberculosis Health Questionnaire is administered and the completed form is filed in the employee's medical record.

2.6.2. A chest radiograph is obtained if:

2.6.2.1. the employee cannot provide documentation of a normal chest radiograph following the discovery of the positive reaction, or

2.6.2.2. the employee's responses to the questions suggest active pulmonary tuberculosis, or

2.6.2.3. the employee did not receive appropriate chemoprevention or treatment, as determined by the University's Employee Medical Director.

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2.6.3. If there is no clinical or radiographic evidence of active pulmonary disease, the employee is medically restricted from entering areas where live nonhuman primates are housed or utilized until there has been a medical evaluation to consider both the likelihood that the reaction indicates a true infection and the estimated risk for progression from latent to active tuberculosis.

2.6.4. If there is clinical or radiographic evidence of active pulmonary tuberculosis, the employee is medically restricted and treated, as outlined in this document.

2.7. HISTORY OF BCG: Persons who have received Bacillus Calmette-Guerin (BCG) immunization will be given TST tests. Interpretation of a reaction will be based upon the size of the reaction, length of time since BCG administration, and risk of prior exposure to tuberculosis. Use of IGRA (Interferon-Gamma Release Assays, i.e. Quantiferon or T-spot) will be conducted where TST specificity is compromised by BCG use after infancy, multiple BCG vaccinations or questionable allergic/indeterminate reactions. IGRA's have much higher specificity than TST's. (See MMWR "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection," Vol.59, No. RR-5, June 25, 2010.)

3. Implementation

- 3.1. Consultation with the DLAR attending veterinarian, Principal Investigator and/or EH&S will occur, as necessary, to assist the Employee Medical Director in the evaluation of specific cases. If a consensus cannot be reached among these individuals, the final decision will rest with the Employee Medical Director.
- 3.2. Individuals refusing tuberculin skin testing, declining the recommended clinical treatment, or failing to submit a completed TB health review form shall be prohibited from entering non-human primate areas or BSL-3 *M. tuberculosis* research labs.
- 3.3. DLAR supervisors, Animal Facility Directors, and the Principal Investigator's designees are responsible to verify current TB status of all entrants (including all visitors) into non-human primate areas or an *M. tuberculosis* lab under their control.
- 3.4. Individuals who manipulate non-fixed primary tissue from non-human primates AND who refuse tuberculin skin testing or fail to submit a completed TB health review form will be reported to the Principal Investigator(s) for the active research protocol. The individual's name will be removed from the protocol, or protocol approval/renewal will be denied until compliance is achieved.