UNIVERSITY OF TOLEDO

SUBJECT: SELECT AGENT AND TOXINS – HANDLING, STORAGE & ACCESS

Procedure No: HM-08-030

PROCEDURE STATEMENT

The University of Toledo will establish and maintain guidelines in order to comply with federal regulations related to the possession of Select Agents and Toxins as defined by the Centers for Disease Control (**CDC**) and United States Department of Agriculture (**USDA**) Animal Plant Health Inspection Service (**APHIS**).

PURPOSE OF PROCEDURE

To ensure proper protocols are established for all staff, students and faculty that are involved in the handling, secure storage and shipment of Select Agents and Toxins at the University of Toledo.

PROCEDURE

I. SCOPE AND APPLICABILITY

This policy describes requirements for the possession, use, receipt or transfer of Select Agents and Toxins. These requirements are designed to protect against misuse of Select Agents. Possession, use, transfer or disposal of these agents may not occur without approval of the Responsible Facility Official (RO), or the Alternate RO located in the Environmental Health and Radiation Safety (EHRS) Environmental Health and Radiation Safety Department. This policy applies to University faculty, staff, students, and visitors, who receive, possess, use, transfer or acquire Select Agent(s) and Toxins while participating in any university-sponsored research activity.

II. DEFINITIONS

"Select Agent" as defined by the CDC and APHIS, means biological agents or toxins deemed a threat to the public, animal or plant health, or to animal or plant products. These agents can be found in the Select Agent List. "Biological agent" means any microorganism (including, but not limited to bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring bio-engineered or synthesized component of any such microorganism or infectious substance, capable of causing death, disease or other biological malfunction in a human, an animal, a plant or another living organism; deterioration of food, water, equipment, supplies or material of any kind; or deleterious alteration of the environment.

"Toxin" means the toxic material or product of plants, animals, microorganisms (including, but not limited to bacteria, viruses, fungi, ricksettsiae or protozoa) or infectious substances, or recombinant or synthesized molecule, whatever their origin and method of production, and includes any poisonous substance or biological product that may be engineered as a result of biotechnology, produced by a living organism; or any poisonous isomer or biological product, homologue, or derivative of such a substance.

"Access" – an individual will be deemed to have access at any point in time if the individual has possession of a select agent or toxin (e.g., ability to carry, possess, use, transfer, or manipulate) or the ability to gain possession of a select agent or toxin. Only authorized persons are permitted access to Select Agents and Toxins. Access to a Select Agents and Toxins can be limited by either security containers or by escorts. For non-laboratory functions including routine cleaning, maintenance and repairs, non-approved individuals will be allowed access to areas where Select Agents and Toxins are accessible only if they are escorted and monitored by an individual who has been approved.

"Authorized person" is an individual who has been approved for access to Select Agents through the successful completion of an FBI security risk assessment (FD-961 Form) and all applicable training.

"Entity" means any government agency (Federal, State or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity. For purposes of this policy, the entity is the University of Toledo.

"Exempt Quantity" means an amount of a Select Agent or Toxin that is below reporting thresholds set forth by the CDC and USDA.

"Responsible Official" (RO) means the individual designated by the entity to act on its behalf. This individual must have the authority and control to ensure compliance with the regulations. The alternate responsible official (ARO) is as assigned by the RO.

A "restricted person" is an individual who falls under one or more of the following categories:

- Is under indictment for a crime punishable by imprisonment for a term exceeding 1 year.
- Has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year.
- Is a fugitive from justice.
- Is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)).
- Is an alien illegally or unlawfully in the United States.
- Has been adjudicated as a mental defective or has been committed to any mental institution.
- (i)Is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country as to which the Secretary of State, pursuant to section 6(j) of the Export Administration Act of 1979 (50 U.S.C. App. 2405(j)), section 620A of chapter 1 of part M of the Foreign Assistance Act of 1961 (22 U.S.C. 2371), or section 40(d) of chapter 3 of the Arms Export Control Act (22 U.S.C. 2780(d)), has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism; or (ii) acts for or on behalf of, or operates subject to the direction or control of, a government or official of a country described in this subparagraph.
- Has been discharged from the Armed Services of the United States under dishonorable conditions.
- Is a member of, acts for or on behalf of, operates subject to the direction or control of, a terrorist organization as defined in section 212(a)(3)(B)(vi) of the Immigration and Nationality Act (8 USC 1182(a)(3)(B((iv).

Restricted persons are prohibited from having access to Select Agents.
"Tier 1 Agents" are a special class of high risk select agents as described by the CDC/USDA that require special handling and security procedures to be followed with regards to this category of agent. These requirements are outlined in the Biosafety, Biosecurity, and Incident Response Manuals for the BSL3 Facility.

III. ROLES and RESPONSIBILITIES

All activities involving registration with federal agencies, intramural or extramural transfers, disposal and exclusion or exemption from regulation must be coordinated through Environmental Health and Radiation Safety (EHRS) and reviewed and approved by the RO and Biosafety Officer. The RO submits all applications to CDC and/or USDA. The ARO conducts the duties of the RO when the RO is unavailable. The Principal Investigator (PI) is responsible to direct a project or program involving Select Agents or Toxins in compliance with all regulatory requirements set forth. The PI is responsible to the University of Toledo for the scientific and technical direction of the project or program. Authorized persons with access to Select Agents are required to attend special training prior to handling Select Agents and Toxins and must follow prescribed work practices. Authorized persons must handle Select Agents and Toxins safely, secure them properly when they are not in use, update inventories regularly and dispose of materials appropriately when work is completed.

Restricted persons are prohibited from having access to Select Agents.

IV. PROCEDURES

A. Select Agent and Toxin Registration

PI's considering work with any Select Agents or Toxins must first contact the University of Toledo RO Environmental Health and Radiation Safety (EHRS) This applies to exempt select agents and toxins as well as those that require federal registration.

Registration of Non-exempt Select Agents and Toxins with CDC/APHIS

PI's, who fall under the regulations, must register their intent to use Select Agent or Toxins with the CDC and/or APHIS. PI's, in collaboration with Environmental Health and Radiation Safety (EHRS), must complete

the application packet and submit it to the RO for submission to CDC and/or APHIS. Researchers also have a requirement to complete permits to import certain select agents covered by the CDC/USDA/APHIS. (Please be aware that this process can take a month or more to complete from start to finish.)

B. Exclusion / Exemption

Certain Select Agents and Toxins that do not meet the regulatory criteria are exempt from registration with the CDC and/or APHIS. A list of exemptions can be found on the CDC's Website.

Excluded Strains of HHS and USDA Select Agents and Toxins: Based upon consultations with subject matter experts and a review of relevant published studies and information provided by the entities requesting the exclusions, the Federal Select Agent Program has determined that certain attenuated select agent strains or less toxic select toxins are not subject to the requirements of the select agent regulations.

An excluded select agent strain or modified toxin will be subject to the regulations if there is a reintroduction of factor(s) associated with virulence, toxic activity, or other manipulations that modify the attenuation such that virulence or toxic activity is restored or enhanced. In addition, excluded select agent strains or modified toxins are not exempt from the requirements of other applicable regulations or guidelines (e.g., NIH guidelines, USDA/APHIS permits, etc.).

Certain toxins are not regulated if the amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed, at any time, the amounts indicated in the table on the *CDC's website.*

The following are requirements of the PI's possessing excluded Select Agent/toxin strains or Exempt toxin quantities:

1. Standard Operating Procedures: Prepare written SOP's for toxin-involved research processes.
2. Personnel Training:
    a. Ensure all staff has attended Laboratory Safety Training at least once.
    b. Provide initial lab-specific safety training to staff on toxin-involved processes, with updates as necessary.
    c. Maintain documentation of training for a period of at least 3 years.
    d. Training should include information on toxin-associated hazards, engineering controls (hoods), personal protective equipment, safe handling, secure storage, proper decontamination & disposal and administrative tasks such as inventorying & record keeping.

PI's must submit exclusion requests to the RO who will review the request and submit it to CDC and/or APHIS if deemed appropriate. Exclusion requests to CDC or APHIS must be signed by the RO and processed by Environmental Health and Radiation Safety (EHRS). Exclusion requests are evaluated by CDC or APHIS on an individual basis and may be granted if the agency determines the material does not pose a significant public health or safety threat.

C. Personnel Security Risk Assessment

Prior to working with or having access to Select Agents all individuals must undergo a security risk assessment (including fingerprinting) by the FBI. This process is arranged through Environmental Health and Radiation Safety (EHRS) with assistance from the Campus Police Department. Individuals wishing to have access to select agents must complete an FD-961 form and undergo fingerprinting in the Campus Police Department. This additional requirement for a background check is over and above any previous background checks performed on individuals wishing to work with select agents and toxins and they must freely submit to the process in accordance with federal law. Individuals will be entered into the On going Suitability Assessment Program, which requires additional interviews, and information collection annually.

D. Training

Select Agent training, provided by Environmental Health and Radiation Safety is required for authorized persons who are allowed access to Select Agents and Toxins. The RO must provide training in biosafety, containment, incident response, and security procedures to individuals with direct access to Select Agents and Toxins. This training will occur annually thereafter for those individuals with access to non-exempt quantities of select agents or toxins. Visitors must be informed of the safety and security requirements and procedures prior to being escorted into areas housing Select Agents and Toxins. In addition to the training provided by the RO, individuals must be trained by the PI in areas specific to the funded biosafety level three research.

E. Security

Stored Select Agents and Toxins must be secured in a locked container, incubator or freezer. Select Agents and Toxins not in storage must be controlled and maintained under constant surveillance. The CDC requires that there be three security levels associated with the secure storage of select agents and toxins.

Access to areas such as labs containing Select Agents and Toxins will be strictly controlled through the use of appropriate security measures. Special keys, activated security I.D.'s and other devices will be utilized to prevent unauthorized access to Select Agents and Toxins. These keys and cards will be jointly issued and tracked by the Environmental Health and Radiation Safety (EHRS) Department with assistance from Campus Police and I.T.

The RO/ARO is the only individual that can issue keys and activate I.D. cards that allow access to regulated amounts of Select Agents and Toxins and does so when all training and background checks have been performed as described in this policy.

F. Record keeping

The RO must keep an up-to-date accurate list of all individuals approved for Select Agent and Toxin access.

The RO must maintain records pertaining to inspections; safety, security and emergency response plans; training; transfer documents and incidents reports.

Principal investigators must maintain a current and accurate Select Agent and Toxin inventory as described in the relevant regulation. Principal investigators must maintain a log(s) as described in the relevant regulation to track all persons who enter the area where select agents are used or stored. The log(s) must record the time of entry and exit for (1) all approved users (2) others, along with the name of the approved escort. The PI must be prepared to provide this collected documentation to the RO upon request of this information.

The RO must maintain registration permits, transfer and receipt documentation and all related documentation.

The RO is required to maintain security records (e.g. transactions from automated access control systems, testing and maintenance of security and ventilation systems and visitor logs) and incident reports relating to the topics of biosafety, containment and biosecurity.

All records and logs must be kept for a minimum of 3 years

G. Transfer and Receipt of Select Agents and Toxins

Extramural transfers of Select Agents and Toxins may not occur without prior authorization of the RO at the facilities of the transferor and recipient. This is accomplished by contacting the the RO to complete an APHIS/CDC Form 2 as required by the CDC. The University RO will request that the PI provide contact information regarding the individual/site requesting a Select Agent or Toxin, transfer or receipt in order to expedite the process.

Intramural transfer of the Select Agents or Toxins must be approved by the RO before the transfer occurs.

The process for Extramural receipt of a Select Agent or Toxin from an outside entity will adhere to the following steps:

1. The RO/PI and the laboratory director/manager will have received prior notification of a pending shipment of a Select Agent or Toxin as the RO will have received a specialized form from the registered shipping facility.
2. The RO/PI will contact the laboratory director/manager to confirm the date of shipment and arrival with the registered shipping facility.
3. The RO/PI will contact the Shipping and Receiving Department on the day of the shipment, and again the next day to notify the the Receiving Department that a dangerous goods shipment of a biologic agent will be arriving via a carrier company on a predetermined date.
4. The RO/PI will request that they, or another designated approved individual be notified immediately when the carrier company arrives.
5. The RO/PI or approved designee will proceed to the dock immediately to receive the Select Agent or Toxin directly from the carrier company driver and take it from there directly to the BSL3 facility where it will be secured.
6. All paperwork associated with the shipment will be collected and maintained by the RO.

H. Destruction and Disposal

Destruction and disposal of Select Agents or Toxins must be done in accordance with federal procedures. The PI must complete a Notification of Destruction Form. This form documents the location, time and method of destruction for approval by the RO. Guidance on the destruction of select agents and toxins is available from the CDC at the following link: https://www.selectagents.gov/

I. Inspections

Prior to issuing a certificate of registration, the CDC or APHIS may inspect or evaluate a facility (entity). Additionally, the RO will inspect the locations of non-exempt laboratories on an annual basis or more often if deemed necessary. The focus of these inspections will monitor compliance with the CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL) Current Edition guidelines. The CDC has the authority to inspect the Registered Spaces at any time.

J. Continued Authorized Use of Select Agents and Toxins

Authorization for possession, use and manipulation of Select Agents and Toxins may be denied or withdrawn by the RO and referred to the appropriate federal authorities for action if:

1. Evidence exists that the PI or research personnel is not or is no longer capable of handling covered Select Agents or Toxins at the applicable Biosafety Level.
2. Evidence exists that the PI or research personnel has handled covered Select Agents and Toxins in a manner outside of acceptable Biosafety Level requirements.
3. Evidence exists that the PI or research personnel has failed to comply with any provisions of the law.
4. Evidence exists that the PI or research personnel has failed to comply with any aspect of this policy.
5. Evidence exists that the PI or research personnel has or intends to use covered Select Agents or Toxins in a manner harmful to the health of humans, animals or the environment.

K. Long-Term Storage

Agents may be placed in Long-Term storage when not accessed for a significant period of time (e.g., 30 calendar days) or when protocols are not active. The agents in long-term storage must be sealed in a manner which prevents or shows evidence of tampering. Agents stored in long-term storage must be checked for integrity of containment periodically. More information on Long-term storage can be found at https://www.selectagents.gov/ig-criteria.html

L. Clinical and Diagnostic Laboratories

Directors of Clinical or Diagnostic Laboratories that identify certain biological agents and toxins from diagnostic or verification testing activities are required to contact CDC and/or APHIS immediately. Directors must contact Environmental Health and Radiation Safety (EHRS) for further instructions.

V. REFERENCES

42 Part 73 Possession, Use and Transfer of Select Agents and Toxins, Interim Final Rule
http://oig.hhs.gov/authorities/docs/SelectAgentsToxinsCMPAuthorityIF.pdf

CDC Select Agent Program
http://www.selectagents.gov/

CDC Biosafety in Microbiological and Biomedical Laboratories (BMBL) Current Edition
http://www.cdc.gov/biosafety/publications/bmbl5/index.htm

VI. FORMS

FD-961
http://www.fbi.gov/about-us/cjis/bioterrorism-security-risk-assessment-form/bioterrorism-security-risk-assessment-form-fd-961

Source: Safety and Health Committee

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