



THE UNIVERSITY OF CHICAGO

MARINE BIOLOGICAL
LABORATORY

SELECT AGENT TOXINS POLICY

APRIL 2022

APPROVAL:

ANNE SYLVESTER DIRECTOR OF RESEARCH

4-26-22

DATE

DAVID MARK WELCH CHAIR, INSTITUTIONAL BIOSAFETY COMMITTEE

4-26-22

DATE

ERIC H. JENSEN BIOSAFETY OFFICER

4-26-22

DATE

TABLE OF CONTENTS

1	POLICY	3
2	ROLES AND RESPONSIBILITIES.....	3
3	PERMISSIBLE AMOUNTS OF SELECT AGENT TOXINS.....	4
4	REQUIREMENTS FOR POSSESSION OF SELECT AGENT TOXINS	5
5	LABORATORY PERSONNEL TRAINING	7
6	INACTIVATION OF SELECT AGENT TOXINS.....	8
7	LABORATORY SAFETY INSPECTIONS	8
8	TRANSFER OF SELECT AGENT TOXINS	9
9	SUSPECTED THEFT, LOSS OR RELEASE	9
10	RECORDKEEPING.....	9
11	REFERENCES.....	10
12	APPENDICES	10

1 POLICY

The Marine Biological Laboratory (MBL) is not a registered entity with the Federal Select Agent Program. Only research involving excluded Select Agents/Toxins at permissible amounts (exempt quantities) is permitted at the MBL. The purchase, use or transfer of Select Agents and Toxins above the permissible amounts requires prior approval by the MBL's Director of Division of Research and the United States Department of Health and Human Services (HHS).

This policy applies to all researchers, faculty, staff, and students who possess or use Select Agent Toxins at the MBL. Responsible Researchers (Course Directors, Resident Faculty, Whitman Scientists, Visiting Scientists, and other Principal Investigators) who possess, use, or transfer any quantity of Select Agent Toxin at the MBL must be registered with the MBL's Institutional Biosafety Committee (IBC).

This policy outlines MBL's institutional requirements for possession of Select Agent Toxins to ensure:

- (a) Safe handling, use, and storage procedures;
- (b) Effective tracking and security of Select Agent Toxins; and
- (c) Compliance with Federal Select Agent Program regulations.

2 ROLES AND RESPONSIBILITIES

2.1 Institutional Biosafety Committee (IBC)

- Providing oversight of the Select Agent Toxins program at MBL.
- Reviewing all research projects involving Select Agent Toxins.
- Ensuring MBL's institutional compliance with the Federal Select Agent Program regulations.
- Resolving any issues of non-compliance with federal regulatory requirements and IBC policies.
- Facilitating registration of MBL as an entity with the Federal Select Agent Program, if necessary.

2.2 Biosafety Officer (BSO)

- Managing purchase requests of Select Agent Toxins.
- Verifying inventories prior to purchase of any new Select Agent Toxin.
- Maintaining copies of inventories.
- Conducting Select Agent Toxins training to laboratory personnel.

2.3 Responsible Researchers

- Complying with federal regulations and MBL Select Agent Toxins policy.
- Registering research projects involving Select Agent Toxins with the IBC.
- Ensuring that all laboratory personnel involved with research described in an IBC protocol are added to the protocol.
- Ensuring Select Agent Toxins are ordered through the MBL's Biosafety Officer.
- Developing written lab-specific Standard Operating Procedures (SOPs).
- Maintaining accurate and up-to-date inventory of Select Agent Toxins.
- Ensuring the maximum permissible amount of Select Agent Toxins is never exceeded.
- Securing Select Agent Toxins against unauthorized access or removal.
- Conducting lab-specific training for personnel in safe handling, PPE, decontamination, storage and security procedures.
- Notifying IBC/BSO of any loss or theft of Select Agent Toxins.

2.4 Authorized Laboratory Users

- Getting prior authorization from Responsible Researcher before ordering any Select Agent Toxin.
- Ordering Select Agent Toxins through the MBL's Biosafety Officer.
- Verifying quantity received and logging amount of new Select Agent Toxin stock material into inventory form (see appendix).
- Updating inventory after using the Select Agent Toxin.
- Completing required laboratory safety training.

3 PERMISSIBLE AMOUNTS OF SELECT AGENT TOXINS

The following Select Agent Toxins are not regulated if the amount under the control of a Responsible Researcher at any time does not exceed the amounts indicated below.

Permissible (Exempt) Quantities of Select Agent Toxins

HHS Toxins	Maximum Amount
Abrin	1000 mg
Botulinum neurotoxins	1 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	10,000 mg
Ricin	1000 mg
Saxitoxin	500 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	100 mg
T-2 toxin	10,000 mg
Tetrodotoxin	500 mg

The following forms of these toxins are also exempt:

- (a) Any toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- (b) Nonfunctional Select Agent Toxins.

There are severe civil and criminal penalties for non-compliance with Federal Select Agent Toxins regulations. Each laboratory possessing or using Select Agent Toxins must maintain an accurate and up-to-date inventory records.

4 REQUIREMENTS FOR POSSESSION OF SELECT AGENT TOXIN

4.1 Authorization/IBC Registration

Responsible Researcher must register research projects involving Select Agent Toxins with the IBC. Contact the Biosafety Officer for assistance at 508-289-7424 or safety@mbi.edu.

4.2 Purchasing Select Agent Toxins

- Select Agent Toxins shall be ordered through the BSO using the MBL Purchase Order (PO) Form (hard copy).
- The BSO will review the PO and verify that: (a) requisition is properly authorized, and (b) order will not unintentionally exceed permissible amount, leading to violation of Federal Select Agent Toxin regulations.
- The BSO will place the order, which will be shipped to MBL Shipping & Receiving Department and delivered to Lillie Room 203.
- Upon receiving the order, the BSO will verify the order against the original PO.
- The BSO will deliver the order to the Responsible Researcher or Authorized User, who will sign a delivery note acknowledging receipt of the order.
- Upon receipt, the Responsible Researcher or Authorized User shall immediately verify the quantity received, log the amount of new stock material into the lab's inventory and lock up the stock materials in the Select Agent Toxins lockbox.
- The BSO will retain a copy of each purchase order and Inventory record.

4.3 Inventory Maintenance

- Accurate inventory of Select Agent Toxins must be kept current using the **Select Agent Inventory Record** (see Appendix). This form is designed to track specific Select Agent Toxin use and personnel access. The form must be kept current within the laboratory.
- The maximum permissible amount may never be exceeded.
- To ensure Responsible Researcher do not inadvertently exceed the permissible amounts of Select Agent Toxins, inventories must be checked prior to purchase. The inventory must also be promptly updated after every container of Select Agent Toxin is:
 - Acquired (by purchase or intra-campus transfer);
 - Depleted (by consumption or intra-campus transfer); and
 - Inactivated.

4.4 Storage and Security

Select Agent Toxins must be secured against unauthorized access. All stock solutions must be kept under lock and key.

- Properly stored with compatible chemicals within adequate secondary containment.

- Provided one layer of physical security (e.g., toxin secured within a locked freezer or secured within a permanently fixed lockbox).
- Select Agent Toxins must be only used by laboratory personnel approved by the Responsible Researcher. Before becoming an Authorized User, the Responsible Researcher must ensure that each person has received training and has been added to the appropriate IBC protocol.
- The laboratory must keep track of who uses the stock (and who has access to the freezer), recording each use in the **Select Agent Inventory Record** form.

4.5 Standard Operating Procedures (SOP)

The Responsible Researcher must develop a written toxin-specific SOP (see Appendix), which should include:

- Appropriate PPE (e.g., gloves, safety goggles or lab coat) provided.
- Safe handling, storage, and use procedures.
- Decontamination/inactivation and disposal procedures.
- Proper use of engineering controls to minimize exposures.

4.6 Engineering Controls

Ensure proper function (current certification) and use of any chemical fume hood or biosafety cabinet where procedures involving Select Agent Toxins are performed.

4.7 Personal Protective Equipment (PPE)

Appropriate PPE such as gloves, eye protection and lab coat, must be provided to laboratory personnel.

5 LABORATORY PERSONNEL TRAINING

The Biosafety Officer will provide initial training to all users prior to use of the select agent. The Responsible Researcher must provide lab-specific safety training to laboratory staff and students involved in use or handling of Select Agent Toxin. Training topics should include:

- Hazards associated with Select Agent Toxins.
- Engineering controls used to minimize exposure (e.g. chemical fume hood, biosafety cabinet).
- PPE to be used when handling Select Agent Toxins.

- Safe handling and storage.
- Proper decontamination and disposal.
- Emergency spill response.
- Administrative requirements (recordkeeping, inventory maintenance, security).

The lab-specific training should be documented within the department and records kept for at least three years.

6 INACTIVATION OF SELECT AGENT TOXINS

Principal Investigators shall only dispose of Select Agent Toxins using approved inactivation methods as described in **Inactivation of Select Agents** (see appendix).

- All generated Select Agent Toxin liquid waste shall be segregated as chemical hazardous waste. Decontaminate the waste using appropriate method.
- Sharps: Dispose glass vial(s), needles, and syringes in a puncture-resistant sharp container.
- Stock vials and other solid waste (e.g., gloves, adsorbent paper): Remove or deface all hazard warning labels on container/vial. Collect in a leak-proof container and place in the biohazard waste container.
- Collect and autoclave solid waste at the end of the Course/project (or more frequently, as deemed appropriate).
- Autoclave or chemically disinfect contaminated PPE before reuse.

7 LABORATORY SAFETY INSPECTIONS

7.1 Laboratory Self-Inspection

The Responsible Researcher must conduct annual self-inspections using the **Inspection for Select Agents** checklist (see appendix), including:

- Verification of appropriate labeling, storage, secondary containment, and security measures.
- Verification that physical and inventories are accurate
- Review of Authorized Users List and verify authorized access to Select Agent Toxins.

Records of self-inspections must be maintained by the department for at least three years after the last date of Select Toxin use, possession, or disposal.

7.2 Laboratory Safety Audit

The BSO will conduct annual audit of each lab with Select Agent Toxins. The inspection will include:

- Review of Authorized Users list to verify authorized access to toxins.
- Verification of appropriate labeling, storage, secondary containment, and security measures.
- Comparison of physical inventory with what is accounted for in the records.
- A copy of the current recorded inventory signed and dated by the Responsible Researcher, will be collected at the time of the audit.

8 TRANSFER OF SELECT AGENT TOXINS

Responsible Researcher shall not authorize purchase of Select Agent Toxins for stock piling, distribution, transfer or sharing. They should acquire Select Agent Toxins ONLY through the Biosafety Officer, use all of the toxins under their custody, and maintain current and accurate inventory.

9 SUSPECTED THEFT, LOSS OR RELEASE

Upon discovery of the theft or loss of Select Agent Toxins, laboratory personnel must immediately notify the Responsible Researcher and BSO/IBC. The BSO/IBC shall notify appropriate regulatory agents. Thefts or losses of Select Agent Toxins must be reported even if the toxin is subsequently recovered or the responsible parties are identified.

10 RECORDKEEPING

The following records shall be maintained at the laboratory's location:

- Copies of each toxin purchase order.
- Select Agent Inventory Record.
- Training records.

The records shall be kept for at least 3 years after the Select Agent Toxin is completely used up or is destroyed.

The Biosafety Officer will maintain records for the initial Select Agent Training, and the Select Agent Inventory Records forms (upon either user leaving MBL or upon completion of Toxin use).

11 REFERENCES

1. **Federal Select Agent Program**
<http://www.selectagents.gov/>.
2. **Permissible Toxin Amounts**. Federal Select Agent Program.
<https://www.selectagents.gov/PermissibleToxinAmounts.html>
3. **Select Agent Toxins Exclusions**. Federal Select Agent Program.
<https://www.selectagents.gov/SelectAgentsandToxinsExclusions.html>
4. ***Biosafety in Microbiological and Biomedical Laboratories*** (BMBL), 5th Edition, 2009. Centers for Disease Control and Prevention (CDC) and the National Institute of Health (NIH).
<https://www.cdc.gov/biosafety/publications/bmb15/BMBL.pdf>
5. ***NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)***. April 2016. Office of Science Policy, National Institutes of Health, Bethesda, MD.
https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf

12 APPENDICES



LAB-SPECIFIC STANDARD OPERATING PROCEDURE (SOP) FOR SELECT AGENT TOXIN

Responsible Researcher:	
Department/Course:	
Building:	Room:
Name of Select Agent Toxin:	Date:
RISK ASSESSMENT	
<ul style="list-style-type: none"> • Maximum amount stored. • Amount used in experiments. • LD₅₀ • Describe risks inherent to procedures (use of powders, aerosol formation, potential routes of exposures, etc.). • Engineering Controls (fume hood, biosafety cabinet, etc.) • Proper PPE (lab coat, gloves, safety goggles; respiratory protection may be required). 	
INACTIVATION AND DISPOSAL PROCEDURES (<i>refer to BMBL Appendix I</i>).	
LABORATORY PERSONNEL TRAINING REQUIREMENTS (<i>list laboratory specific training required to work with material</i>).	
SPILL/ACCIDENT RESPONSE PROCEDURES (<i>describe what to do in the case of a spill or exposure</i>).	

OCCUPATIONAL HEALTH INFORMATION <i>(describe available and/or required vaccines, prophylactic treatments etc.).</i>		
STORAGE/SECURITY <i>(describe how the material will be securely stored).</i>		
INVENTORY MAINTENANCE <i>(describe how the inventory will be maintained).</i>		
LIST OF Authorized USERS		
Name	Signature	Date

Responsible Researcher (Signature): _____ **Date:** _____

Biosafety Officer (Signature): _____ **Date:** _____



INSPECTION FOR SELECT AGENTS

Responsible Researcher:	Email:
Laboratory Supervisor:	Email:
Department/Course:	Phone:
Building:	Room #:
Inspected By:	Inspection Date:

General Safety	YES	NO	N/A
Laboratory has a written SOP for Select Agent Toxin.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
SDS is available for the Select Agent Toxin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Proper PPE is available and used during handling procedures	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rooms where Select Agent Toxins are used are properly posted	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Waste associated with the Select Agent Toxin is being properly decontaminated prior to disposal	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Authorized Users and Safety Training			
Authorized Users have been reviewed and verified active list is current?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
All Authorized Users have been provided safety training on the procedures involving Select Agent Toxin?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Training documentation maintained for a minimum of 1 year?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Inventory Verification			
Inventory has been reviewed and is consistent with the actual amounts of Select Agent Toxin(s) in the laboratory?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Inventory log is current and up to date	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Storage and Physical Security Measures			
Access to Select Agent Toxins is restricted to authorized personnel	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
All Select Agent Toxins containers labeled properly?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
All Select Agent Toxins are stored within secondary containment in a locked freezer, or secured within a permanently fixed lockbox?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

LIST ANY OTHER DEFICIENCIES FOUND
LIST CORRECTIVE ACTIONS

Responsible Researcher (Name): _____

Responsible Researcher (Signature): _____ **Date:** _____

Biosafety Officer (Signature): _____ **Date:** _____



INACTIVATION OF SELECT AGENTS

NaOCl = Sodium hypochlorite; NaOH = Sodium hydroxide

SELECT AGENT TOXIN	Autoclaving (121°C; 1 hour)	2.5% NaOCl + 0.25N NaOH	2.5% NaOCl	1.0% NaOCl	0.1% NaOCl
Abrin	YES	YES	YES	YES	YES
Botulinum neurotoxins	YES	YES	YES	YES	YES
Diacetoxyscirpenol (DAS)	NO	YES	NO	NO	NO
Ricin	YES	YES	YES	YES	YES
Saxitoxin	NO	YES	YES	YES	YES
Staphylococcal enterotoxins (A-E)	YES ^b	YES	YES	YES	YES
T-2 Toxin	YES	NO	NO	NO	NO
Tetrodotoxin	NO	YES	YES	YES	NO

YES = Complete inactivation; NO = No inactivation.

a = Exposure (**30 minutes**) to various concentrations of sodium hypochlorite with or without sodium hydroxide; b = assumed inactivation.

Conotoxin inactivation depends on the presence or absence of disulfide bonds.

1. For conotoxins with disulfide bonds: incubate with an excess of dithiothreitol (DTT) (10-20mM buffered solution, pH 8.7) for at least 1 hour at room temperature or 30 minutes at 50°C. Add an equal volume of 50-100mM solution of iodoacetamide (buffered solution, pH 8.7) and incubate for 1 hour at room temperature.
2. For conotoxins without disulfide bonds, incubate in a chemical fume hood in a closed glass vial with 6N HCl for 24 hours at 90-110°C.