Toxin Best Practices for a Non-Toxic Workplace

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Abstract

Select agents and toxins are biological materials that have the potential to pose a severe threat to public health and safety, animal and plant health, or animal and plant products. The Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA) allow for the storage and use of select toxins in permissible quantities without full enrollment in the Federal Select Agent Program (FSAP) (42 CFR, Part 73). It can be a challenge for programs to ensure regulatory compliance regarding permissible limits of select toxins. Without full FSAP regulation awareness, principal investigators (PI's) using toxins in exempt quantities may lack program oversight for monitoring access and usage, and such a lack could pose a serious biosecurity threat. To address this gap, NIH regularly visits select toxin laboratories to ensure regulatory awareness and appropriate recordkeeping. This year, we implemented a survey across all NIH select toxin laboratories to ensure compliance and reveal areas for improvement. We provide details of the questionnaire reflecting the status of best practices for the following categories: Toxin Logbook, Select Toxin Quantity, Toxin Security/Access, and Toxin Ordering/Acquisition. While results demonstrated compliance, with all laboratories well below the permissible limit, this initiative revealed areas for collaborative improvement. We achieved implementing improved security measures, increased regulatory awareness, and enhanced documentation methods. This experience uncovered a need to provide standard operating procedures (SOPs) for inactivation and proper disposal of select toxins used at the NIH.

Introduction

Select agents and toxins are carefully regulated in biomedical research to ensure proper possession, use and transfer of these potential bioterrorism agents. However, toxins are permitted to be in a lab without a registration with the FSAP if the amount possessed by the PI does not exceed the amounts indicated in Table 1. Although these agents do not require FSAP registration, it is important that laboratories adhere to best practices such as tracking, transferring, and securing the inventory. This ensures that the total amount of toxin is always maintained below the permissible limits. Furthermore, when transferring toxin, there are requirements that an entity document due diligence, which ensures that the PI receiving the toxin is eligible and has a legitimate need to handle the toxin. Finally, the toxin must be secured against theft, loss or release during the period between identification and either the transfer or destruction of the toxin. For this study, we define compliance as at least 2 means of security. , not including the campus nor the building.

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**

Table 1: Select Toxin Permissible Amounts ~ The maximum amount of select toxin that a PI can maintain without obtaining approval from the FSAP.

Resources:

1. https://www.selectagents.gov/compliance/guidance/toxin/docs/Select_Toxin_Guidance.pdf
2. https://www.ecfr.gov/current/title-42/chapter-I/subchapter-F/part-73

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Methods

To measure compliance, a list of 14 questions were created that focused on the following categories: Toxin Logbook, Select Toxin Quantity, Toxin Security/Access, and Toxin Ordering/Acquisition (Table 1). Furthermore, improvements and updates were made to the Toxin Exclusion Form (TEF) that investigators and researchers sign as their attestation to remain below the permissible limit. Additionally, the TEF informs all laboratory personnel of the unique regulatory aspects of performing Due Diligence for any potential transfers regardless of amount, and the requirement to report any suspicious activity regardless of the 'exempt' status. Our findings represent all the laboratories surveyed, except those without inventory or wished to inactivate their registrations. Finally, we authored an overview of the best practices for working with select toxins, which was distributed to all laboratories.

Toxin Logbook	Logbook is kept in a secure location?
	Logbook is current and inventory records reflect total amount (in mg)?
	Inventory is centrally tracked by an individual with toxin access?
	Generation/Use/Disposal marked by user and described?
	TEF and Best Practices form updated for the logbook?
Select Toxin Quantity	PI and personnel are aware of the permissible limit for the toxin (s)?
	PI/Personnel are informed of the regulatory aspects regarding usage?
	Select Toxin quantities in possession are within limits?
Toxin Security / Access	Toxin is stored in a secured and locked location, accessible only by registered users?
	Are all aliquots of the toxin kept centrally and tracked accurately?
	All individuals with access have either signed the TEF or PI Dashboard?
Toxin Ordering / Acquisition Rules	Is all toxin obtained via a commercial source?
	Has any toxin come from or gone out to another source/user (collaborator, other facility or laboratory)?
	Have the important aspects regarding toxin usage as outlined in our "Best Practices" form been explained to the PI and laboratory personnel?

Table 2: Exempt Select Toxin survey questionnaire ~ A list of 14 questions asked to NIH laboratories about their permissible select toxin storage and use.

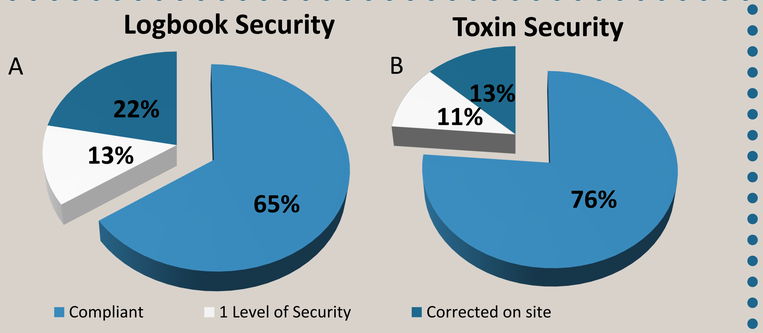

Figure 1: Security ~ A) Security of select toxin inventory logbook, measured as a percent for all laboratories, compliance measured by at least 2 means of security. B) Security of select toxin, measured as a percent for all laboratories, compliance measured by at least 2 means of security.

Figure 2: Toxin Security Solutions ~ Examples of additional means to secure select toxins. A) Locking refrigerator box B) Portable safe with cable and/or C) Freezer lock.

Results

Overall, the results of this survey showed a high rate of compliance to regulations. Every laboratory was below the permissible limit of select toxins. Figure 1 shows that 65% of the laboratories had 2 levels of security for the inventory logbook (Fig. 1A). Of the remaining 35%, 22% were able to add additional security on site and 13% required further efforts to achieve 2 levels of security. Similarly, for the toxin security, 76% of laboratories demonstrated 2 levels of security, 13% were able to add additional security on site and 11% required further efforts to achieve 2 levels of security. (Fig. 1B). For laboratories that required additional measures, security devices such as locking refrigerator boxes (Fig. 2A), portable safes with a cable (Fig. 2B), or freezer locks (Fig. 2C) were recommended. As it is necessary to determine exact inventory amount, we examined the accuracy of the inventory and associated documentation. Accuracy of inventory was measured by ensuring that the logbook was current, centralized, and that the records reflected the total amount of toxin remaining in mg (Fig. 3A). Accuracy of documentation was measured by whether all the users of the toxin and the PI signed the most recent TEF and online registration (Fig. 3B). Finally, additional information such as the commercial toxin source, and knowledge of regulations and limits were collected (Fig. 4).

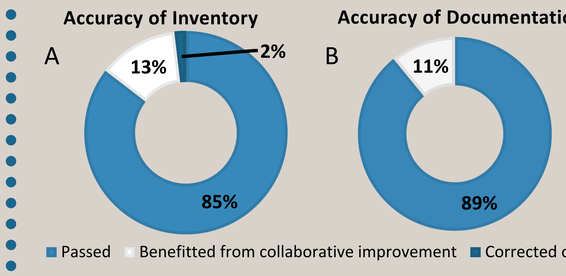

Figure 3: Accuracy of Records~ A) Inventory accuracy was measured by whether the inventory records were up to date, kept in a central location, and reflected the total amount of toxin remaining in mg. B) Documentation accuracy was determined by whether all users and the PI signed the current TEF and online registration (both are used).

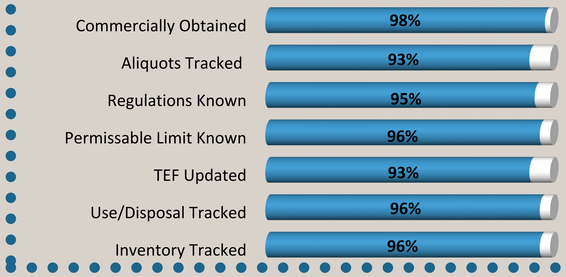

Figure 4: Toxin Ordering and Access ~ Most laboratories demonstrated high compliance to questions focused on toxin sourcing, access, and FSAP regulation knowledge.

Conclusion

Overall, compliance with select toxin regulations and expectations was high and this study revealed areas of improvement regarding redundant security and better recordkeeping, many of which were able to be implemented on site. After the interim period of the pandemic, a collaborative 'correction to center' was useful for some laboratories. Our experience with laboratories revealed their own creative solutions for additional select toxin security (Fig. 2) and the benefit of electronic logbooks and inventory systems (such as FreezerPro and barcoding). Furthermore, the laboratory survey process uncovered a need to provide SOPs for the inactivation of, and proper disposal of select toxins studied at the NIH.