Abstract

The APHIS/CDC Form 3, Report of Theft, Loss or Release of Select Agents and Toxins (TLR incident report) is the mechanism by which the theft, loss or release of a biological select agent and toxin (BSAT) is reported to the United States Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS) or Health and Human Services (HHS)/Center for Disease Control and Prevention (CDC). A total of seven hundred and twenty seven (727) TLR Incident Reports were received by CDC between 2004 and 2010. Based on information contained in these reports, there were:

- No reports of the theft of any BSATs,
- One confirmed loss of a BSAT occurred during shipment out of 3412 transfers of BSAT conducted during that time period.
- Eleven total laboratory acquired infections (LAls) associated with BSAT releases reported to CDC between 2004 and 2010, in an average annual population of approximately 10,000 individuals with approved access to BSATs. No fatalities resulted from these infections and there were no reported cases of secondary transmission to other humans.
- Annual increases in the number of TLR reports submitted to CDC from 16 reports in 2004 to 269 reports in 2010.
- Approximately half of the reports were submitted by entities registered with CDC and approved to possess BSATs (59%) with slightly less than half submitted by entities exempt from registration and inspection (41%), (primarily diagnostic laboratories). In 2009 and 2010, the number of TLR incident reports from exempt entities 104 and 148, respectively) exceeded those submitted by registered entities (88 & 96, respectively). The majority of TLR Incident Reports from registered entities involved Biosafety Level 3 (BSL-3) laboratories. Most reports from exempt entities involved Biosafety Level 2 (BSL-2) laboratories.
- The majority of reports from both registered and exempt entities involved bacterial agents.

These results show that the Federal Select Agent Program has been successful in implementing a monitoring program, increasing compliance of registered and exempt laboratories (as evidenced by increasing numbers of reports) and effective investigation that identified some LAls, and resolved other loss & release reports to determine that biosafety and security in U.S. labs is being sustained.

Introduction

After the 2001 anthrax attacks in the United States, Congress recognized the growing threat posed by BSATs as potential weapons of mass destruction. Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and the Agricultural Bioterrorism Protection Act of 2002 expanded the authority of the federal government to regulate the possession, use or transfer of agents and toxins that have the potential to pose a severe threat to public health and safety, to animal health and animal products, or to plant health and plant products (biological select agent and toxin, BSAT) (42 Code of Federal Regulations [CFR] Part 73, 9 CFR Part 121, and 7 CFR Part 331, respectively). These regulations gave the federal government the power to specify conditions that must be met by all individuals, private and public organizations, academic institutions and government agencies in order to be lawfully in possession of biological select agents and toxins (BSAT). The enforcement of these regulations has been delegated to CDC and APHIS by the HHS and USDA Secretaries, respectively. The Division of Select Agents and Toxins (DSAT) at CDC has been assigned the responsibility for oversight of the BSAT regulations found in 42 CFR Part 73.

One of the key elements of the select agent regulations is the requirement imposed on all entities (e.g., laboratories or individuals) to immediately report any theft, loss or release (TLR) of BSATs to either CDC or APHIS (42 CFR § 73.19). This applies to entities that are required to register with CDC or APHIS (e.g., those possessing, using, or transferring select agents) and undergo inspections as well as to those exempted under 42 CFR § 73.5 and 73.6. Exempt entities primarily consist of diagnostic laboratories that are not registered with CDC or APHIS to possess BSATs, but may encounter them in their routine diagnostic activities. Both registered and exempt entities must also submit a more detailed report within seven calendar days following the occurrence or recognition of a TLR incident. These requirements allow CDC or APHIS to ensure that all TLR incidents are reported to law enforcement authorities when necessary, to assess risk to public health, worker safety and animal or plant resources, and to respond with appropriate actions as needed.
In the current manuscript, we present data reported to CDC from 2004-2010 following implementation of a nationwide program for monitoring the potential theft, loss, or release of BSATs.

**Materials and Methods**

**TLR Incident Reporting Requirements**—Reporting requirements for all entities in possession of BSATs are found in 42 CFR § 73.19 entitled “Notification of theft, loss, or release.” Specifically, “Upon discovery of the theft or loss of a select agent or toxin, an individual or entity must immediately notify CDC or APHIS and appropriate Federal, State, or local law enforcement agencies. Thefts or losses must be reported even if the select agent or toxin is subsequently recovered or the responsible parties are identified” (42 CFR 73.19[a]). In addition, “A completed APHIS/CDC Form 3 must be submitted within seven calendar days” (42 CFR 73.19[a][2]).

In addition, “Upon discovery of a release of a select agent or toxin causing occupational exposure or release of a select agent or toxin outside of the primary barriers of the biocontainment area, an individual or entity must immediately notify CDC or APHIS” (42 CFR 73.19[b]). “A completed APHIS/CDC Form 3 must be submitted within seven calendar days” (42 CFR 73.19[b][2]).

The 2008 Federal Select Agent guidance document (Select Agents and Toxins Theft, Loss or Release Information Document) defines an “occupational exposure” as “any event which results in any person in a registered facility or lab not being appropriately protected in the presence of an agent or toxin.” This may include reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potential infectious materials that may result from the performance of a person’s duties. For example, a sharps injury from a needle being used in select agent or toxin work would be considered an occupational exposure. This definition for any occupational exposure is derived largely from the Occupational Safety and Health Administration (OSHA) regulation 29 CFR § 1910.1030 (Bloodborne pathogens).

**Event data collection and processing**—Information contained in APHIS/CDC Form 3, Report of Theft, Loss or Release of Select Agents and Toxins submitted by reporting entities to CDC from 2004 through 2010 was used in this analysis. Information derived from these forms and other communications that is relevant to this manuscript includes: 1) the reporting entity type (registered, exempt), the biocontainment facility type, the agent, and the event type (theft, loss or release).

**Disposition of reports.** The first response by CDC after initial notification of a TLR incident involves an immediate assessment of the public health risk posed by the incident. The initial notification could be sent immediately or within 7 days.

The second phase of the TLR incident report disposition process involves a number of steps including:

1. **Data collection and processing**—CDC collects and reviews all information provided by an entity in the initial report of the event, information provided in the Incident report form, information collected through verbal communications and written correspondence during the post-event evaluation process, and other information obtained during inspections and investigation of the event. If appropriate, referrals to law enforcement and/or consultations with subject matter experts are made at this time.

2. **Review and evaluation**—CDC conducts a review of factors that may have contributed to the occurrence of the TLR event, such as deficiencies in training, equipment malfunctions or inadequacies in safety procedures. These evaluations include attempts to identify steps that can be taken to reduce the likelihood of a recurrence of the event, such as improved engineering or work practice controls.

3. **Follow-up and report closure**—CDC requests confirmation that appropriate medical evaluation and interventions are being provided for potentially exposed workers. In addition, CDC requests periodic reports of potentially exposed worker health status, when necessary, and that any adverse change in the health status of the potentially exposed workers related to this event is immediately reported to CDC. CDC also provides contact information for subject matter experts in other organizational units at CDC to entities and occupational health providers for assistance, if requested.

4. CDC also requests written assurance, when appropriate, that all specimens and samples that may contain BSATs are either properly destroyed, secured or transferred to another entity approved for storage of the BSATs. Depending upon the seriousness of the incident, CDC may perform onsite visits to enhance incident evaluation and fact-finding or to verify the application of remediation procedures.

**Data analysis**—Information received by CDC from entities reporting TLR events was collected from the sources discussed above and compiled into an Excel spreadsheet. Information regarding the type of agent, laboratory type, activities associated with the TLR event, entity type, and other pertinent facts were analyzed to identify patterns and trends that may be useful for improving laboratory safety and security. For the calculation of rates of reports per 1000 workers, the total number of workers with approved access to select agents was used as a denominator. For calculation of reports per 100 registered entities, the total number of registered entities obtained from the National Select Agent Registry (NSAR) data base was used as a denominator.

The rate of report submissions per 100 registered entities or per 1000 workers with security risk assessment (SRA) approval was determined for each year between 2004 and 2010. The rate of report submissions per 100 registered entities or per 1000 workers was calculated by dividing the number of each type of report by the number of entities with completed registration documentation (i.e., registered entities) x 100 or by the number of workers with
approved security risk assessments at registered facilities x 1000, respectively.

The total number of BSAT shipments approved by CDC was determined by counting the number of approved requests for transfers.

**Results**

A total of 727 TLR Reports were received by CDC between 2004 and 2010 (Table 1). During this time period, there were no thefts of BSATs reported to CDC. Of the 727 reports received, 88 (12%) were loss reports and 639 (88%) were release reports. The final disposition of BSATs described in the 88 loss reports was reconciled in all but one report. In this particular case, a shipment of *Coccidioides immitis* was lost during transit. An investigation of this incident led by the FBI concluded that this shipment was apparently destroyed during processing at a commercial shipping facility in the United States.

There were 11 laboratory acquired infections (LAIs) that resulted from the incidents described in the 639 release reports. The rate of increase in release reports subsided to less than 10% of registered entities in 2007 to 25 in 2010 but the number of these reports fluctuated between 2004 and 2010. The rate of release report submissions tripled between 2006 and 2007 and increased by nearly 60% again in 2008. The rate of report submissions per 100 registered entities increased by nearly three-fold in 2007 from the previous year (Figure 1). Additional increases occurred each year successively thereafter from 47 reports in 2007 to 80 in 2008, to 88 reports in 2009 and to 96 reports in 2010. There was also an increase in the number of loss reports from registered entities from 5 reports in 2007 to 25 in 2010 but the number of these reports fluctuated during the 7 year period.

The annual distribution of TLR Reports submitted between 2004 and 2010 is shown in Table 1. The number of reports received annually ranged from 16 in 2004 to 269 in 2010. There was a substantial increase in the total number of reports each year throughout the entire time period. Approximately 70% (62 of 88) of all loss reports were submitted between 2007 and 2010, and approximately 94% (601 of 639) of all release reports were received during this same 4-year period. The number of release reports from registered entities increased by nearly three-fold in 2007 from the previous year (Figure 1). Additional increases occurred each year successively thereafter from 47 reports in 2007 to 80 in 2008, to 88 reports in 2009 and to 96 reports in 2010. There was also an increase in the number of loss reports from registered entities from 5 reports in 2007 to 25 in 2010 but the number of these reports fluctuated during the 7 year period.

The rate of report submissions per 100 registered entities is shown in Figure 2 (left axis) along with the number of registered entities (right axis) for each year. The number of entities registered to possess BSATs during this time period ranged from a low of 136 in 2004 to a maximum of 327 registered entities in 2005.

The rate of release reports ranged from 2.8 reports in 2005 to 29.6 reports per 100 registered entities in 2010. The rate of release report submissions tripled between 2006 and 2007 and increased by nearly 60% again in 2008. The rate of increase in release reports subsided to less than 10% in 2009 and 2010. The rate of loss report submissions de-

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**Table 1**

Number of BSAT loss and release reports received by CDC between 2004 -2010.

<table>
<thead>
<tr>
<th>Year</th>
<th>Loss #</th>
<th>Loss (%)**</th>
<th>Release #</th>
<th>Release (%)</th>
<th>Annual Report Total #</th>
<th>Annual Report Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>8</td>
<td>(9.1)</td>
<td>8</td>
<td>(1.3)</td>
<td>16</td>
<td>(2.2)</td>
</tr>
<tr>
<td>2005</td>
<td>12</td>
<td>(13.6)</td>
<td>9</td>
<td>(1.4)</td>
<td>21</td>
<td>(2.9)</td>
</tr>
<tr>
<td>2006</td>
<td>6</td>
<td>(6.8)</td>
<td>21</td>
<td>(3.3)</td>
<td>27</td>
<td>(3.7)</td>
</tr>
<tr>
<td>2007</td>
<td>5</td>
<td>(5.7)</td>
<td>52</td>
<td>(8.1)</td>
<td>57</td>
<td>(7.8)</td>
</tr>
<tr>
<td>2008</td>
<td>15</td>
<td>(17.0)</td>
<td>113</td>
<td>(17.7)</td>
<td>128</td>
<td>(17.6)</td>
</tr>
<tr>
<td>2009</td>
<td>17</td>
<td>(19.3)</td>
<td>192</td>
<td>(30.0)</td>
<td>209</td>
<td>(28.7)</td>
</tr>
<tr>
<td>2010</td>
<td>25</td>
<td>(28.4)</td>
<td>244</td>
<td>(38.9)</td>
<td>269</td>
<td>(37.0)</td>
</tr>
<tr>
<td>Total</td>
<td>88</td>
<td>(100)</td>
<td>639</td>
<td>(100)</td>
<td>727</td>
<td>(100)</td>
</tr>
<tr>
<td>Annual Average</td>
<td>13</td>
<td>-</td>
<td>91</td>
<td>-</td>
<td>104</td>
<td>-</td>
</tr>
</tbody>
</table>

* = There were no thefts reported between 2004-2010

** = percent of total reports in category for 2004-2010
Figure 1
Annual numbers of BSAT release event reports from registered and exempt entities between 2004 and 2010. A comparison between the number of reports received from registered (dark bars) and exempt (light bars) entities is shown graphically for each year between 2004 and 2010. The actual number of reports submitted by both types of entities each year is also shown above the bars. There were no reports submitted by exempt entities in 2004 and 2005.

Figure 2
Annual rates of BSAT reports of loss and release events submitted to CDC per 100 registered entities, 2004-2010. The rate of reports of loss events per 100 registered entities between 2004 and 2010 is graphically illustrated using lines connecting solid squares. The annual rate of release event reports is indicated using open circles. The scale for both loss and release report rates are shown on the left side of the graph. The number of entities registered with CDC to possess BSATs each year that was used to calculate the rates shown in this graph is also indicated for each year using “X” symbols. The reference scale for the number of registered entities is shown on the right side of the graph. The numerical values for loss and release rates as well as the number of registered entities are shown above each symbol.
clined from 5.9 in 2004 to 1.7 in 2007 but then increased to 7.7 reports per 100 registered entities in 2010.

The rate of report submissions per 1000 workers with security risk assessment (SRA) approval between 2004 and 2010 is shown in Figure 3 (left axis) along with the number of SRA approved workers for each year (right axis). The number of SRA approved workers at registered entities ranged between a low of 8,185 workers in 2004 to a maximum of 10,979 workers in 2009. There was a small (< 4%) decline in 2010 to 10,639 approved workers. On average, there were 9,768 SRA approved workers annually between 2004 and 2010. The rate of release report submissions ranged from 1 report in 2004 to approximately 9 reports per 1000 workers in 2010. Most of this increase occurred in 2007 (+167%) and 2008 (+54%). Additional annual increases of approximately 8% and 9% in this rate were observed in 2009 and 2010, respectively. The rate of loss report submissions fluctuated between 0.6 in 2006 and 2.3 per 1000 workers in 2010.

Prior to 2006, there were no TLR reports received from exempt entities. The number of release reports from exempt entities increased from 4 reports in 2006 to 148 reports in 2010 (Figure 1). After 2007, there was a rapid rise in the number of reports received from exempt entities each year, but unlike reports received from registered entities, the increase in report submissions did not subside in 2009 and 2010. The number of release reports submitted by exempt entities exceeded those submitted by registered entities in both 2009 and 2010. There was only one loss report submitted by an exempt entity during the entire time period. The submission rates per entity or per worker for exempt entities could not be determined because the total number of exempt entities or the number of workers at these entities is not known.

Ninety-two percent of the loss reports from regulated and exempt entities were associated with laboratory biocontainment (i.e., BSL) facilities instead of animal biocontainment (i.e., ABSL) facilities (Table 2). Most (~68%) of these events involved BSL-3 laboratories at registered facilities. Seven loss reports were submitted by registered entities performing animal work in ABSL-3 laboratories. Nearly two-thirds (65.9%) of all loss reports were inventory discrepancies. Other losses were categorized as discarded samples (14%) and shipping/transport errors (18%). There was only one loss report submitted by an exempt entity.

Eighty-five percent (537 of 639) of all release reports occurred in BSL facilities compared with ABSL facilities. However, more release reports were received from exempt than registered BSL facilities (290 vs. 247 reports, respec-

Figure 3
Annual rates of BSAT reports of loss and release events per 1000 workers with access approval.
The rate of release event reports and loss reports between 2004 and 2010 per 1000 workers with security clearances is graphically illustrated using lines connecting solid squares. The annual rate of release event reports release reports submitted to CDC per 1000 workers is indicated using open circles. The scale for both loss and release report rates are shown on the left side of the graph. The number of workers with approved security risk assessments each year that was used to calculate the rates shown in this graph is also indicated for each year using “X” symbols. The reference scale for the number of approved workers is shown on the right side of the graph. The numerical values for loss and release rates as well as the number of approved workers are shown above each symbol.
Laboratory and Animal biocontainment facility types associated with BSAT loss and release reports.

<table>
<thead>
<tr>
<th>Laboratory Type</th>
<th>Registered Entities</th>
<th>Exempt Entities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Loss Reports % d</td>
<td># Release Reports % d</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSL2</td>
<td>21 24</td>
<td>64 19</td>
</tr>
<tr>
<td>BSL3</td>
<td>59 68</td>
<td>169 49</td>
</tr>
<tr>
<td>BSL4</td>
<td>0 0</td>
<td>14 4</td>
</tr>
<tr>
<td>BSL</td>
<td>80 a 92</td>
<td>247 72</td>
</tr>
<tr>
<td>ABSL2</td>
<td>0 0</td>
<td>8 2</td>
</tr>
<tr>
<td>ABSL3</td>
<td>7 8</td>
<td>89 26</td>
</tr>
<tr>
<td>ABSL4</td>
<td>0 0</td>
<td>1 &lt;1</td>
</tr>
<tr>
<td>ABSL</td>
<td>7 b 8</td>
<td>98 28</td>
</tr>
<tr>
<td>Total # of reports</td>
<td>87 100</td>
<td>345 100</td>
</tr>
</tbody>
</table>

a = # of reports from laboratory biocontainment facilities (BSL)
b = # of reports from animal biocontainment facilities (ABSL)
c = Total # of reports (BSL + ABSL laboratories)
d = % of total reports

tatively). Ninety-one percent of reports from exempt laboratory BSL facilities involved BSL-2 laboratories, whereas most (~68%) of these reports from registered entities were associated with BSL-3 facilities. Most (98 of 102) of the reports from ABSL facilities were submitted by registered entities. Approximately 90% of these reports from registered entities involved ABSL-3 containment facilities. There were three reports from exempt ABSL-2 facilities and 1 from an exempt ABSL-3 entity (Table 2).

The number and types of BSATs described in the release reports could be determined for both registered and exempt entities. The total number of each type of agent is shown in Table 3 along with information about the numbers of agents reported by registered and exempt entities. There were 22 release reports in which more than one BSAT was involved. The total number of agents reported in the 639 release reports received by CDC was 676.

Both registered and exempt entities listed bacterial species as the most predominant type of agent in these reports. However, bacteria constituted a substantially larger fraction of all agents reported by exempt entities compared to registered facilities (81% vs. 63%, respectively). Sixteen percent of agents reported by exempt entities were fungi but this type of agent was rarely reported (<3% of total agents) by registered facilities. Together, bacterial and fungal agents accounted for 97% of all agents reported by exempt entities. Viral agents were very rarely (<2% of total agents) reported by exempt entities but accounted for 23% of all agents associated with release reports submitted by registered entities. Release reports involving rickettsial agents were uncommon overall (3.6% of total) and extremely rare at exempt entities (0.7% of exempt total). There was only 1 report from an exempt entity that involved a toxin whereas 22 reports involving toxins were submitted by registered entities.

The annual distribution, type of select agent, type of entity and type of containment facility in which the 11 laboratory acquired infections occurred that were reported to CDC between 2004-2010 are shown in Table 4. There were five LAs in 2004, two cases in 2007, one case in both 2008 and 2009, and two cases reported in 2010. There was only 1 TLR incident in which more than one LAI resulted from the release. This release occurred in 2004 and resulted in lab-acquired tularemia in three lab workers. Ten of the 11 LAs involved bacterial agents whereas the remaining case resulted from exposure to a fungal agent.

LAs occurred in both registered (8 cases) and exempt (3 cases) facilities. The majority of reports (5; some reports involved more than one case) and cases (7) involved BSL-2 laboratories in both registered and exempt entities. The remaining 4 LAs occurred in BSL-3 laboratories located in registered facilities. All LAs reported by exempt facilities occurred in BSL-2 laboratories.

There were 3412 approved shipments of BSAT between 2004 and 2010. There was only shipment that was lost during transit. An investigation by law enforcement agencies concluded that the shipment was destroyed during shipment.

Discussion

This is, to the best of our knowledge, the first formal report describing the results of a national BSAT TLR reporting system focusing on high risk biological agents. After monitoring over 300 registered entities, that possess, use, or transfer BSATs each year between 2004-2010, the key findings from the present study include: 1) there were no reports of a theft of any BSAT between 2004-2010; 2) there was only one instance out of more than 3400 shipments in which a select agent was actually lost during ship-
Table 3
Number and type of BSATs associated with release reports received by CDC.

<table>
<thead>
<tr>
<th>Agent Type</th>
<th>All Entities</th>
<th>Registered Entities</th>
<th>Exempt Entities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>(%)*</td>
<td>#</td>
</tr>
<tr>
<td>Toxins</td>
<td>23</td>
<td>(3.4)</td>
<td>22</td>
</tr>
<tr>
<td>Fungi</td>
<td>58</td>
<td>(8.6)</td>
<td>11</td>
</tr>
<tr>
<td>Bacteria</td>
<td>479</td>
<td>(70.9)</td>
<td>238</td>
</tr>
<tr>
<td>Rickettsia</td>
<td>24</td>
<td>(3.6)</td>
<td>22</td>
</tr>
<tr>
<td>Viruses</td>
<td>92</td>
<td>(13.6)</td>
<td>87</td>
</tr>
<tr>
<td>Total</td>
<td>676</td>
<td>(~100)</td>
<td>380</td>
</tr>
</tbody>
</table>

* = percent of total reports in category for 2004-2010

Table 4
Laboratory Acquired Infections caused by BSATs between 2004-2010.
The annual distribution, type of select agent, type of entity and type of containment facility in which the 11 laboratory acquired infections occurred that were reported to CDC between 2004-2010.

<table>
<thead>
<tr>
<th>Year</th>
<th>Agent</th>
<th># Cases</th>
<th>Entity type</th>
<th>Laboratory Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Brucella melitensis</td>
<td>1</td>
<td>Registered</td>
<td>BSL 2</td>
</tr>
<tr>
<td>2004</td>
<td>Coccidioides species</td>
<td>1</td>
<td>Registered</td>
<td>BSL 3</td>
</tr>
<tr>
<td>2004</td>
<td>Francisella tularensis</td>
<td>3</td>
<td>Registered</td>
<td>BSL 2</td>
</tr>
<tr>
<td>2007</td>
<td>Brucella melitensis</td>
<td>1</td>
<td>Registered</td>
<td>BSL 3</td>
</tr>
<tr>
<td>2007</td>
<td>Brucella melitensis</td>
<td>1</td>
<td>Exempt</td>
<td>BSL 2</td>
</tr>
<tr>
<td>2008</td>
<td>Brucella melitensis</td>
<td>1</td>
<td>Registered</td>
<td>BSL 3</td>
</tr>
<tr>
<td>2009</td>
<td>Francisella tularensis</td>
<td>1</td>
<td>Registered</td>
<td>BSL 3</td>
</tr>
<tr>
<td>2010</td>
<td>Brucella suis</td>
<td>1</td>
<td>Exempt</td>
<td>BSL 2</td>
</tr>
<tr>
<td>2010</td>
<td>Brucella suis</td>
<td>1</td>
<td>Exempt</td>
<td>BSL 2</td>
</tr>
</tbody>
</table>

One of the key provisions for improving accountability of BSATs in the United States was the establishment of the regulatory requirement that all entities in possession of BSATs must keep accurate and current inventory records of BSATs held in long term storage (42 CFR § 73.17). Prior to the publication of the current select agent regulations in 2002, there were no regulatory requirements for maintaining any inventory records of BSATs present in laboratories. Although most laboratories in possession of BSATs did have inventory records before promulgation of the inventory record keeping requirement, there was considerable variation in the accuracy and completeness of these records. For many entities with large collections of BSATs, including those with archival materials, generation of accurate inventory records for all BSATs in their possession required substantial resources and time to complete. In order to ensure and maintain ongoing compliance with these inventory accountability requirements, CDC routinely con-
ducts inventory “spot” checks of BSAT inventories during inspections. These spot checks have provided a mechanism through which the accuracy of BSAT inventories can be monitored.

Another important component of the inventory accounting responsibility is the requirement that all entities in possession of BSATs must immediately report any theft and the loss, even temporarily, of these materials (42 CFR § 73.19[a]). This immediate reporting requirement allows a response by law enforcement and regulatory agencies to be initiated in a timely manner. After these discrepancies are identified and reported to CDC or APHIS, a review by CDC of the circumstances surrounding this event is conducted that includes notification of the FBI in cases where the discrepancy cannot be rapidly reconciled.

The shipment of BSATs also represents an activity that could result in the theft or loss of these materials. Accordingly, the select agent regulations require pre-shipment authorization by either CDC or APHIS and notification to the regulatory agencies when materials leave the shipper and arrive at their destination. There were 3412 successful shipments of BSATs approved by CDC between 2004 and 2010. There was only one shipment that was lost during shipment between registered entities. It was determined by law enforcement officials that this shipment was destroyed during transit.

The select agent regulations also address the threat to public health and safety posed by an accidental release of BSATs from facilities using these materials for scientific or commercial purposes. Regulated entities “must develop and implement a written biosafety plan that is commensurate with the risk of the agent or toxin, given its intended use.” (42 CFR § 73.12[a]). There is also the additional requirement, that “the biosafety and containment procedures must be sufficient to contain the select agent and toxin.” (42 CFR § 73.12[b]). In the event that the biosafety and containment procedures in place do not contain the BSATs, the select agent regulations require that all entities that possess, use, or transfer BSATs must immediately report any release to CDC or APHIS. Prior to the implementation of the provisions of 42 CFR Part 73, there was no systematic reporting system at any level of government that monitored the number of laboratory workers and the type of infections and exposures associated with this occupation (Sewell, 1995).

Biological laboratories, and the work done therein, can be complex and the determination that a a release from primary containment has occurred may not be a straightforward process. Accordingly, the Federal Select Agent Program has provided the regulated community with guidance, including example scenarios, on the types of situations that would be considered to be releases and therefore reportable. This guidance can be found at the National Select Agent Registry web site (www.selectagents.gov). We have observed a significant increase in TLR Reports submitted to CDC since this guidance was first posted in early 2008. One possible explanation for this increase could be the outreach and education efforts that DSAT has conducted on the TLR reporting requirements. These efforts include a guidance document that was published in January of 2008 as well as more thorough inspections. The requirement for reporting all TLR events immediately after the occurrence or recognition of the event enables CDC to identify and assess any potential public health or security threats posed by the event. In addition, any time sensitive steps needed to protect workers from potential risks resulting from the release of a BSAT are identified as soon as possible after notification. CDC also uses information provided in the TLR Reports, as well as information collected through other sources such as verbal communications, written correspondence during the post-event evaluation process, information obtained during inspections and investigations of the reported event to identify new approaches for improvements in safety and security practices. Immediate reporting of exposures to BSATs that may pose serious public health threats also allows a more effective provision of assistance to entities that lack experience with medical or epidemiological issues associated with these agents, and provides occupational health professionals the opportunity to intervene with medical surveillance and countermeasures earlier in the potential infection process, when these measures are likely to be more effective. Ironically, intervening with prophylactic therapies early in the response to the report may obscure the number of actual infections resulting from release events of BSATs.

Other studies have attempted to assess the risk of infection associated with work in biomedical laboratories (Wedum & Kruse, 1969; Miller et al., 1987), but have encountered difficulties in achieving this goal due to problems with identifying subclinical infections, atypical incubation periods and routes of infection (Sewell, 1995). Other factors such as fear of reprisal or embarrassment may contribute to underreporting of laboratory acquired infections.

The specificity of these reporting criteria should be considered when reviewing the data presented in this manuscript. These reported events do not describe situations where a total loss of containment of the BSATs and a release into the environment outside of the containment facility may have occurred. Since there are redundant containment barriers and procedures in place in all registered facilities that work with BSATs in the United States, these additional safety barriers and procedures greatly reduce the likelihood that any BSAT will escape outside of the laboratories. Any risk for a release of a BSAT beyond the redundant containment barriers of the facility is immediately assessed based on the information we receive during the initial and follow up reports.

Overt occupational exposures represent a recognizable event in which the worker exposed to the BSAT may be at risk for developing a laboratory acquired infection. This type of release can be minimized through training, proper use of personal protective equipment (PPE) and improved engineering controls for sharp instruments (e.g., contaminated needles). None of the LAIs reported to CDC resulted
from overt exposures to BSATs (Table 4).

The second type of release event defined in the regulations (i.e., a release outside of the primary containment barriers); however, can represent a less recognizable threat to workers in biocontainment laboratories. All 11 LAls resulted from either unrecognized and/or unreported exposures, presumably through the aerosol release of the BSATs. These observations are entirely consistent with studies by Pike (1976) who found no distinguishable accidents or exposure events in more than 80% of LAls. Harding and Byers (2000) also reported only a small number of recognized containment breaks in a study of LAls.

The regulatory requirement or pre-access approval by CDC for all individuals working with BSATs in CDC-registered facilities allows for a reasonable estimate of the population for which the incidence of LAls can be determined. During the seven years in which report data was available for this study, the average annual rate of LAls in BSAT facilities registered with CDC was 1.6 per 10,000 authorized workers. In order to place this rate in an overall context of occupational illnesses in similar workplaces, a comparison may be made with incidence rates of occupational illnesses in scientific research and development facilities, as reported by the Department of Labor (NAICS Category 5417, rates from 2006 through 2010). These rates ranged from a high of 22.3 illnesses per 10,000 workers in 2006 to a low of 15.9 illnesses per 10,000 workers in 2009. Although these metrics may not be directly comparable, this information suggests that BSAT facilities are at least as safe, if not safer, than facilities in the overall U.S. research and development sector.

The reporting requirement of any suspected TLR provides information about the characteristics of events occurring in BSAT laboratories and the circumstances surrounding these events. Initial analysis of this information has provided some insights that may improve biosafety practices in laboratories working with BSATs under differing conditions. For instance, detection of differences between registered entities and entities exempted from registration requirements, such as clinical and diagnostic laboratories, has allowed CDC to consider targeted recommendations that more appropriately address the risks associated with different laboratory operating conditions in these types of facilities. The predominance of potential release events at exempt entities involving just two types of agents (i.e., bacteria and fungi), which are predominantly manipulated in BSL-2 facilities, contrasts with the broader spectrum of agents reported by registered entities that occurred most frequently in BSL-3 laboratories. The marked differences between these entity types in the frequency of potential release events with viral agents and toxins were also noteworthy. The requirement for exempt entities to report the identification of BSATs and any TLR events provides a mechanism for agencies responsible for the regulatory oversight of BSATs to obtain assurance that these materials are either destroyed or transferred to facilities with approved security measures in place. These reports also allow assessment of the factors that are associated with potential release events in animal biosafety facilities and maximum containment laboratories.

A recent report by the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight recommended the establishment of a non-punitive incident reporting system for high- and maximum containment biological laboratories that possess, use, or transfer both BSAT and non-BSAT agents. Such a system, the Task Force reasoned, could provide valuable information in assessing risk and developing more effective biosafety programs in these facilities. Although the CDC TLR reporting system is a regulatory requirement and failures to report could potentially result in punitive actions by the federal government, our experience suggests that the system envisioned by the Trans-Federal Task Force could provide valuable insights related to incidents in a wide range of biological laboratories. The data provided through this system could be helpful in identifying specific combinations of agents and/or activities for which risk assessment and control activities can be focused. This expansion of monitoring to non-BSAT associated events may provide a broader understanding of the incidence of such events and inform biosafety and biosecurity guidance.

The findings in this report are subject to a number of limitations. The number of reports received by CDC likely is an underestimate of the true number of suspected losses and releases of BSAT, especially in the early years of the program because there was little encouragement for exempt entities to report TLR events prior to 2005 and guidance regarding TLR reporting was not provided to the regulated community until 2008.

Additionally, releases are likely to have been unrecognized and therefore unreported. In spite of these limitations, the reports that have been submitted contain a substantial amount of information about potential problems with the safety and security of BSATs in the United States. This information can provide insights into approaches to improve safety and security in these facilities.

The data collected by CDC between 2004 and 2010 of monitoring suspected BSAT TLRs indicate that the risk of exposure to BSATs managed by US laboratories to the general population is low. However, the potential misuse of these agents and toxins remains a risk to public health at the national and international level. Effective biosafety and biosecurity programs in US laboratories will continue to be critical tools to effectively manage this risk.

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Part 73 of Title 42, Code of Federal Regulations (Select Agents, and Toxins) (HHS).


Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight. Available at: www.phe.gov/Preparedness/legal/boards/biosafetytaskforce/Pages/default.aspx


Training Announcement—6th Annual Leadership Institute

The 6th Annual Leadership Institute “Managing Unmanageable Situations: Management Techniques and Strategies for Biosafety Professionals” will be held from April 15-18, 2013 at the Charleston Marriott in Charleston, South Carolina.

The core focus of the 2013 ABSA/Emory/ERGFRF Biosafety Leadership Institute will be to provide management instruction, guidance, and practice for biosafety professionals to utilize in designing and implementing effective biosafety programs in their home institutions.

Each participant of the 2013 Leadership Institute will leave with a personalized plan that complements the missions and goals of their own respective institutions. By engaging with an expert faculty and networking with peers, each participant will be equipped to demonstrate how their program plays a vital role in facilitating research and enhancing the sustainability of their respective institutions. For more information, please visit www.absa.org/eduleadership.html.