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## Transfer of select agents and toxins: 2003–2013

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### Abstract

The Federal Select Agent Program (FSAP), which is comprised of the Centers for Disease Control and Prevention Division of Select Agents and Toxins (DSAT) and the United States Department of Agriculture Agricultural Select Agent Services, regulates entities that possess, use, or transfer biological select agents and toxins (BSAT) within the United States and must pre-approve all BSAT transfers within or into the U.S. As part of the FSAP, DSAT regulates BSAT that pose a severe threat to public health and safety. From March 2003 to December 2013, DSAT approved 4,402 BSAT transfers. The select agents most commonly transferred were bacteria and fungi, accounting for approximately 73 percent of all transfers. Transfers between commercial entities were the most common entity type transfer, and entities most frequently transferred BSAT to entities within the same region. Nearly 70 percent of the DSAT approved transfers included BSAT that, as of December 4, 2012, are classified as Tier 1 agents. Tier 1 agents present the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence. The requirement to pre-approve transfers of BSAT allows the FSAP to monitor and track shipments to alert the FSAP of theft, loss, or release of BSAT during shipment, thereby protecting public health and safety. During the study period, only one package was lost during shipment, which contained a non-Tier 1 BSAT. The Federal Bureau of Investigation investigated the loss and concluded that the BSAT package was most likely damaged by the commercial carrier and discarded. There were no incidents of theft or release associated with BSAT shipments noted during the study period.

### Keywords

Select agent and toxin; transfer; biosafety; biosecurity; CDC; DSAT

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The authors declare that this research was conducted in the absence of commercial or financial relationships that could be construed as a conflict of interest.

## Introduction

Following the publication of the Antiterrorism and Effective Death Penalty Act of 1996 (Public Law 104–132, 1996), the Centers for Disease Control and Prevention (CDC) began monitoring the transfer of biological select agents and toxins (BSAT) that pose a severe threat to public health and safety within and into the U.S. The transfers were regulated in accordance with 42 Code of Federal Regulations (CFR) § 72.6 (Department of Health and Human Services, 1996), which outlined the regulated BSAT and shipping requirements for each package, and required entities to inform the CDC after BSAT transfers were completed. In the aftermath of the *Bacillus anthracis* mailings in the U.S. in 2001, Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and are hereinafter referred to as the Bioterrorism Response Act, which granted the authority to regulate BSAT of human concern to the HHS and BSAT of plant and animal concern to the USDA (Public Law 107–188, 2002a; Public Law 107–188, 2002b).

Under the authority of the Bioterrorism Act, the United States Government collectively published 42 CFR § 73.3 (Select Agent Regulation, 2012a), 7 CFR § 331.3 and 9 CFR § 121.3 (Select Agent Regulation, 2012b) on December 13, 2002 as the Interim Final Rule to implement provisions of the Bioterrorism Response Act; these three regulations went into effect in February 2003 and are hereinafter referred to as the select agent regulations (SAR). HHS delegated authority to regulate BSAT of human concern to the CDC (Department of Health and Human Services, 2006) Division of Select Agents and Toxins (DSAT) and USDA delegated authority to regulate BSAT of plant and animal concern to the Animal and Plant Health Inspection Services (United States Department of Agriculture, 2003) Agricultural Select Agent Services (AgSAS); DSAT and AgSAS work together to regulate BSAT as the Federal Select Agent Program (FSAP). According to the SAR, entities that possess, use, or transfer an HHS or USDA BSAT listed in section 3 of the SAR, or an overlap BSAT (regulated by both DSAT and AgSAS) listed in section 4 of the SAR, must register with the FSAP, which includes a review of safety and security provisions during an on-site inspection prior to BSAT possession, to ensure entity compliance with the SAR. The SAR changed the paradigm for transferring BSAT by requiring entities to receive approval from the CDC and USDA prior to transfer.

The SAR has been modified several times since the SAR went into effect in 2003. In 2005, the SAR was revised to include significant changes to security requirements (Select Agent Regulation, 2005). SAR revisions published in 2012 identified BSAT that present the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence as Tier 1 and included substantial enhancements to the security, incident response, and training requirements for entities possessing Tier 1 BSAT (Select Agent Regulation, 2012a; Select Agent Regulation, 2012b). In addition, the list of HHS and overlap BSAT was modified from 50 to 44 agents on October 4, 2012 by adding three viruses and removing three toxins, two fungi, two viruses, one virus subtype, and one rickettsia species (Select Agent Regulation, 2012a). The lists of HHS, USDA, and overlap BSAT are reviewed by the FSAP on a biennial basis.

As described in sections 3 (c) and 4 (c) of the SAR, the FSAP regulates all BSAT as well as nucleic acids that encode for infectious forms of select agent viruses or functional forms of select toxins that can be expressed *in vitro* or *in vivo*, or are in a vector or recombinant host genome and can be expressed *in vitro* or *in vivo* (Select Agent Regulation, 2012a; Select Agent Regulation, 2012b). Entities may apply for exclusion to the regulations for BSAT that have been attenuated or rendered less toxic or potent, which is decided on a case-by-case basis; however, if virulence or toxicity is restored to an excluded agent or toxin, the BSAT will again be subject to the SAR including transfer pre-approval.

According to the transfer requirements outlined in section 16 of the SAR, all BSAT transfers within and into the U.S. must be approved by the FSAP prior to shipment and can only be received by FSAP registered entities (Select Agent Regulation, 2012a; Select Agent Regulation, 2012b). The FSAP reviews each BSAT transfer request to ensure that the receiving entity and principal investigator are registered with the FSAP. Entities that initiate transfers that are not registered with the FSAP including, but not limited to, entities outside the U.S. or local offices of physicians, veterinarians and third-party diagnostic clinics that identify BSAT in clinical and environmental samples, are denoted as non-registered entities (NRE). DSAT approves the transfers of HHS BSAT, AgSAS approves the transfer of USDA BSAT, while the transfer of overlap BSAT may be approved by either agency.

Each shipment must be packaged, labeled, and shipped in accordance with all federal and international regulations including, but not limited to, the U.S. Department of Transportation's Hazardous Material Regulations (Department of Health and Human Services, 2009). The BSAT transferring entity provides the FSAP with the tracking information so that the FSAP can monitor the shipment. The requesting Responsible Official (RO) must notify the FSAP within two business days that the shipment has been received. If the package is damaged during shipment, missing BSAT material, or is not received within 48 hours of the expected delivery time, the requesting RO must notify the FSAP and submit an *APHIS/CDC Form 3, Report of Theft, Loss, or Release of Select Agents and Toxins* to the FSAP within 7 calendar days as required in section 19 of the SAR (Select Agent Regulation, 2012a; Select Agent Regulation, 2012b).

For this report, we reviewed all HHS and overlap BSAT transfers from March 2003 to December 2013 to characterize trends associated with the transfer of BSAT and to identify the most frequently transferred agents, routes of transfer, and the types of entities involved. This report represents the first in-depth review for DSAT approved transfers of HHS and overlap BSAT between entities registered with the DSAT.

## Material and Methods

### Data collection

All information reported for each transfer is maintained in the FSAP National Select Agent Registry database. For this retrospective review, a dataset was extracted from the database which included all DSAT approved transfers to DSAT-registered entities reported for the period March 12, 2003 (date when BSAT transfer reporting provisions became effective) and December 31, 2013. The data were compiled into Microsoft Excel for data analysis. Data

were analyzed by agent, U.S. state of transfer origin (sender location), U.S. state of transfer delivery (recipient location), entity type, and carrier type. For security purposes, the sender and recipient state information was categorized into four regions: Northeast, Midwest, South, and West. Transfers that originated from outside the U.S. (n = 153) were excluded from the regional transfer analysis because the country-specific transfers were too few in number to establish consistent routes of transfer. The carrier methods used to transfer BSAT were categorized into commercial carrier or non-commercial, based on the method reported by the entity initiating the transfer.

Information about entity type was collected from the self-reported *APHIS/CDC Form 1 (Application for Registration for possession, use, and transfer of Select Agents and Toxins)* (Form 1) and categorized as defined below. NREs were omitted (n=249) from the entity type review because NRE senders could transfer BSAT material without reporting the entity type.

- Academic, combining academic (private), academic (state), and academic (not specified) fields in the Form 1;
- Commercial, combining commercial (profit) and commercial (not specified) fields in the Form 1;
- Government (non-federal), combining government (non-federal), government (state/local), and government (not specified) fields in the Form 1;
- Government (federal) and private (non-profit) entity type categories remained unchanged.

### Data analysis

To compare the frequency of transfers between regions, we standardized the annual number of transfers per region by calculating transfers per entity. The average number of transfers per entity were calculated by dividing the annual transfers initiated from each region by the number of entities registered with DSAT for each region for that year. To compare the frequency of transfers between entity types, we standardized the average transfers per entity type by dividing the annual number of transfers initiated per entity type by the number of entities registered with DSAT for that entity type for that year. To analyze shipping frequencies by day of the week, the transfers between registered entities were calculated as a percentage of the total number of transfers for the study period for each day of the week in which transfers were shipped and received. The percentage of transfers using each shipping method was determined from the shipping methods reported by the initiating entity for each day that a transfer was shipped. The average calendar days in transit are the average of the number of whole calendar days for all transfers that were initiated on each day of the week, rounded to the nearest tenth. To calculate the percentage of transfers arriving by Friday of the same week, the database was queried for all transfers shipped on each day of the week and the number of transfers arriving by Friday of the same week was divided by the total number of transfers shipped on that day. All data obtained from the database were compared with archived paper report forms to verify that the information was accurately entered into the databases.

## Results

Between March 2003 and December 2013, we approved 4,402 HHS and overlap BSAT transfers between registered entities. Four hundred forty-two transfers included more than one agent, resulting in 5,305 BSAT transferred during the study period. Of the more than 500 entities across the U.S. that had registered with DSAT between March 2003 and December 2013, nearly 60 percent had received at least one DSAT approved BSAT transfer while 48 percent had shipped at least one BSAT during that time. Eleven entities had received and eight entities had sent more than 100 transfers during the study period, and these entities accounted for 43.4 and 46.8 percent of all BSAT transfers, respectively (data not shown). We approved approximately 400 HHS and overlap BSAT transfers requested by DSAT-registered entities per year, ranging from a 12-month low of 395 in 2009 to a high of 522 in 2004 (Figure 1). Since 2004, the number of DSAT registered entities has remained between 284 and 336, with the total number of entities declining on average 2.4 percent annually since 2006. After SAR amendments in 2005 and 2012, the number of annual transfers declined 17.8 percent from 2006 to 2007 and 20.4 percent from 2012 to 2013 (Fig. 1).

### Transfers sent and received by day of the week

DSAT monitors the length of time in which BSAT packages remain in transit to alert DSAT of potential cases of theft, loss, or release. Approximately 95 percent of BSAT transfers were initiated between Monday and Thursday with more than 98 percent of those shipments arriving by Friday of the same week (Table 1). For shipments initiated between Monday and Friday, the average number of calendar days per BSAT transfer varied from a high of 1.1 on Monday to a low of 0.6 on Friday. Shipments requiring more than two days of transit time accounted for 3.1 percent of all transfers and nearly 40 percent of these transfers were shipped on Thursday or Friday (data not shown). BSAT transfers initiated on Thursday and Friday, more often utilized a non-commercial carrier and had the shortest transit times, averaging 0.8 and 0.6 days in transit, respectively (Table 1).

### Transfers by region

To identify geographic trends and important routes of shipment, BSAT transfers within the U.S. were analyzed according to the regions in which each sending and receiving entity was located (Fig. 2A). Transfers between entities in the Midwest accounted for the highest transfers per entity of any regional transfer in the study, averaging 0.8 over the study period. In 2005, 2006 and 2012, the transfers per entity between Midwest entities was more than 1.0 (Fig. 2B), due to transfers of botulinum neurotoxin (BoNT) and BoNT-producing species of *Clostridium* transfers. While the Northeast to the South transfer per entity rate remained below 0.4 for the majority of the study period, these transfers averaged 1.1 transfers per entity in 2004 (Fig. 2C). Of the Northeast to South transfers during this period, transfers initiated from government (federal) entities accounted for 93.1 percent of transfers (data not shown); however, no changes in the specific type of BSAT agent transferred were associated with the increase in Northeast to South transfers in 2004. For transfers between entities in the West, the transfers per entity were nearly 1.0 in 2011 and 2012 (Fig. 2D), and were associated with transfers of BoNT and *F. tularensis* (data not shown).

### Transfers by entity type

DSAT approved transfers between registered entities were analyzed to determine the frequency with which each entity type transfers BSAT. We observed that transfers between commercial entities were the highest average number of transfers for all entity-to-entity transfer types during the study period, averaging 1.5 transfers per entity and ranged from 0.8 in 2003 to 2.2 in 2012 (Fig. 3A). The transfer of BoNT and BoNT-producing species of *Clostridium* accounted for over 90 percent of transfers between commercial entities during the study period (data not shown). Transfers from government (federal) entities to government (federal), academic, private (non-profit), and government (non-federal) entities exceeded 1.5 transfers per entity in 2004 (Fig. 3B), due to the inclusion of *B. anthracis* in nearly 60 percent of all transfers initiating from government (federal) entities that year (data not shown). Transfers per entity from private (non-profit) to academic and private (non-profit) entities exceeded 1.0 on multiple occasions from 2008–2013 (Fig. 3C). *Yersinia pestis* and *B. anthracis* accounted for approximately 43 and 39 percent, respectively, of the transfers between private (non-profit) entities observed in 2008 and 2010, respectively; however, no BSAT-specific increases in transfers were associated with the increases in transfers from private (non-profit) to academic entities (data not shown).

### Bacteria and fungi transfers

Of the 5,305 BSAT transferred during the study period, select agent bacteria and fungi were the most commonly transferred organisms and accounted for more than 73 percent of all transferred BSAT (Fig. 4A). *B. anthracis*, *F. tularensis*, BoNT-producing species of *Clostridium*, and *Y. pestis*, all of which are classified as Tier 1, were the most frequently transferred BSAT bacteria and fungi species during the study time period (Fig. 5) and accounted for nearly 50 percent of all transferred BSAT. *B. anthracis* accounted for approximately 20 percent of all bacteria and fungi transfers over the course of the study (Fig. 4A), including 217 transfers in 2004 (Fig. 5).

### Toxin transfers

From 2003 to 2013, transfers including select toxins accounted for approximately 16 percent of all BSAT transfers (Fig. 4B). BoNT is the only toxin classified as a Tier 1 BSAT and was one of the five most transferred BSAT during the study period (Fig. 5). BoNT accounted for more than 85 percent of all select toxin transfers (Fig. 4B) and we documented over 70 BoNT approved transfers per year, observing substantial increases in BoNT transfers from 2005–2007, and in 2012–2013 (Fig. 5). Other than BoNT, we documented less than 10 toxin transfers for all select toxins per year except for 2005 and 2013 when there were 11 and 10 ricin transfers, respectively (data not shown). BoNT was the only select toxin that averaged at least one transfer each year during the study time period.

### Virus transfers

During the study period, transfers including select agent viruses accounted for approximately 11 percent of all BSAT transfers (Fig. 4C). Eastern equine encephalitis virus (EEEV), Venezuelan equine encephalitis virus (VEEV), and monkeypox virus (MPXV) together accounted for nearly 60 percent of all HHS and overlap BSAT virus transfers during



the study period. Increases in transfers were observed for EEEV in 2009 and 2011, MPXV in 2006, and VEEV in 2006 and 2007 (data not shown). DSAT approved fewer than 10 transfers per year for any select agent virus requiring Biosafety Level-4 (BSL-4) containment facilities.

## Compliance

During the study period, 21 shipments involving potential SAR violations were referred to the HHS-Office of Inspector General (HHS-OIG) for further investigation and potential enforcement action. Of the 21 transfer incidents referred to HHS-OIG, eight resulted in civil monetary penalties ranging from \$15,000 to \$450,000. All but three of these incidents involved transfers not approved by DSAT prior to shipment. Of the remaining three incidents, one involved a package that was lost during transit, one involved the failure to comply with applicable laws regarding shipping and packaging, and in one incident it could not be confirmed that a violation of the select agent regulations had actually occurred. The lost package was investigated by the FBI who found no criminal intent and concluded that the package was most likely inadvertently destroyed and discarded by the commercial carrier.

## Discussion

This report provides the first comprehensive review of DSAT regulatory oversight of BSAT transfers for the period between March 2003 and December 2013. In this study, we have identified important routes of transfer that will be used to significantly enhance monitoring, including transfers between specific entities of the same region and same entity type. We observed that the number of transfers increased prior to and decreased following the implementation of the SAR amendments in 2005 and 2012 (Fig. 1). Approximately one year prior to each amendment, a Notice of Proposed Rulemaking was published that alerted entities of the potential upcoming changes, and entities may have transferred BSAT prior to the publication of the amendment. BSAT transfer requirements, such as DSAT approval prior to shipment and registration of receiving entities with DSAT, did not change in either amendment. However, each amendment contained significant changes to other components of the SAR that may have influenced transfers. The list of regulated BSAT was modified in 2005 and 2012 to add or remove BSAT that may have affected the number of transfers. For example, we approved 174 *Coccidioides* sp. transfers prior to the 2012 BSAT list modification, and removing this agent may have contributed to the overall reduction in transfers observed in 2013. In addition, the introduction of enhanced security requirements in 2005 and Tier 1 requirements in 2012 may have influenced an entity's decision to possess BSAT and we observed that several entities transferred BSAT prior to the implementation of the amendments. However, not all increases appear to be associated with regulatory changes as some increases in transfers were likely associated with an increase in the transfer of a specific BSAT, such as the increase in *B. anthracis* transfers in 2004 during the investigations into U.S. Postal Service mailings (Fig. 5) (Jernigan, D.B. et al, 2002).

In addition to the regulatory oversight provided by DSAT, registered entities themselves play an important role in ensuring the safety and security of BSAT transfers by carefully

scheduling and packaging transfers. With only 3.1 percent of transfers exceeding two calendar days in transit, the data indicate that entities schedule transfers to minimize shipping times and thereby reducing the potential for loss of viability as well as the possibility of a BSAT theft, loss, or release. More than 98 percent of transfers were received by Friday, suggesting that entities likely schedule BSAT transfers to arrive when authorized personnel are available to take possession of the shipment. During the study period, we did not receive any reports of a stolen shipment, which indicates that the security provisions established by DSAT and executed by entities were sufficient to maintain the security of BSAT during transfer. In addition, we did not receive any reports of transfer-related releases during the study period, indicating that entities complied with federal regulations to package BSAT appropriately for shipment. After analyzing all days of transfers by entity type or region, we observed that the number of transfers that were sent or received on Saturday and Sunday were quite low and meaningful conclusions could not be drawn.

When the number of entities responsible for transferring BSAT was analyzed, 60 percent of entities registered with DSAT had received at least one DSAT approved BSAT transfer during the study period, while 48 percent of the entities had shipped a BSAT. One potential explanation for the number of laboratories that had not frequently shipped or received BSAT is that some entities, such as some diagnostic laboratories that only possess unregulated BSAT positive controls including attenuated strains or genomic fragments, register with DSAT to prepare for the possession of any BSAT specimens that are identified by the entity. Therefore, unregulated positive control BSAT strains can be transferred between diagnostic laboratories without DSAT approval and those transfers do not need to be reported to FSAP. Another possible explanation is that diagnostic laboratories often perform presumptive tests on specimens that do not have an identified agent or toxin; the SAR do not apply to specimens that have a presumptive diagnosis and transfers of diagnostic specimens do not require DSAT approval. In addition, entities such as diagnostic laboratories do not usually perform research and therefore do not transfer BSAT to collaborators.

During the study period, only one package was lost by a commercial carrier (Henkel, R.D., 2012), which suggests that the transfer of BSAT between regulated entities in the U.S. is done in an efficient, safe, and secure manner. We were alerted to the lost transfer by the receiving entity when the package did not arrive at the expected time, as required in the SAR. The FBI conducted an investigation and concluded that the package was damaged by the commercial carrier and discarded. In response to this incident, we initiated a policy in 2010 that requires entities to provide tracking information to the FSAP at the time of shipment. Closely monitoring the shipment of each BSAT, including contacting entities if a package has not been received within 48 hours of expected delivery, allows us to rapidly respond to theft, loss, or release of BSAT during shipment.

When HHS and overlap BSAT transfers approved by DSAT were analyzed by region, we observed that entities most frequently transferred BSAT within the same region. This observation was consistent for all four regions; however, transfers between entities in the same region were higher for certain regions. For example, when we standardized the number of transfers per region to the number of entities located in the transferring region, we observed that transfers per entity were highest between entities within the Midwest region



and within the West region (Figure 2). A possible explanation for the frequent transfer between regions is that entities may obtain BSAT more efficiently if the other entity is in a relatively close proximity and, therefore, are more likely to obtain BSAT from other entities registered for the BSAT in the same region.

Entities most frequently transfer BSAT to entities of the same type. The FSAP does not limit the amount of transferred material or the number of transfers requested and carried out by any entity; however, the FSAP must approve each transfer. Transfers between commercial and between private entities occurred more frequently than between any other entity type (Figure 3). Government (federal) entities often perform multiple clinical specimen transfers over the course of a year, such as the transfer of specimens in the *B. anthracis* mailings investigation in 2004, or to share BSAT with other laboratories. Commercial and private entity transfer activity may be explained by transfer of environmental and quality control samples of BSAT, including BoNT-producing species of *Clostridium*. One possible explanation for the observation that entity types frequently transfer BSAT amongst themselves is that many entity types have similar work objectives and use similar BSAT, and established collaborations may exist between entities in the same region.

Although DSAT has regulated only 14 bacteria and fungi during the study period, these organisms were the most frequently transferred material during the 11-year study time period, followed by toxins and viruses. More entities are registered with DSAT for bacteria and fungi than toxins or viruses, in part, because entities do not have to register with DSAT for permissible amounts of toxins and only a few entities maintain a BSL-4 laboratory required to work with most of the HHS and overlap BSAT viruses. The type of select toxin and select agent virus material regulated by the FSAP may provide another possible explanation for the large percentage of bacteria and fungi transfers. FSAP does not regulate transfers that contain permissible amounts of select toxins, or transfers that include nucleic acids that are not immediate precursors to infectious viruses, including reverse genetics plasmids or virus genomes that do not utilize host polymerases (e.g., negative strand RNA viruses and some DNA viruses including MPXV). Of the 27 viruses regulated by DSAT since the Bioterrorism Response Acts, the regulations apply to the immediate precursors of 9 select agent viruses, while the same material is not regulated for the other 18 viruses. The genetic material of the two most frequently transferred viruses, EEEV and VEEV (Fig. 4C), is regulated and we require pre-approval to transfer both the live virus and genomes of these agents.

Over the course of this study, we observed numerous limitations that affected our conclusions and interpretations of the data. For example, we observed that 19 entities accounted for almost half of all BSAT transfers, representing less than five percent of all entities registered during the study period. Therefore, while the focus of this study is to report the regulation of BSAT transfers for all entities registered with DSAT, the regional and entity type trends observed do not apply to all entities. DSAT is currently identifying individual entities that frequently transfer BSAT and will continue to monitor their activity to ensure that BSAT transfers are transferred in a safe and secure manner. Another limitation of this report is that the data does not include USDA BSAT transfers regulated by AgSAS. Lastly, because of the limitations of the data collected, including a relatively short time

period and multiple amendments during that time frame, we were unable to perform statistical analyses to identify statistically significant relationships between the entity types, regions, and types of BSAT transferred during this time period. Larger sets of data collected over a longer period of time may permit a statistical analysis.

The efficient, safe, and secure transfer of BSAT between regulated entities in the U.S. is a fundamental component of an effective preparedness and response program, and the data in this report reflect achievement of that objective. During the study period, DSAT approved 4,402 transfers of BSAT between regulated entities in the U.S. We did not receive any reports of thefts or releases and only one reported loss of BSAT in transit (Henkel, R.D., 2012). Greater than 99 percent of these transfers were executed in compliance with the SAR indicating an effective partnership between regulated entities and federal regulators. The vast majority of individuals involved in the packaging and shipping of these materials complied with the regulations, and ensured that their packages were appropriately shipped to maximize the probability for a rapid, safe, and secure delivery. We will continue to monitor all BSAT transfers to ensure compliance with the SAR to protect the safety and security of BSAT and the public.

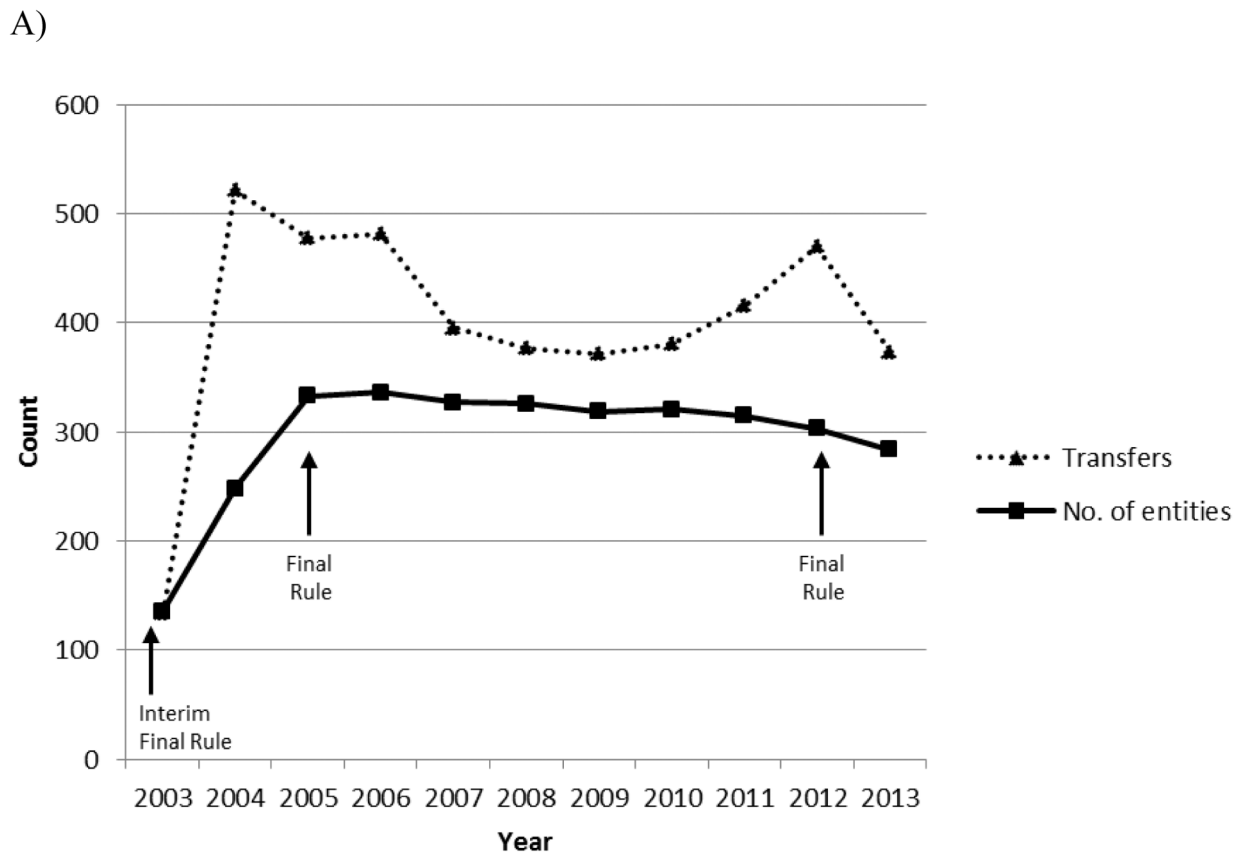
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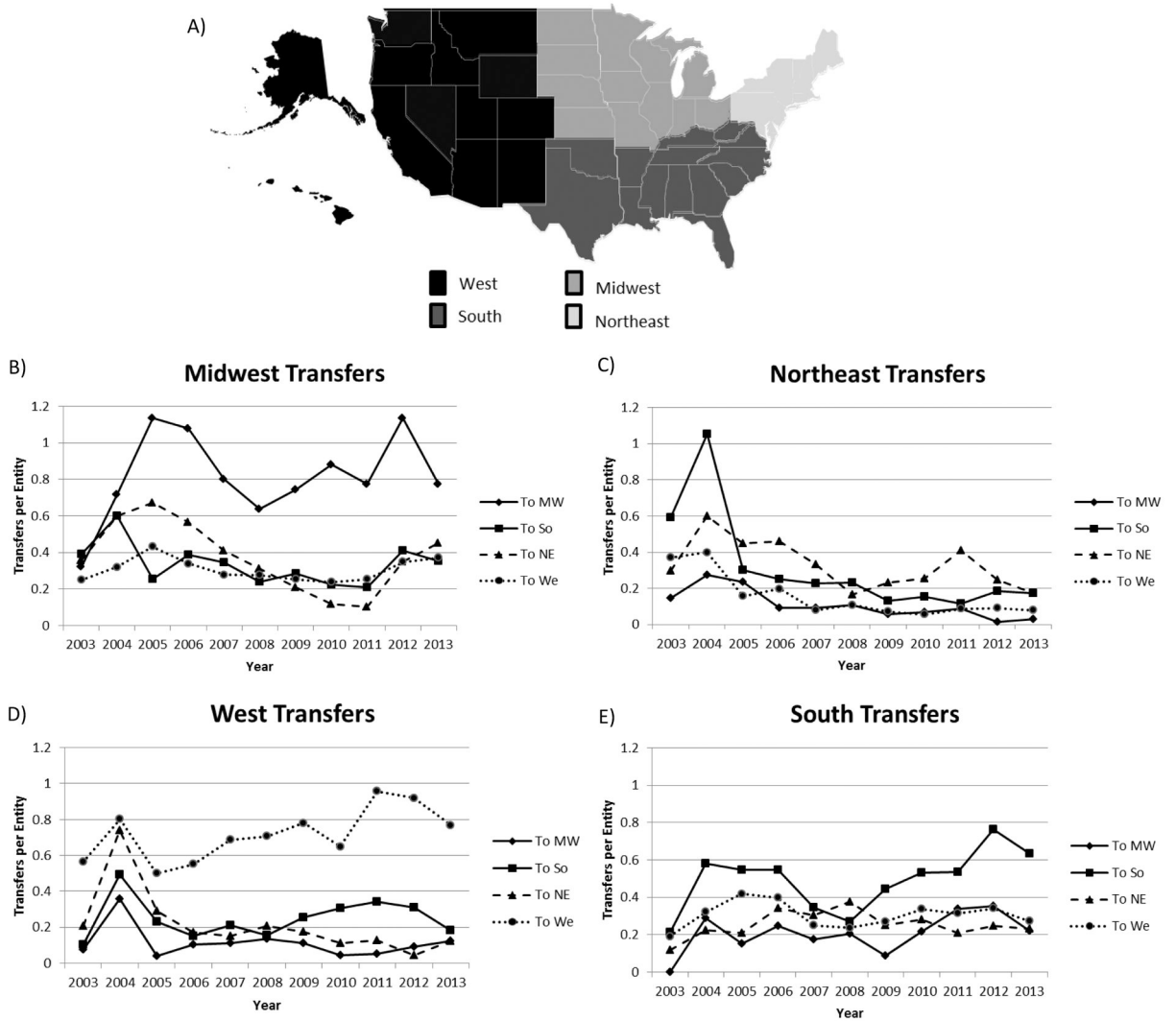
## References

- Department of Health and Human Services. (1996). Additional Requirements for Facilities Transferring or Receiving Select Infectious Agents. Fed. Reg 61, 29327–29333. Available at <http://www.gpo.gov/fdsys/pkg/FR-1996-06-10/pdf/96-14707.pdf>.
- Department of Health and Human Services. (2006). Public Health Security and Bioterrorism Preparedness and Response Act Delegation of Authority. Fed. Reg 71, 67130 Available at <http://www.gpo.gov/fdsys/pkg/FR-2006-11-20/pdf/06-9263.pdf>.
- Department of Health and Human Services. (2009). Biosafety in Microbiological and Biomedical Laboratories. 5th ed Washington, DC Available at <http://www.cdc.gov/biosafety/publications/bmbl5/index.htm>.
- Henkel RD, Miller T, Weyant R (2012). Monitoring Select Agent Theft, Loss and Release Reports in the United States—2004–2010. Appl. Biosafety 17: 171–80.
- Jernigan DB, Raghunathan PL, Bell BP, Brechner R, Bresnitz EA, Butler JC, Cetron M, Cohen M, Doyle T, Fischer M, Greene C, Griffith KS, Guarner J, Hadler JL, Hayslett JA, Meyer R, Petersen LR, Phillips M, Pinner R, Popovic T, Quinn CP, Reefhuis J, Reissman D, Rosenstein N, Schuchat A, Shieh WJ, Siegal L, Swerdlow DL, Tenover FC, Traeger M, Ward JW, Weisfuse I, Wiersma S, Yeskey K, Zaki S, Ashford DA, Perkins BA, Ostroff S, Hughes J, Fleming D, Koplan JP, Gerberding JL National Anthrax Epidemiologic Investigation Team. (2002). Investigation of bioterrorism-related anthrax, United States, 2001: epidemiologic findings. Emerg. Infect. Dis 8: 1019–28. [PubMed: 12396909]
- Public Law 104–132. (1996). Antiterrorism and Effective Death Penalty Act of 1996. Available at <http://www.gpo.gov/fdsys/pkg/PLAW-104publ132/pdf/PLAW-104publ132.pdf>.
- Public Law 107–188. (2002a). Public Health Security and Bioterrorism Preparedness and Response Act, Title II--Enhancing Controls on Dangerous Etological Agents and Toxins, Subtitle B—Department of Agriculture. See 7 USC § 8401. Available at <http://www.gpo.gov/fdsys/pkg/PLAW-107publ188/pdf/PLAW-107publ188.pdf>.

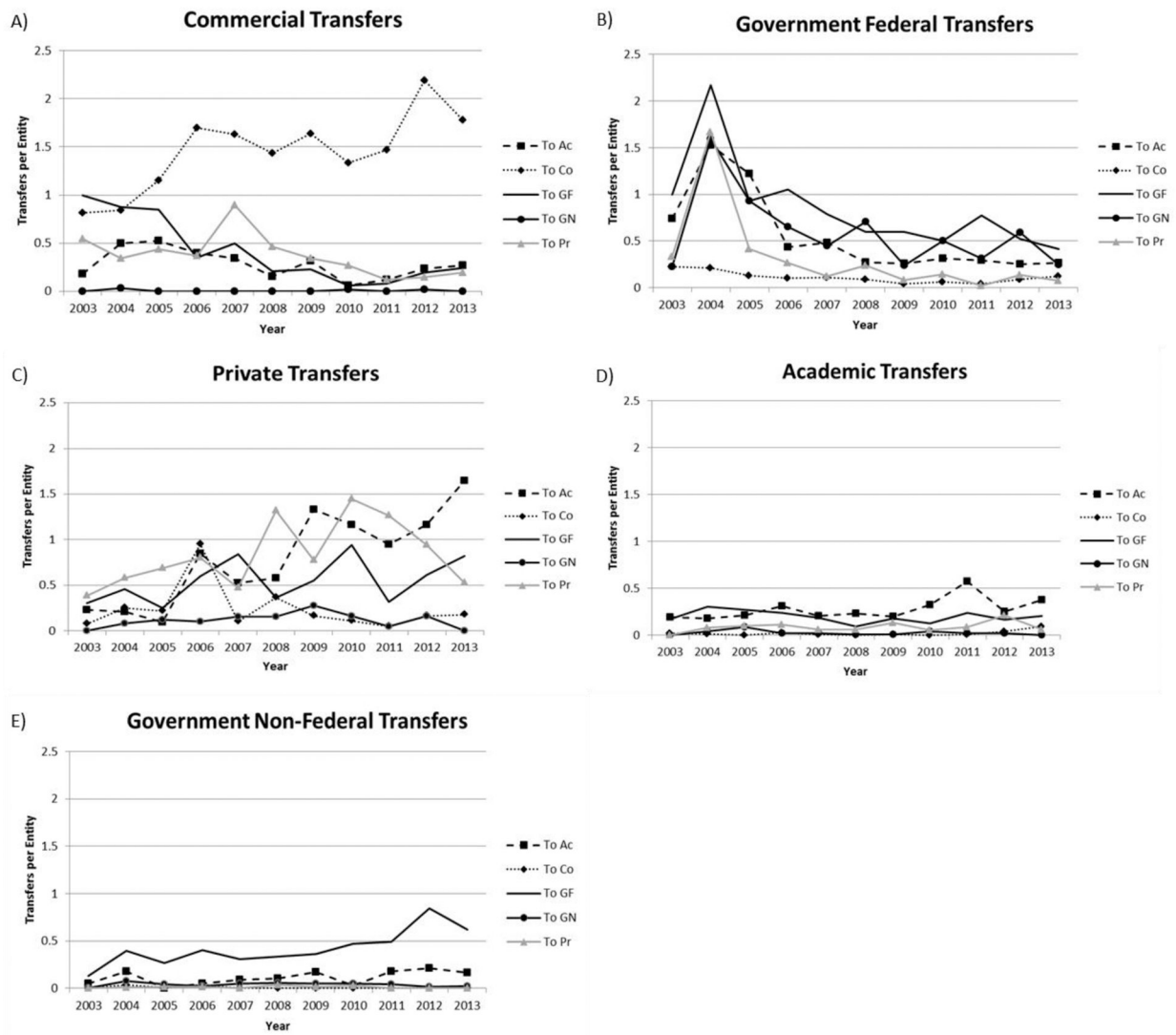
- Public Law 107–188. (2002b). Public Health Security and Bioterrorism Preparedness and Response Act, Title II--Enhancing Controls on Dangerous Etiological Agents and Toxins, Subtitle A-- Department of Health and Human Services. See 42 USC § 262a. Available at <http://www.gpo.gov/fdsys/pkg/PLAW-107publ188/pdf/PLAW-107publ188.pdf>.
- Select Agent Regulation. (2005). 42 CFR Part 73: Possession, Use, and Transfer of Select Agents and Toxins; Final Rule. Available at <https://oig.hhs.gov/authorities/docs/05/032905FRselectagents.pdf>.
- Select Agent Regulation. (2012a). 42 CFR Part 73: Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review; Final Rule. Available at <http://www.gpo.gov/fdsys/pkg/FR-2012-10-05/pdf/2012-24389.pdf>.
- Select Agent Regulation. (2012b). 7 CFR Part 121, 9 CFR Part 331: Agricultural Bioterrorism Protection Act of 2002; Biennial Review and Republication of the Select Agent and Toxin List; Amendments to the Select Agent and Toxin Regulations; Final Rule. Available at <http://www.gpo.gov/fdsys/pkg/FR-2012-10-05/pdf/2012-24434.pdf>.
- United States Department of Agriculture. (2003). 7 C.F.R. Part 2.80: Delegations of Authority By The Secretary of Agriculture and General Officers of the Department. Available at <http://www.gpo.gov/fdsys/pkg/CFR-2003-title7-vol1/pdf/CFR-2003-title7-vol1-sec2-80.pdf>.



**Figure 1. DSAT approved transfers and number of registered entities per year, 2003–2013.** The arrows indicate the enactment of the Bioterrorism Act of 2002 and revisions to the Select Agent Regulations in 2005 and 2012.



**Figure 2. Average annual BSAT transfers per entity, 2003–2013.** DSAT approved annual transfers per entity were analyzed by the regions in which the sending and receiving entities were located. A) The United States was divided into four regions geographically. B) to E). The average annual number of transfers per entity was analyzed by the region where the sending entity was located for the B) Midwest (MW) (n=60), C) Northeast (NE) (n=65), D) West (We) (n=89), and E) South (So) (n=82). The number in parentheses for each region is the average number of entities for each region, rounded to the nearest whole number. The data do not include transfers from outside the United States.

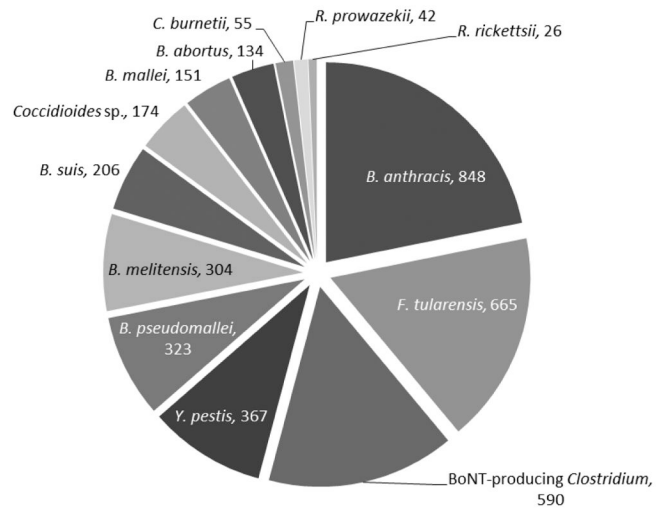


**Figure 3. Average annual BSAT transfers per entity by entity type, 2003–2013.**

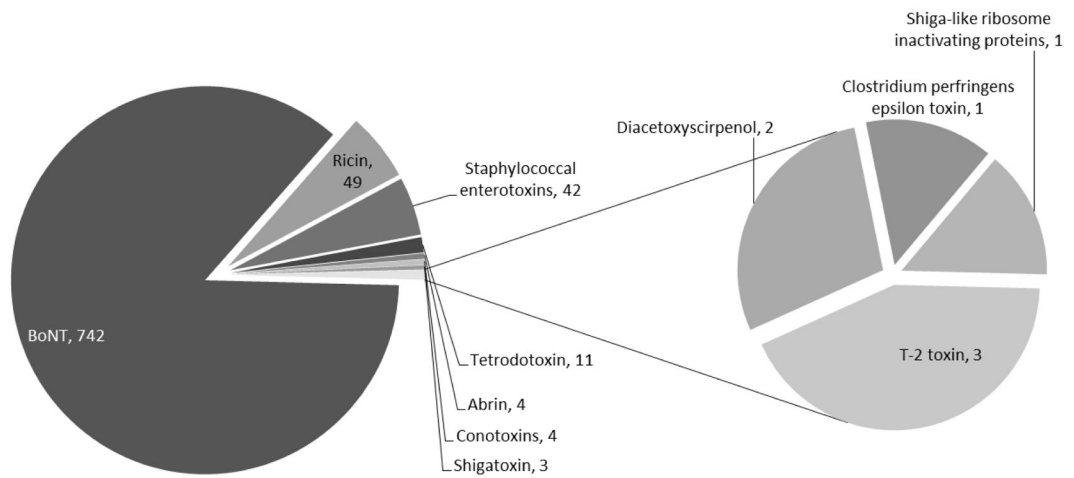
DSAT approved annual BSAT transfers per entity type were analyzed by the sending and receiving entity types. The average annual number of transfers per entity was analyzed by the type of entity sending the BSAT for A) commercial (Co) (n=40), B) government (federal) (GF) (n=48), C) private (non-profit) (Pr) (n=20), D) academic (Ac) (n=88), and E) government (non-federal) (GN) (n=100) entities. The number in parentheses for each entity type is the average annual number of entities for each entity type, rounded to the nearest whole number. The data do not include NRE entity types.



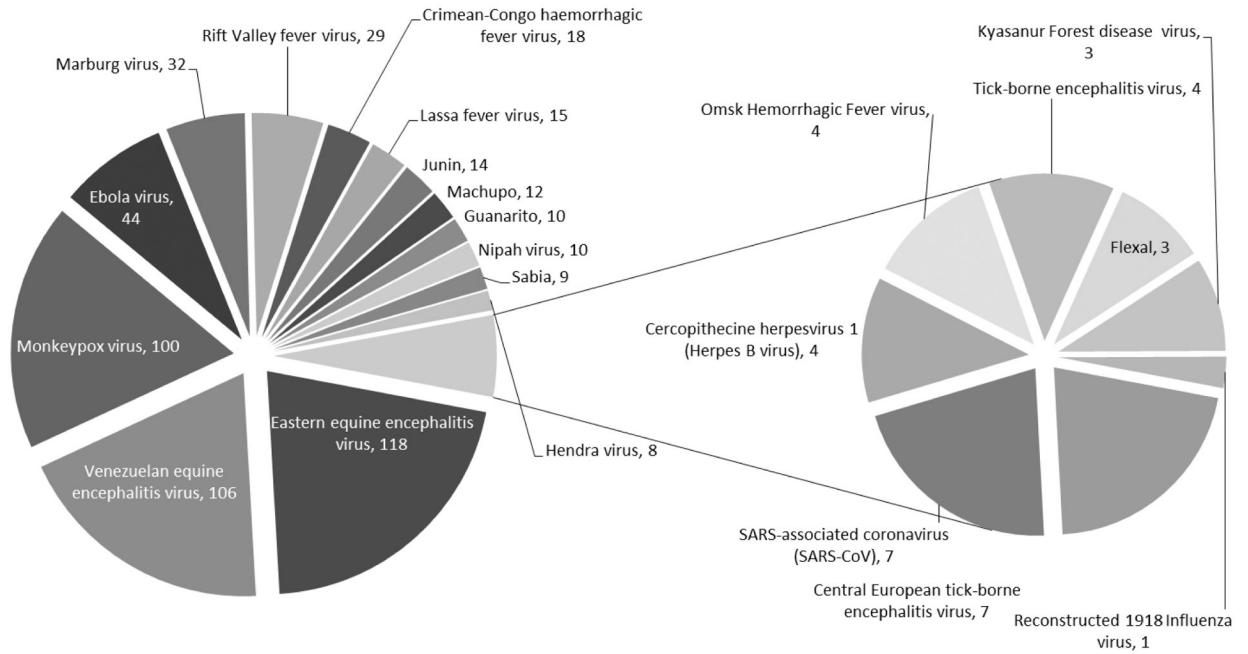
A)



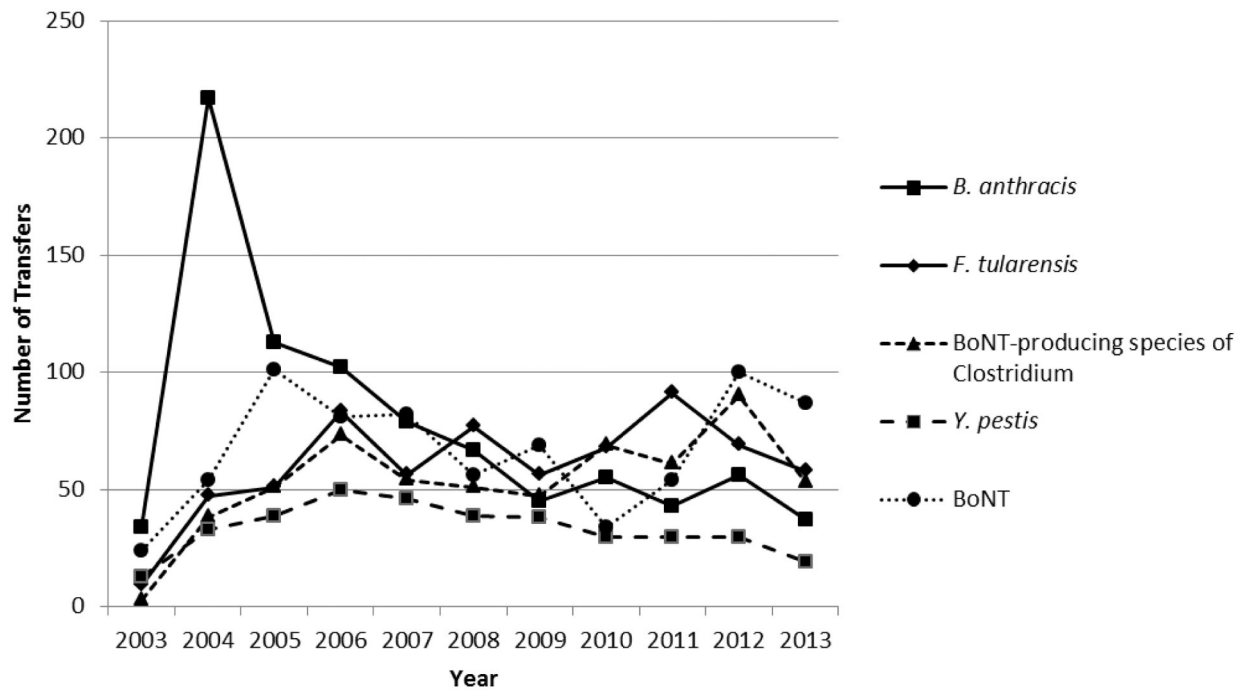
B)



C)



**Figure 4. HHS and Overlap BSAT transfers by type of agent or toxin, 2003 – 2013.**  
 The total number of DSAT approved transfers for each HHS and Overlap A) bacteria and fungi (n=3885), B) toxins (n=862), and C) viruses (n=558).



**Figure 5. Most frequently reported BSAT in DSAT approved transfers by year, 2003–2013.** The total number of transfers for the study period: *B. anthracis* (n=848), *F. tularensis* (n=665), BoNT-producing species of *Clostridium* (n=590), *Y. pestis* (n=367), and BoNT (n=742).

**Table 1.**  
**DSAT approved transfers within the United States by day of week on which the BSAT was shipped or received, type of carrier, and transit time, 2003–2013.**

The percent of shipments transferred and received on each day of the week was calculated from the total number of transfers. The percentage of shipments using a carrier was calculated as a percentage of all the reported shipment methods for each day that a transfer was shipped. The average calendar days in transit are the average of the number of calendar days for all transfers that were initiated on each day of the week.

Day of the week	Percent shipped per day of the week (Total number)	Percent received per day of the week (Total number)	Percent of shipments using commercial carriers	Avg. calendar days in transit from date shipped	Percent of shipments arriving by Friday of same week
Monday	25.5 (1059)	3.3 (136)	75.9	1.1	99.7
Tuesday	32.2 (1338)	24.8 (1029)	74.0	1.0	99.3
Wednesday	26.1 (1084)	30.6 (1270)	75.3	1.0	98.4
Thursday	11.8 (492)	29.1 (1209)	50.0	0.8	93.6
Friday	4.1 (171)	11.9 (495)	29.2	0.6	86.0
Saturday	0.1 (3)	0.2 (9)	33.3	4.6	-
Sunday	0.1 (4)	0.1 (3)	50	0.5	-