CDC 90 Day Internal Review of the Division of Select Agents and Toxins

The nation relies on research to improve the rapid detection of biological threats and to develop the medical countermeasures to prevent and treat them. The Federal Select Agent Program oversees the possession, use, and transfer of biological select agents and toxins which have the potential to pose a severe threat to human, animal, or plant health or to animal or plant products. The Federal Select Agent Program consists of the Centers for Disease Control and Prevention (CDC)/Division of Select Agents and Toxins (DSAT) and the Animal and Plant Health Inspection Service (APHIS)/ Agriculture Select Agent Services (AgSAS). The CDC 90-day Internal Review Work Group focused on the program operated by DSAT and has not yet involved AgSAS to reconcile recommendations that have impact on both programs.

The Internal Review Workgroup noted ongoing reviews of biosafety and biosecurity conducted by the U.S. Government (USG) since Executive Order 13546 was published in 2010. The Internal Review Workgroup did not duplicate recommendations from these reviews, but complements them with 9 observations leading to 10 actionable recommendations in three broad categories (inspections, incident reporting, and transparency) to improve the CDC select agent and toxin regulatory program.

Inspections

Observation A: Some regulated entities have reported variability in the skills and approach of inspectors.

> **Recommendation 1**: Reduce potential variability of inspections. DSAT shall identify activities in inspection checklists that can be completed in quantitative as distinguished from a qualitative manner. Activities requiring qualitative analysis shall be the focus of added specificity and enhanced training and coordination among inspection teams to reduce potential variation.

Observation B: About 20-30% of final inspection reports are not issued within the DSAT 30-day target (interval between the inspection and the final report), delaying timely resolution of findings.

> **Recommendation 2**: Increase timeliness of inspection reports. DSAT shall initiate routine analyses of inspection report timeliness data to identify modifiable characteristics of DSAT reports delayed beyond 30 days. DSAT shall report timeliness metrics and performance goals to the regulated community annually.
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> DSAT shall work with AgSAS to implement a policy for providing interim reports to entities when final reports are likely to be delayed.
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> DSAT shall present staffing and retention plans to support the program's inspection goals, as well as recommendations from this and related federal reports.

Observation C: Select agent laboratories do not currently implement a standardized risk assessment process to identify the highest risk activities.

> **Recommendation 3**: Review and implement options for standardized risk assessment. CDC, in collaboration with APHIS, shall convene an independent scientific body to review the science and practice of risk assessment in the modern select agent laboratory and provide recommendations that improve the effectiveness and timeliness of the inspection process.

Observation D: Clear descriptions of progressive categories of the severity of inspection findings will enable the Federal Select Agent Program to refine penalties and corrective actions to the appropriate level of risk and to convey the appropriate level of concern when reporting findings.

> **Recommendation 4**: Design and implement a pilot program to better characterize the severity of inspection findings. In collaboration with APHIS, DSAT shall develop and implement a pilot program to characterize and score inspection findings according to severity level. A 12-month pilot program shall be implemented to include sharing scores with entities and gather feedback to improve the process.

Observation E: Enforcement options for DSAT are limited and difficult to scale to the range of safety and security findings on inspections. Most compliance issues and violations are resolved through negotiated corrective action plans.

> **Recommendation 5**: Prioritize and strengthen enforcement actions to the highest risk violations. DSAT shall produce a list of violations and findings identified for corrective action since the initiation of the DSAT Corrective Action Plan program. DSAT shall order the list according to the level of oversight concern (i.e., severity). The list shall then be reviewed by a DSAT-convened panel of experts for feedback on the completeness of the list, the DSAT assessment of severity, and the enforcement action taken.
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> **Recommendation 6**: DSAT shall produce a report on other approaches to increasing compliance with regulations (e.g., consultative services and incentives) based on review of other regulatory programs (e.g., nuclear research, aviation safety).

Observation F: The Internal Review Workgroup acknowledged uncertainties and gaps in understanding how best to strengthen biosafety and to implement measures that appropriately balance the ability to conduct life-saving research with biological select agents and toxins and the need to ensure the safety and security of the public and the workers in these institutions.

> **Recommendation 7**: Analyze trends and associations between inspection findings and risk. In collaboration with AgSAS, DSAT shall draw on CDC scientific expertise to conduct an assessment of inspection and investigation data to:
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> - Describe trends in safety and security findings, including sentinel events and levels of containment breach
> - Identify associations between negative findings and other characteristics of the entity and work conducted by the entity
> - Identify associations within the data collected during inspections to identify domains of findings that could inform how inspections could be made more efficient and effective
> - Design and begin validation of a risk scoring method for inspections.

Incident Reporting

Observation G: The terminology used in the APHIS/CDC Form 3 (*Report of Theft, Loss, or Release of Select Agents and Toxins*) does not convey the level of risk to safety and security or the extent of concern. For example, the term 'release' is currently being used to describe both a vial spilled within a

biosafety cabinet with multiple layers of containment and a potential event in which *Bacillus anthracis* spores escape the facility to the surrounding community. Better defining the terms, including sub-categories of 'release' and 'loss' that convey a gradient in risk, would improve the distinction between significant incidents that pose risk to laboratory staff or the public from those incidents that pose low, if any, risk due to the layers of protection that are in place.

> **Recommendation 8**: Make reporting more informative about the actual and potential risk of reported incidents. DSAT, with AgSAS, shall complete a review to update the APHIS/CDC Form 3, to include subcategories of "release" and "loss" and additional fields to more consistently categorize an incident with regard to such matters as the type of release (e.g., potential release, spill within secondary containment, occupational exposure, possible breach of facility containment, etc.), type of exposure (e.g., none, intact personal protective equipment (PPE), skin, mucosal, waste water, etc.), and the understanding of safety and security risk levels relative to human illness. Input shall be solicited from the regulated community and interested stakeholders before the new form is put into practice.

Observation H: Molecular diagnostic methods are constantly improving and may offer faster and more sensitive confirmation than culture. The Federal Select Agent Program currently defines identification of a select agent as growing the agent in culture, such that if there is a disease confirmed with molecular diagnostic methods but not culture, the threshold for the laboratory to report the discovery of a select agent is not met (APHIS/CDC Form 4). The possession, use, and transfer of the associated clinical samples would not fall under Federal Select Agent Program safety or security regulations.

> **Recommendation 9**: Keep pace with scientific advances including through incorporation of molecular diagnostic methods. The Federal Select Agent Program shall develop a plan to update policies or initiate regulatory changes to include molecular testing methods as an option for the confirmation of the presence of select agents and toxins in clinical samples drawn for suspicion of biological select agent or toxin-associated disease. The plan should include an assessment of the impact of changing the definition of select agent and toxin identification on Form 4 reporting.

Transparency and Public Understanding

Observation I: Inspection reports and corrective action plans are typically only provided to the inspected entity. The Internal Review Workgroup expressed interest in sharing inspection data to increase public understanding of the work of biological select agents and toxins registered entities.

> **Recommendation 10**: Without risking the security of regulated entities and the agents and toxins they work with, increase public reporting of inspection processes and findings. DSAT shall present a decision briefing for releasing more informative aggregate information regarding inspection findings on a routine basis (consistent with terminology enhancements in Recommendation 4) and an approach to develop concurrence on this approach with AgSAS and federal biosecurity experts.