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Environmental Biodetection and Human Biosurveillance Research and Development for National Security

Priorities for the Department of Homeland Security Science and Technology Directorate

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Preface

Biological threats are among the priorities addressed by the biodefense community and, more broadly, the U.S. homeland security enterprise. Early detection of such threats is a foundation for preparedness and timely, effective response to a biological attack. As potential adversaries become more decentralized and capable in the development and deployment of biological weapons, U.S. research and development (R&D) must strive to stay ahead to effectively detect biological threats and minimize their effects.

The U.S. Department of Homeland Security (DHS) Science and Technology Directorate (S&T) asked the Homeland Security Operational Analysis Center (HSOAC) to assess priorities for its investments in R&D, specifically addressing biological threats. The project entailed three tasks: (1) assess the relevant policy and practice landscape for national biosurveillance and biodetection efforts; (2) conceptualize how R&D can be brought to bear to improve biosurveillance and biodetection; and (3) review and assess DHS S&T R&D in support of biosurveillance and biodetection programs.

This report aims to describe the results of analyses addressing these tasks. HSOAC examined in detail the current and projected S&T R&D portfolio related to biological threats and also sought to understand relevant R&D supported by non-DHS sponsors. During the course of this study, discussions were under way about reorganization of DHS S&T, the research sponsor. Related budget uncertainties challenged S&T's ability to plan R&D investments with confidence. This study recognized those uncertainties and focused on the project tasks as outlined. Therefore, S&T asked HSOAC to assess potential priorities and establish a framework to help inform priority-setting in the face of such uncertainties. The findings should be of interest to S&T management, the new Countering Weapons of Mass Destruction Office, DHS management, and federal, state, local, tribal, and territorial agencies that benefit from S&T.

This research was sponsored by S&T and conducted within the Acquisition and Development Program of the HSOAC federally funded research and development center (FFRDC).

About the Homeland Security Operational Analysis Center

The Homeland Security Act of 2002 (Section 305 of Public Law 107-296, as codified at 6 U.S.C. § 185), authorizes the Secretary of Homeland Security, acting through the Under Secretary for Science and Technology, to establish one or more FFRDCs to provide independent analysis of homeland security issues. The RAND Corporation operates HSOAC as an FFRDC for DHS under contract HSHQDC-16-D-00007.

The HSOAC FFRDC provides the government with independent and objective analyses and advice in core areas important to the department in support of policy development, decision-making, alternative approaches, and new ideas on issues of significance. The HSOAC FFRDC also works with and supports other federal, state, local, tribal, and public- and private-sector organizations that make up the homeland security enterprise. The HSOAC FFRDC's research is undertaken by mutual consent with DHS and is organized as a set of discrete tasks. This report presents the results of research and analysis conducted under HSHQDC-17-J-00156, Assessment of DHS Biosurveillance and Biodetection Efforts.

The results presented in this report do not necessarily reflect official DHS opinion or policy.

For more information on HSOAC, see www.rand.org/hsoac.

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Summary

The 2001 anthrax attacks in the United States serve as a reminder of the country's vulnerability to biological weapons. Evolving technologies and greater capabilities of adversaries in recent years have increasingly put such weapons within the ready reach of those who could do the United States harm. Therefore, national biodefense is a critical element of national security.

Environmental biodetection (BD) and human biosurveillance (BSV) are part of the foundation of national biodefense. For purposes of this assessment, we refer to *environmental biodetection* as detection of biothreat agents in the environment, specifically in air, and *human biosurveillance* as detection of biothreat agents in humans.[1] U.S. research and development (R&D) must strive to stay ahead of U.S. adversaries by effectively detecting biological threats and minimizing their effects. The U.S. Department of Homeland Security (DHS) Directorate for Science and Technology (S&T) chemical and biological defense (CBD) program supports important R&D to improve technologies and operations related to BD and BSV.

The objective of this assessment was to provide S&T with an overall qualitative characterization of its added value within the U.S. biodetection and biosurveillance enterprise, potential directions for R&D to strengthen technological elements of each system, and a summary of opportunities to enhance the return on future investments in biodetection and biosurveillance systems in general. The Homeland Security Operational Analysis Center (HSOAC) team addressed the objective through three tasks: (1) assess the relevant policy and practice landscape for national BD and BSV efforts, (2) conceptualize how R&D can be brought to bear to improve BD and BSV, and (3) review and assess R&D within DHS S&T in support of BD and BSV. S&T asked HSOAC to focus specifically on biological threats in humans and aerosol threats in the environment and to consider the role of DHS in the larger interagency context. S&T intends for the outcomes from these analyses to help shape S&T investments, which should be consistent with U.S. and DHS goals for biodetection and biosurveillance. Such investments ultimately aim to save lives while saving money and increasing operational efficiency in the event of a bioterrorist attack.

To carry out the project tasks, the HSOAC team reviewed the S&T R&D portfolio and relevant documentation, interviewed key S&T leaders, and collected and examined inventories of R&D sponsored by other agencies. Such R&D was identified through searches of key federal R&D databases, openly published papers, and agency websites. The team created conceptual frameworks to help organize, characterize, and present R&D activity. Specifically, the team created (1) taxonomies to organize and characterize relevant R&D activity, (2) logic models that depict environmental biodetection and human biosurveillance operational activi-

[1] Although biothreats to animals and plants are real, the sponsor asked HSOAC to focus specifically on threats to humans.

ties, (3) logic models for S&T R&D, and (4) a conceptual mapping of this R&D to the architecture of the National Strategy for Biosurveillance.

Policy and Practice Landscape

As part of the Federal Select Agent Program, the U.S. Centers for Disease Control and Prevention and the U.S. Department of Agriculture maintain the list of select agents of concern to government planners. Most of the agents of greatest concern—labeled Tier 1—can be transmitted via air. This makes air monitoring and timely, accurate environmental biodetection particularly important. Timely detection can trigger responses to help minimize human exposure and disease. Similarly, timely detection of exposure or disease in humans (whether from airborne pathogens or pathogens transmitted through other mechanisms) can trigger responses to provide appropriate chemoprophylaxis (if warranted), clinical care, and, potentially, additional prevention measures.

The policy context for environmental biodetection and human biosurveillance is complex, stemming from multiple national strategies that address different aspects of biodefense and national security. For example, the National Security Strategies in recent years (White House, 2006, 2010, 2015, 2017) have addressed pandemics and other biothreats with increasing prominence. The 2001 anthrax attacks spurred legislation that resulted in the first U.S. National Health Security Strategy in 2009 and an update in 2015 (U.S. Department of Health and Human Services [HHS], 2009, 2015). In 2012, the White House issued the first National Strategy for Biosurveillance—a short document based on four core pillars: scanning and discerning the environment, identifying and integrating essential information, alerting and informing decisionmakers, and forecasting and advising impacts. It remains the extant national guidance for the U.S. biosurveillance enterprise. Other national strategies issued from 2004 through 2014 address domestic and global health security, medical countermeasures, public health preparedness, and biodefense. These strategies all address health and security (and some carry titles or include text using the term *health security*), whole-of-government efforts, and biodefense (i.e., countering biological threat agents); most of them also address BSV and R&D.

Biodefense is a national enterprise with multiple players. Multiple federal agencies have responsibilities related to biodetection and biosurveillance. The HSOAC team developed operational logic models to depict the conceptual flow of activities to concrete outputs and desired intermediate and end outcomes for biodetection and biosurveillance, agnostic about the responsibilities of specific agencies. These are useful to understand what biodetection and biosurveillance are supposed to do and accomplish.

Regarding agency responsibilities, DHS has a unique federal niche for environmental biodetection, as defined in this study (i.e., detection of biothreat agents in air); in contrast, multiple agencies have significant responsibilities and programming related to human biosurveillance—notably, in addition to DHS, HHS and the U.S. Department of Defense. The two relevant DHS operational programs are BioWatch (for environmental BD) and the National Biosurveillance Integration System (for human BSV). BioWatch is a system of sampling units placed in approximately 30 metropolitan areas and used at special events to detect selected threat agents collected from air samples. The technology used by BioWatch for sample collection and testing has evolved relatively little since the program's inception in 2003. The role of

the National Biosurveillance Integration System is suggested by its name—to serve as a focal point for integrating and analyzing interagency biosurveillance information to be used across the federal government. Both programs have been under close watch by the U.S. Government Accountability Office and others that have questioned their lack of specified requirements, utility, cost, and effectiveness.

Non-S&T R&D Landscape

Although the primary focus of this study was to examine the S&T portfolio and assess the current and potential future contributions of S&T-supported R&D to environmental biodetection and human biosurveillance, the HSOAC team wanted to examine the nature and breadth of non-S&T R&D to determine whether S&T does or can fill gaps—or even whether S&T could, in principle, adapt early phase R&D supported by other funding sources—to meet DHS needs. Therefore, the team conducted searches to identify R&D directly or potentially relevant to environmental biodetection or human biosurveillance. The searches were wide-ranging and intended to be illustrative rather than exhaustive. After eliminating duplicates and applying retention and exclusion criteria, the team analyzed an inventory of 152 R&D activities relevant to environmental biodetection and 282 relevant to human biosurveillance. (The team used counts of activities, rather than funding level, as the most feasible surrogate for R&D level of effort in this study because funding information was not available for about 20 percent of the inventory items.) The majority of inventory items (106, 70 percent for BD; 268, 85 percent for BSV) represented funded projects identified through searches of two large federal databases (the National Institutes of Health [NIH] RePORTER, which captures R&D within HHS, and Federal RePORTER, which captures R&D from other federal agencies, including the National Science Foundation [NSF]); the remainder, in roughly equal proportions, were identified through searches of published papers and federal agency websites.

The team used these illustrative inventories to examine the nature of non-S&T R&D related to environmental biodetection and human biosurveillance. Specifically, the team captured information on the funding source, level of maturity of the R&D (i.e., technology readiness level [TRL]) as gleaned from reading project or published abstracts, and whether the R&D specified any security orientation (i.e., addressed biothreat agents or a context of health security; however, this was not a specific criterion for inclusion of R&D activities in the inventories). To capture the topic addressed by the research, the team created and applied a taxonomy for environmental BD (Table S.1) and another for human BSV (Table S.2). These were refined iteratively as new inventory items were identified, but the team did not systematically search for R&D activities within each taxonomy area. Each taxonomy included broad themes (labeled Tier 1) and a series of more specific subthemes (labeled Tier 2). The taxonomy for environmental BD includes sample collection and processing, sample testing, system configuration, and concept of operations (CONOPS), with different Tier 2 elements within most of these. The taxonomy for human BSV includes data sources and reporting, biological diagnostic test R&D, data analysis, system configuration, and CONOPS, again with multiple Tier 2 categories within them. The team classified each inventory item using the final taxonomies.

Table S.1
Taxonomy for Environmental Biodetection

Tier 1	Tier 2
Sample collection and processing	Air handling
	Collection
	Transport
	Extraction
Sample testing: primary detection, confirmation, characterization	Real-time detection
	Nucleic acids
	Proteins
	Other
	Whole-of-agent properties
	Enabling technologies
System configuration	Number, location, and type of sensors
	Assay complement selection
CONOPS	None

The HSOAC team's inventory included 152 distinct non-S&T R&D activities related to environmental BD and 282 related to human BSV.[2] Most of the BD R&D in the HSOAC inventory has been supported by HHS, DoD, and NSF; most BSV activity in the HSOAC inventory has been supported by HHS and NSF. Most of the R&D for both BD and BSV is at early stage of maturity (TRLs 1–3 for DHS applications) and addresses development of tests for environmental or clinical samples. There was less R&D activity identified related to system configuration or CONOPS, and about one-fifth of both BD and BSV R&D addresses security concerns. These findings suggest areas for which DHS could potentially adapt outputs from early stage research supported by others rather than supporting such (early stage, basic) research itself. Several relevant areas of R&D—test development in particular (second Tier 1 category listed for both biodetection and biosurveillance in Tables S.1 and S.2)—are already being well covered by non-S&T funders, and some of the non-S&T R&D addresses security concerns that are also of interest to DHS. The findings also suggest gaps that could be priorities for DHS R&D (for example, addressing system configuration and especially CONOPS).

S&T R&D

The primary interest of this study was to examine the S&T's CBD R&D portfolio and identify areas of value added and potential priorities for future investments. The HSOAC team used the two taxonomies to characterize S&T R&D and captured information from the sponsor about

[2] There was insufficient information to normalize the R&D activities across the various sources. Some activities were related to individual published academic articles, and others referred to entire research programs. We use the term *activity* to refer to a general body of work in a given area defined by our taxonomy.

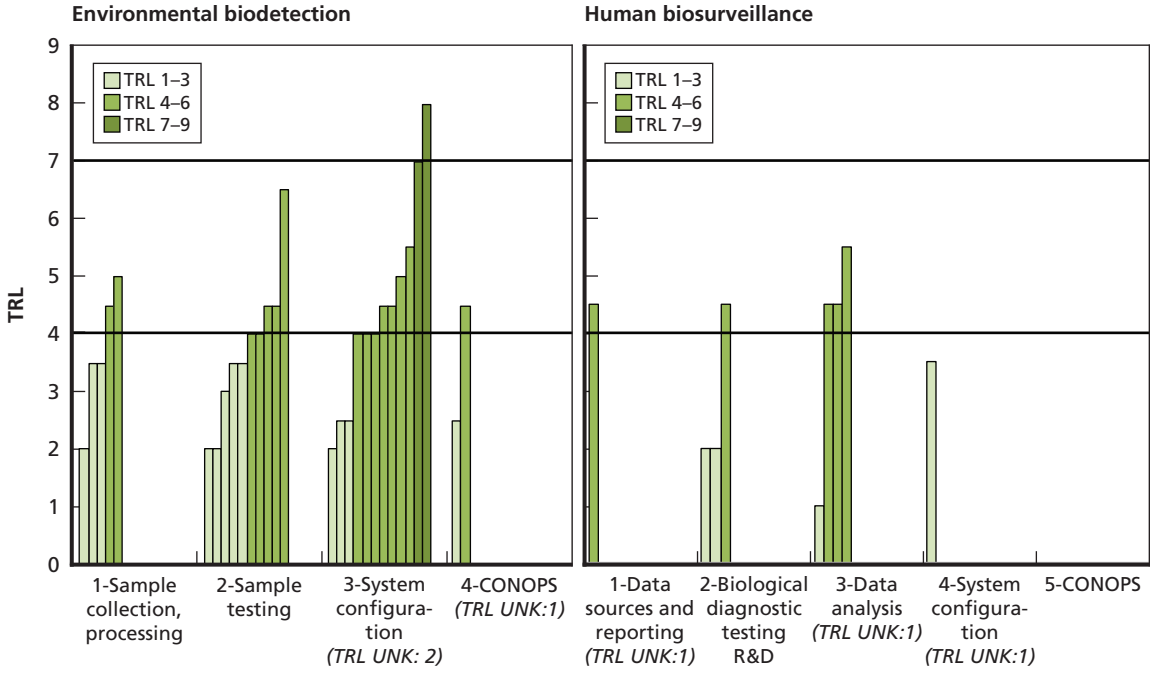
Table S.2
Taxonomy for Human Biosurveillance

Tier 1	Tier 2
Data sources and reporting	Clinical providers: physician's offices, hospitals, and clinics
	Emergency providers: emergency departments and poison control
	Work or school absenteeism
	Laboratories
	General public
	Traditional media
	Social media
	Digital evidence from human behavior
	Standoff/portal monitors
	Device-based detection
Biological diagnostic testing R&D	Nucleic acids
	Proteins
	Other
	Whole-of-agent properties
	Enabling technologies
	Presyndromic detection
Data analysis	Establishment of baseline
	Anomaly detection
	Determination of natural versus synthetic origin
	Integration of data from different sources
	Projected trajectory of current outbreak
	Forecasting of future disease events
System configuration	Choice of data types and reporting frequency and procedures
	Communications network and infrastructure
CONOPS	Strategies and processes for reporting and deploying diagnostic tests
	Strategies and processes for data analysis and integration
	Strategies and processes for sharing situational awareness and alerting

targeted customers and a timeline for each project or program. The team also grouped all S&T activities into S&T-specific themes for purposes of both complementary analysis and development of coherent S&T R&D logic models for environmental BD and human BSV.

S&T supports a greater volume of R&D addressing environmental BD than for human BSV (Figure S.1). R&D in both areas aims to serve the needs of both internal (DHS) and external (non-DHS) customers, although systematic assessment of customer use or satisfac-

Figure S.1
S&T Environmental Biodetection and Human Biosurveillance R&D Portfolio



NOTES: Each bar represents a single R&D project or activity. UNK = unknown.
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tion has not been undertaken to verify the extent to which targeted customers use S&T R&D outputs.

S&T's BD research is largely in the areas of test development and system configuration and spans all three maturity levels. Its BSV research addresses development of diagnostic tests, software, prototypes, and tools and data analysis; it spans early and midstage maturity levels (i.e., no testing of systems approaching readiness for deployment).

The HSOAC team developed R&D logic models, which visually depict and collect similar types of activities across both environmental BD and human BSV and call out specific customers both within DHS and external to DHS. It should be noted that the intermediate outputs and intermediate outcomes in these logic models are described as *anticipated* because the HSOAC team did not speak with any of S&T's customers to validate their use or intended use of S&T's outputs. Contacting S&T's customers was beyond the scope of this project, but it is a potentially useful activity for DHS to consider going forward. Engaging with customers can provide both evidence and data to help document and measure how R&D outputs are contributing to desired outcomes. It also would be a useful means of identifying other paths that lead to outcomes or identify barriers or obstructions preventing S&T's R&D from achieving its intended purpose. Such information also can inform strategic planning, assist leadership with identifying R&D activities that show evidence of achieving outcomes, and allow for informed decisions to address identified barriers or rebalance the research portfolio.

In broad terms, S&T's environmental biodetection and human biosurveillance R&D is trying to achieve its mission through enabling desired intermediate outcomes. These intermediate outcomes include earlier, more-rapid, and more-precise detection of biological agents in

the environment or in people and more information for decisionmakers so that they can make better-informed decisions about initiating appropriate mitigation actions more rapidly.

Opportunities and Recommendations

The understanding of the policy and practice landscape, non-S&T R&D relevant to environmental biodetection and human biosurveillance, and S&T's R&D portfolio gained through this study provides the basis for analysis of opportunities for future S&T investment. Our analyses of non-S&T R&D are based on counts of activities rather than the level of effort (funding amounts) because we wanted to sample from a broader range of sources of information about R&D activity, some of which do not provide funding amounts. Nonetheless, our surrogate measure of activities accomplishes our aim of identifying areas in which R&D is being carried out and where there might be gaps.

As noted above, DHS has a unique niche within the federal government in the area of **environmental biodetection**—detection of biothreat agents in air. Based on our review of the open literature and policy landscape, there is no other federal organization that has a similar operational program on a comparable scale. S&T's heavy orientation toward R&D in this area reflects the role of DHS, yet the DHS operational program—BioWatch—remains under scrutiny. Its technology has advanced very little since its inception in 2003. Internal efforts to transition to a next-generation technology (autonomous collection and testing equipment) were hampered by lack of defined technical and operational requirements, performance measurement against those requirements, and justification of cost-effectiveness.

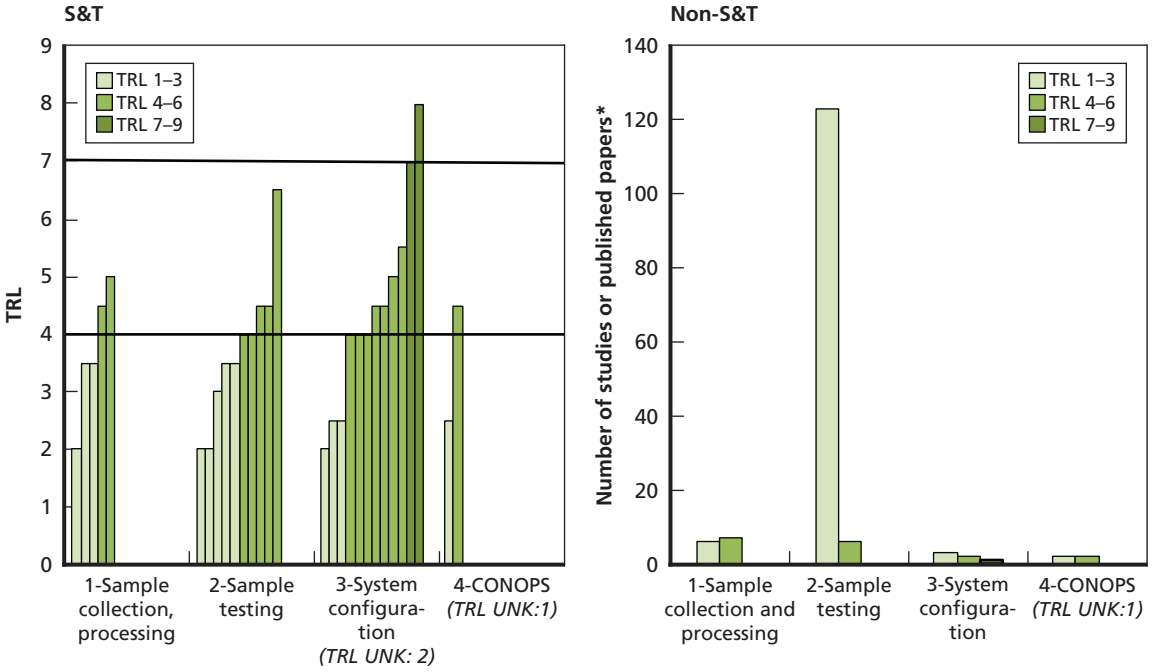
Both S&T and other funding agencies support BD test development, with non-S&T BD R&D sample test development projects more prevalent in our sample of activity than projects in the other taxonomy Tier 1 categories of sample collection and processing, system configuration, and CONOPS (Figure S.2). S&T supports four activities in the early stage of development (TRLs 1–3) and eight at higher TRL levels, compared with more than 120 and fewer than ten, respectively, supported by other agencies. S&T can selectively support research that meets specific DHS needs while monitoring outputs from early stage research funded by others and identifying outputs that could be adapted to meet DHS needs.

Our investigation identified several federal agencies—including DHS—that have missions and programming in human biosurveillance. Perhaps because of this priority, other agencies support human BSV R&D addressing test development to a greater extent than S&T does (Figure S.3). Because DHS is not a primary surveillance data collection agency, it should (and does) focus less on R&D related to data sources and reporting. However, it also supports little to no R&D addressing biosurveillance systems configuration or CONOPS or more-mature R&D that is closer to ready for application, all of which would be relevant to its National Biosurveillance Integration Center.

The discussion of opportunities above gives rise to five recommendations related to directions for future S&T R&D investments. These are conditional on DHS decisions regarding continued DHS programming related to environmental biodetection and human biosurveillance and are as follows:

- Develop a DHS strategic plan for environmental biodetection and human biosurveillance R&D, consistent with DHS's role in national biodefense.

Figure S.2
Comparison of S&T and Non-S&T Biodetection R&D Activity, by TRL



* Surrogate for R&D activity.

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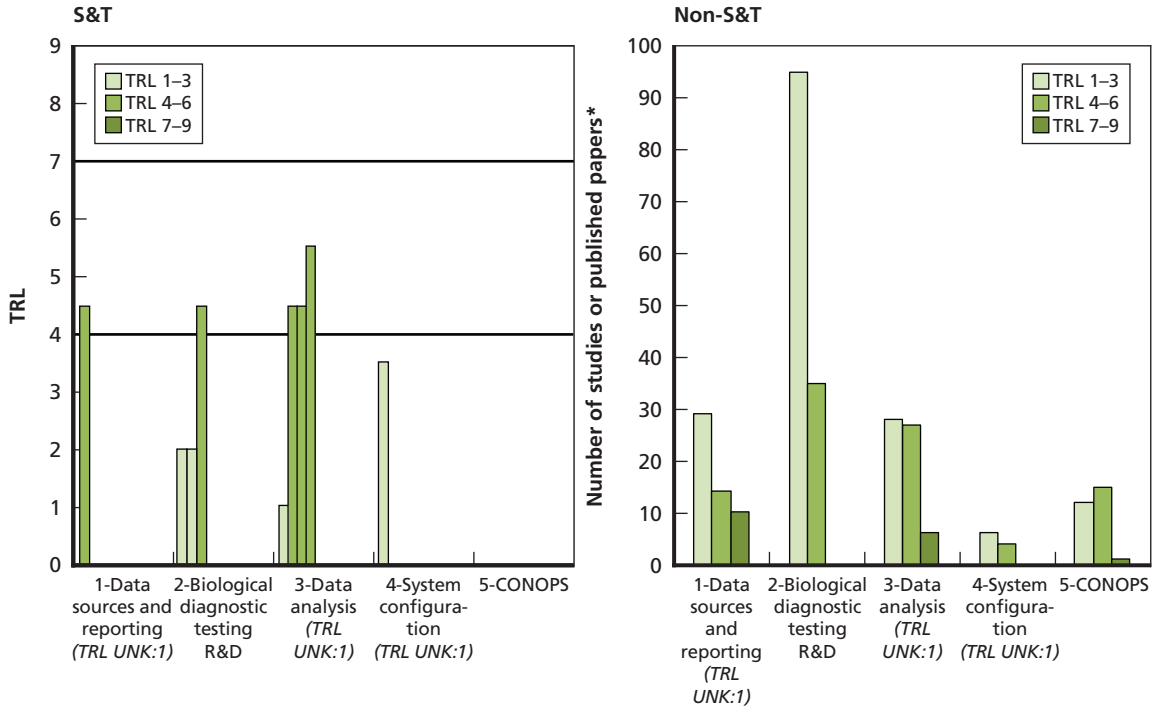
Figure S.3
Comparison of S&T and Non-S&T Biosurveillance R&D Activity, by TRL



* Surrogate for R&D activity.

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- Prioritize biodetection R&D over biosurveillance R&D, given DHS's unique federal government role in this area.
- Prioritize R&D addressing CONOPS, given the relative lack of R&D in this area by either S&T or other agencies and the shorter-term potential for real-world application.
- Actively monitor R&D (at all stages of maturity) supported by other agencies, and adapt relevant outputs to meet DHS needs—for example, addressing biodetection and biosurveillance test development, and biodetection aerosol applications.
- Prioritize midstage and later stage R&D (TRLs 6–9) to complement or balance the current predominantly earlier stage research (TRLs 1–3).

A DHS strategic plan should lay out clear desired intermediate and end outcomes consistent with DHS's role in national biodefense and then construct a program of R&D and other activities aligned to help achieve them. A set of methods (e.g., R&D logic models) can then be used as a planning tool to help guide future investments and to develop metrics for monitoring progress toward defined outcomes.

These recommendations help focus future directions for DHS R&D investments in the areas of environmental biodetection and human biosurveillance. Again, they depend at least in part on the future of current DHS operational programs in these areas—BioWatch and the National Biosurveillance Integration Center. To the extent they remain as department (and federal) priorities and housed within DHS, there are clear needs for R&D to help improve both. Also, DHS components (e.g., U.S. Secret Service, U.S. Coast Guard) must be able to access R&D outputs to help them improve their capabilities to carry out their missions.

Potential next steps could include consultation with internal (DHS) and external (non-DHS) customers currently or potentially targeted by S&T R&D to verify needs and uses of R&D in furtherance of their respective missions; use of logic models or other planning tools to develop a strategic R&D plan for addressing biodetection or biosurveillance needs; and development and implementation of measures for tracking uptake and use of S&T R&D outputs and progress toward the intermediate objectives shown in our R&D logic models.

Acknowledgments

The HSOAC project team thanks John Fischer, leader in the U.S. Department of Homeland Security's Science and Technology Directorate, for his support for the research and insightful guidance throughout the project. We also wish to thank the program directors with whom we spoke, who shared valuable information and insights about specific research and development activities. We also thank RAND researchers Gary Cecchine and Donald Prosnitz for their thoughtful reviews and constructive comments on the report and Isaac Porche, director of HSOAC's Acquisition and Development Program, for his wise guidance throughout the project.

Abbreviations

AIDO	Analysis for Investigation of Disease Outbreaks
ASPR	Office of the Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
BD	biodetection
BKC	Biodefense Knowledge Center
BSV	biosurveillance
BSVE	Biosurveillance Ecosystem
BTRA	Biological Terrorism Risk Assessment
CBD	chemical and biological defense
CBRN	chemical, biological, radiological, or nuclear
CDC	Centers for Disease Control and Prevention
CDP	Center for Domestic Preparedness
CONOPS	concept of operations
DHS	U.S. Department of Homeland Security
DNDO	Domestic Nuclear Detection Office
DoD	U.S. Department of Defense
DoE	U.S. Department of Energy
DTIC	Defense Technical Information Center
DTRA	Defense Threat Reduction Agency
EMS	emergency medical services
EOP	Executive Office of the President
EPA	Environmental Protection Agency

FEMA	Federal Emergency Management Agency
FY	fiscal year
GAO	U.S. Government Accountability Office
HHS	U.S. Department of Health and Human Services
HIV	human immunodeficiency virus
HSE	homeland security enterprise
HSOAC	Homeland Security Operational Analysis Center
HSPD	homeland security presidential directive
IARPA	Intelligence Advanced Research Projects Agency
ICE	Immigration and Customs Enforcement
IOM	Institute of Medicine
MALDI-TOF-MS	matrix-assisted laser desorption ionization time-of-flight mass spectrometry
N/A	not applicable
NAS	National Academies of Science, Engineering, and Medicine
NASA	National Aeronautics and Space Administration
NBIC	National Biosurveillance Integration Center
NBIS	National Biosurveillance Integration System
NIH	National Institutes of Health
NRC	National Research Council
NSF	National Science Foundation
OHA	Office of Health Affairs
OI&A	Office of Intelligence and Analysis
OLA	Office of Legislative Affairs
OSTP	Office of Science and Technology Policy
PCR	polymerase chain reaction
R&D	research and development
RNA	ribonucleic acid
S&T	Science and Technology Directorate

SERS	surface-enhanced Raman spectroscopy
SLTT	state, local, tribal, and territorial
STTR	Small Business Technology Transfer
TRL	technology readiness level
TSA	Transportation Security Administration
UNK	unknown
USCG	U.S. Coast Guard
USDA	U.S. Department of Agriculture
USSS	U.S. Secret Service
VA	U.S. Department of Veterans Affairs
VACUUM	Viable Aerosol Collection Utility Unit Man-Portable
WHO	World Health Organization

CHAPTER ONE

Introduction

The intentional biological attack within the continental United States involving anthrax-laced letters mailed to offices in Florida, Washington, D.C., and various media outlets in September 2001 resulted in the deaths of five people and the reported illness of 17 others from inhaling anthrax (National Public Radio, 2011). This event brought to light the country's vulnerability with regard to detecting possible biological threats. Following this event and the creation of the U.S. Department of Homeland Security (DHS), DHS established environmental biodetection (BD) and broad biosurveillance (BSV) operations intended to help the country prevent, detect, and respond to biological events. Several years later, the 2014 West Africa Ebola outbreak highlighted the potential domestic risks posed by naturally occurring pathogens, when four individuals, who had either recently traveled to West Africa or provided care to people who had contracted the disease, tested positive for Ebola in the United States over the course of two months.

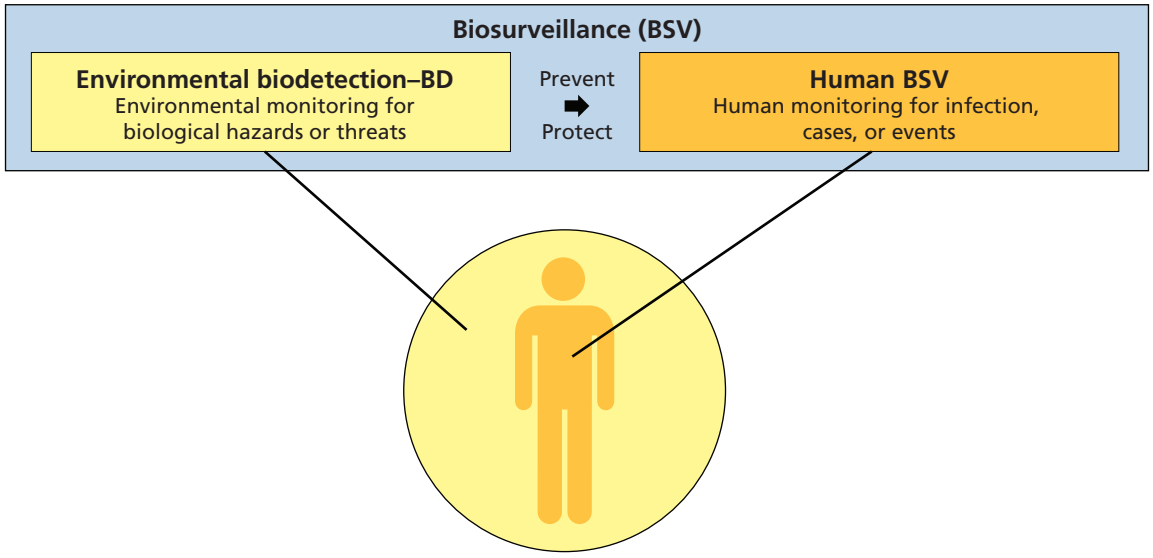
Both intentional attacks and the natural emergence of new pathogens pose challenges to biodefense. For example, in March 2018, the World Health Organization (WHO) included "Disease X" on a list of 11 priority diseases in the *Research and Development Blueprint* for severe emerging diseases with the potential to spread widely and without available, effective preventive or therapeutic measures (WHO, 2018). WHO describes Disease X as "[representing] the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease, and so the *Blueprint* explicitly seeks to enable cross-cutting research and development (R&D) preparedness that is also relevant for an unknown 'Disease X' as far as possible." The WHO *Blueprint* was first issued in 2015 and is updated roughly annually. It refers to emerging infectious diseases, which have been on the U.S. and global policy agenda since the first U.S. domestic and global strategies were issued in the 1990s. Retrospective examinations have documented the number of emerging pathogens dating back before the 1990s. For example, Jones and colleagues report on 335 diseases that emerged between 1940 and 2004, of which more than 100 were discovered in the United States (perhaps because of more comprehensive surveillance and testing), with an overall global average of 5.2 per year and U.S. average of more than one per year (Jones et al., 2008). This growing understanding that there are diseases, both known and unknown, that have the potential to result in grave harm to the United States and other countries highlights the important role that DHS and U.S. federal organizations have with regard to doing R&D to protect us from potential biothreats, whether intentional or naturally occurring.

Therefore, biological threats are among the priorities addressed by the biodefense community and, more broadly, the homeland security enterprise (HSE). Early detection of biothreat agents is a foundation for preparedness and timely, effective response to biological attack or naturally occurring new pathogens with pandemic potential. For purposes of this assessment,

we refer to *environmental biodetection* (detection of biothreat agents in the environment, specifically in air because of the scope of the DHS operational program in this area) and *human biosurveillance* (detection of biothreat agents in humans); both fall within what professionals typically conceptualize as *biosurveillance* (see Figure 1.1).

As technologies relevant to bioterrorism advance and potential adversaries become more

Figure 1.1
Environmental Biodetection and Human Biosurveillance



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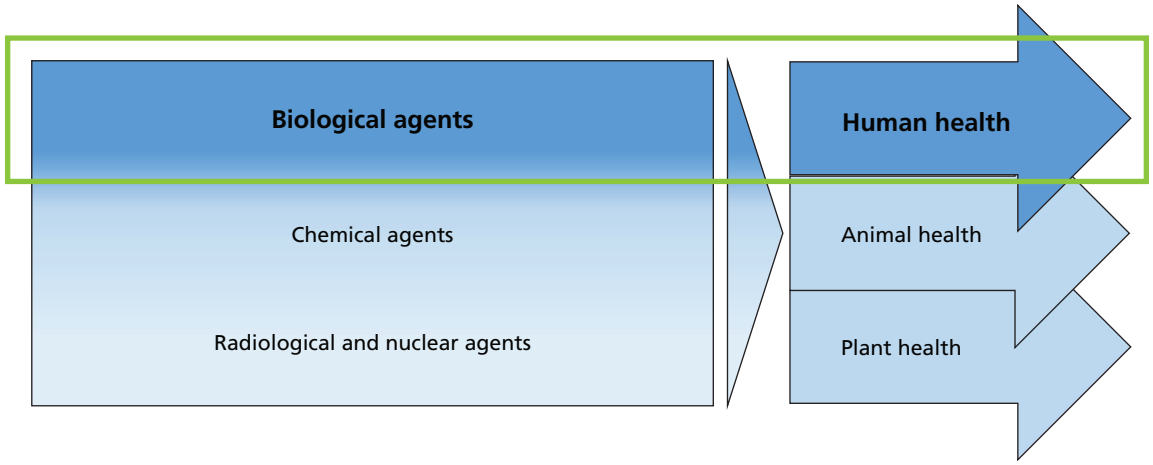
decentralized and sophisticated with regard to the development and deployment of biological weapons, U.S. R&D must strive to stay ahead to effectively detect biological threats and minimize their impact. However, fiscal realities dictate efficiency in R&D investments. In the context of both the need for adequate biodefense and the need for DHS to appropriately allocate funds, the DHS Science and Technology Directorate (S&T) asked the Homeland Security Operational Analysis Center (HSOAC) to assess priorities for its investments in R&D.

Study Objectives, Scope, and Tasks

The objective of this assessment is to provide S&T with an overall characterization of its qualitative added value within the U.S. biosurveillance enterprise; potential directions for R&D to strengthen technological elements of biodetection and biosurveillance within DHS; and a summary of opportunities to enhance return on future investments in BD and BSV systems in general. S&T intends for the outcome of this analysis to help shape S&T investments for biodetection and biosurveillance. Ultimately, such investments aim to save lives while increasing operational efficiency to detect and respond to a bioterrorist attack.

S&T asked HSOAC to focus specifically on biological threats in humans and aerosol threats within the environment (Figure 1.2) and to consider the role of DHS within the larger interagency context.

Figure 1.2
Project Scope: Biological Agents Affecting Humans



SOURCE: White House, 2012.
RAND *RR2398-1.2*

The project entailed three tasks: (1) assess the relevant policy and practice landscape for national BD and BSV efforts, (2) conceptualize how R&D can be brought to bear to improve BD and BSV, and (3) review and assess DHS S&T R&D in support of BD and BSV programs.

Methods

To address Task 1, the HSOAC team reviewed key U.S. government policy documents that are relevant to biothreats and national security. To address Tasks 2 and 3, the team reviewed the S&T portfolio of R&D activity. The team also met with key S&T staff, including a division director and six key program managers. The team then created conceptual frameworks to organize, characterize, and present R&D activity. Specifically, we created (1) taxonomies to organize and characterize relevant R&D activity, (2) logic models that depict environmental BD and human BSV operational activities, (3) logic models that depict S&T R&D, and (4) conceptual mapping of R&D to the architecture of the National Strategy for Biosurveillance (see Chapter Two).

The team also developed inventories of relevant non-S&T R&D activities related to environmental BD and human BSV based on the searches described below, then characterized each R&D item based on the two taxonomies, technology readiness level (TRL), sponsor, and security orientation (i.e., review of abstract for mention of select agents; viral hemorrhagic fever; or security-related context, such as "bioterror" or "military"). The purpose of examining non-DHS R&D was to assess whether and how non-DHS R&D might inform S&T R&D investments. The team used counts of activities, rather than funding level, as the most feasible surrogate for R&D level of effort because funding amounts were not available for about 20 percent of non-S&T R&D inventory items (mostly journal publications and agency websites); the team's aim was to obtain a sense of the nature and breadth of R&D activity in specific areas from a broader range of sources rather than precise funding information from a narrower range of sources. If some activities, such as high TRL R&D projects, have unusually

large financial investments or some funders invest more in each activity on average than others, then analyses based on the level of financial investment could be substantially different from those based on the number of activities.

The search terms were drawn from the two taxonomies, and the taxonomies were iteratively updated to reflect the inventory results. However, we did not systematically search for R&D activities within each taxonomy area. The inventories of non–S&T-sponsored BD and BSV research were derived from searches of federal R&D databases, searches for published papers indexed in the Web of Science databases,[1] and searches on federal agency websites, as described in the rest of this section.

Federal Research Databases

We drew heavily from two key databases of federally supported research:[2]

- National Institutes of Health (NIH) RePORTER database: Captures projects supported by agencies across the U.S. Department of Health and Human Services (HHS), including the Food and Drug Administration and the U.S. Centers for Disease Control and Prevention (CDC)[3]
- Federal RePORTER database: Captures projects from the National Aeronautics and Space Administration (NASA), the National Science Foundation (NSF), the Environmental Protection Agency (EPA), and the U.S. Department of Veterans Affairs (VA), as well as projects from portions of the U.S. Department of Defense (DoD), the U.S. Department of Agriculture (USDA), and the U.S. Department of Education.

We searched for projects funded from fiscal year (FY) 2013 through FY 2018 using such terms as "surveillance," "air sampling," and "biodefense" (details of federal database searches are presented in the appendix).

Published Papers

To identify published papers documenting relevant work, we searched Web of Science, a large source of indexed scientific publications that covers many disciplines and allows for tailored searches. We initially searched for documents that included the search terms "biosurveillance or "biodetection." In order to reflect relatively recent R&D, publication searches were restricted to January 2010 through September 2017. These search terms generated an initial set of publications. We then did additional searches of Web of Science using search terms that included "bio-detection," "biosensors," "biosensing," "biomonitoring," and "biodefense." In cases in which the search terms produced too many documents to review manually, the returned results were filtered by limiting them to publications in the following categories: nanoscience and

[1] Web of Science is a large searchable database of scientific publications across disciplines and journals that allows for tailored searches (Clarivate, undated).

[2] Although other databases of federal spending (e.g., USAspending.gov) contain a larger number of records than the two databases searched, the search functionality and information present (e.g., lack of detailed project abstracts, inclusion of numerous non–R&D efforts) were not conducive to identifying efforts relevant to this project. Because of the comparatively comprehensive nature of the two databases, the results might underestimate the relative activities of federal agencies whose research activities we characterized using other sources.

[3] The NIH RePORTER database did not include activities funded by the HHS Biomedical Advanced Research and Development Authority (BARDA).

nanotechnology, applied physics, optics, biotechnology applied microbiology, biophysics, biochemical research methods, biomedical engineering, microbiology, spectroscopy, biology, and chemical engineering. We also specifically searched for DHS-funded research publications. To do this, we searched Web of Science by funding agency using "DHS," "DHS S&T," "DHS Science," and "Department of Homeland Security." The final collection of Web of Science papers was then reviewed manually. We identified papers relevant to this project by manually reviewing titles and abstracts of the search results and retained papers that pertained to or described methods for detecting, collecting, and alerting in regard to bio-related events. Although Web of Science includes papers funded by a broad range of sponsors, including industry, state and local governments, and foundations, the small set of illustrative papers we selected contained only work funded by the U.S. government, foreign entities, and an academic institution. Nonetheless, the inclusion of those activities did diversify our inventory.

Research Funded by the Department of Defense

Because of the security orientation of DoD, we explored a wide variety of sources to identify as comprehensive as possible a set of openly available DoD-supported BD and BSV research and initiatives. We queried centralized databases—the Federal RePORTER database described above and the Defense Technical Information Center (DTIC)[4]—using the terms "biosurveillance," "biodetection," "biodefense," "emerging pathogen detection," and phrasing variants. DTIC information surveyed included the R-2s (budget justification documents) at the DoD Investment Budget Search website, which describe research, development, testing, and evaluation programs by program element for the president's budget submission to Congress. To avoid duplicates, when searches returned multiple R-2s for a program element, we consulted only the most recent. Databases provided limited insight into defense-oriented BD and BSV research. The Federal RePORTER database focuses on scientific research grant awards from DoD, among other federal agencies, but not all elements of DoD are represented in the database. DTIC is a repository of final reports on DoD-funded research but has relatively limited unclassified content in the areas of biological agent detection and surveillance. To supplement the centralized database search, we searched public websites of organizations that are DoD-aligned or DoD-funded. We first identified a list of relevant organizations aligned with DoD or with defense-focused research, including DHS and U.S. Department of Energy (DoE)–funded national laboratories. The organizations explored further were as follows:

- **Office of the Secretary of Defense:** Defense Threat Reduction Agency (DTRA), Defense Advanced Research Projects Agency, Defense Health Agency, Joint Program Executive Office for Chemical and Biological Defense
- **Department of the Army:** Army Research Laboratory, U.S. Army Edgewood Chemical Biological Center, U.S. Army Medical Research Directorate
- **Department of the Navy:** Navy Medical Research and Development, Naval Research Laboratory
- **Department of the Air Force:** Air Force Research Laboratory

[4] DTIC was searched via the public portal. Thus, identified research does not include any that generated for-official-use-only or classified final reports.

- **DoE-funded national laboratories:** Los Alamos National Laboratory, Oak Ridge National Laboratory, Lawrence Livermore National Laboratory, Lawrence Berkeley National Laboratory, Pacific Northwest National Laboratory
- **Other:** Johns Hopkins Applied Physics Laboratory, Lincoln Laboratory, National Biodefense Analysis and Countermeasures Center.

For each of these organizations, we searched publicly available websites for information on research foci, funded projects, and finished projects. The quality and quantity of information available varied by organization. To account for variations in the amount of information available for each organization, we first searched publicly available websites for indexes of funded projects. We examined projects that were funded between 2014 and 2017 for relevance to BD and BSV.[5] Second, we searched organizational charts or charts describing areas of focus to identify current lines of research within the organization. Third, we searched recent news or similar public announcements from the past year to identify any recently completed projects that fell within the BD and BSV subject areas.

Research in the Commercial Sector

Beyond advertising of products that are currently available, the information that companies make public about ongoing research is highly variable. To address this challenge, we identified biodetection and biosurveillance research in the commercial sector through examination of Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) awards. These are federally funded opportunities for small businesses that aid development and commercialization of technologies or products that align with federal government priorities. Eleven agencies, including DHS, currently participate in the SBIR program, and five (DoD, HHS, DoE, NASA, and NSF) participate in the STTR program. The SBIR/STTR database has a comprehensive list of all opportunities that were funded in the past few FYs. We filtered this database for the "chemical biological defense" flag and the three most recently funded years (FY 2015 to FY 2017).[6] We identified companies conducting early BD or BSV research by scanning funded requests for proposals for BD and BSV keywords.[7] Because commercial R&D activities use a range of funding types in addition to SIBR/STTR funds, our list is not comprehensive. In particular, it does not capture the work of large companies not eligible for SIBR/STTR funds or any work entirely self-funded by industry.

Once we identified papers and research projects, we scanned titles and abstracts for relevance to the BD or BSV frameworks. Projects without clear links to "environmental air monitoring for biological hazards/threats" and "human monitoring of biological agents for infection/ cases/events" were excluded. Other exclusion criteria included international research that was not directly relevant to detecting aerosolized bioagents or human BSV, projects about

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[5] The data collected were intended to reflect a snapshot of current or recently completed research related to BD and BSV. For this reason, searches of publicly available information sources were limited to within approximately four years (i.e., 2014 to 2017).

[6] The requests for proposals we identified directly from the SIBR/STTR database were funded by DoD. The NIH and Federal RePORTER searches identified additional SIBR/STTR-funded activities that, although relevant, were not categorized with the "chemical and biological defense" topic code. After we completed our searches, the SIBR/STTR program updated its website and no longer offers searches by topic flag.

[7] Keywords searched included "biosurveillance," "biodetection," "biodefense," "emerging pathogen detection," "biological agent detection," "biological threat detection," and phrasing variants.

sexually transmitted diseases or such chronic diseases as cancer that are not relevant to detection of biothreat agents in the environment or humans, nonhuman study, and food safety. We retained projects working on fundamental and enabling technologies, such as those intended to characterize single cells rapidly (e.g., use of Raman spectroscopy to determine whether a cell is cancerous based on surface markers and intracellular components) or reduce the time to identify a biological agent that could be adapted to either environmental BD or human BSV, even if the projects were not directly relevant and would otherwise fall within the exclusion categories. We estimated the stage of maturity (TRL) for each retained project, specifically related to DHS responsibilities in the areas of environmental BD in air and human BSV. Science (basic research) projects are at TRLs 1–3, technology development projects are at TRLs 4–6, and product development projects are at TRLs 7–9 (DHS, undated-c). Although abstracts from project proposals and published papers are not written with TRL in mind, we reviewed the available information (mainly abstracts) and categorized the TRL for each activity into a larger group of TRLs 1–3, TRLs 4–6, or TRLs 7–9, rather than assigning more-specific levels.

Road Map for Report

The remainder of this report describes the policy and practice landscape relevant to environmental biodetection and human biosurveillance, including national strategies and the responsibilities of DHS and other federal agencies (Chapter Two); the non-S&T R&D landscape related to biodetection and biosurveillance (Chapter Three); analysis of S&T R&D (Chapter Four); and analysis of opportunities and recommendations related to S&T R&D investments (Chapter Five).

CHAPTER TWO

Policy and Practice Landscape

As noted in the introduction, biothreat agents have been recognized as a significant security threat to the United States. The CDC and USDA maintain the list of select agents of concern to government planners as part of the Federal Select Agent Program (Federal Select Agent Program, undated). Most of the agents of greatest concern—labeled Tier 1—can be transmitted via air: the pathogens causing anthrax, botulism, glanders, melioidosis, Ebola fever, tularemia, Marburg fever, smallpox, and plague. This makes air monitoring and timely, accurate environmental BD particularly important. Timely detection can trigger responses to help minimize human exposure and disease. Similarly, timely detection of exposure or disease in humans (whether to airborne pathogens or pathogens transmitted through other mechanisms) can trigger responses to provide appropriate chemoprophylaxis (if warranted), clinical care, and, potentially, additional prevention measures. Thus, environmental biodetection and human biosurveillance are foundational to national biodefense.

This chapter summarizes the biodefense policy and practice landscape. We first summarize key policy documents relevant to biodefense, and then, briefly, the practice landscape—the missions and responsibilities of DHS and other federal agencies, especially as they relate to environmental biodetection and human biosurveillance.

Policy Landscape: National Strategies

The team reviewed national strategies that are relevant to biothreats and national security, including those in which environmental biodetection and/or human biosurveillance play a role. These are described briefly next.

National Biodefense Strategy. The Blue Ribbon Study Panel on Biodefense was established in 2014 to assess gaps and provide recommendations related to defense against biological threat agents (biodefense) (Blue Ribbon Study Panel on Biodefense, 2015). The panel held four daylong sessions of public meetings during 2014 and 2015 and issued a report and recommendations in October 2015. The panel concluded that the United States does not adequately address biological threats and called for focused leadership to foster coordination and collaboration and drive innovation. Among its 33 recommendations were calls for institutionalization of biodefense at the level of the White House, development of a national strategy and implementation plan, improvements in biosurveillance (among other preparedness and response elements, such as medical countermeasures), and improvements in environmental detection and the DHS National Biosurveillance Integration System (NBIS) (described in more detail later in this chapter). The National Biodefense Strategy Act of 2016 (6 U.S.C. § 104) called for

development of a national strategy and implementation plan for biodefense within 275 days. As of April 2018, the final strategy had yet to be released.

National Security Strategy (2017). The National Security Strategy, issued by the White House, reflects overall U.S. policy related to national security. The linkages between health and national security have been progressively strengthened within these strategies in recent years, from brief mention of pandemics in the 2006 strategy (White House, 2006) to a section on pandemics and infectious diseases within a larger section on international order in the 2010 strategy (White House, 2010) and a dedicated section on global health security in 2015 (White House, 2015). The most recent National Security Strategy, issued in December 2017, has a section on combating biothreats and pandemics within the section on securing U.S. borders and territory, under the first pillar related to protecting the American people, homeland, and American way of life (White House, 2017). These threats can be intentional, accidental, or naturally occurring. The most recent National Security Strategy specifies three priority actions: detect and contain biothreats at their source (linked to global health security), support biomedical innovation, and improve emergency response.

National Health Security Strategy and Implementation Plan, 2015–2018 (2015). The Secretary of HHS issued the first legislatively mandated National Health Security Strategy in December 2009 (HHS, 2009). It is also a whole-of-government effort and includes two overarching goals and nine objectives addressing such issues as community resilience, workforce, situational awareness (including biosurveillance), the health care system, medical countermeasures, prevention and mitigation of environmental and other threats, global health partnerships, and innovation. The required quadrennial update, with associated implementation plan, was issued by the HHS Assistant Secretary for Preparedness and Response in early 2015 (HHS, 2015). It includes five objectives, related to resilient communities, medical countermeasures and nonpharmaceutical interventions, health situational awareness (including biosurveillance), the health care and emergency management system, and global health security.

Global Health Security Agenda (2014). The United States led the development of a multinational initiative to strengthen the capabilities of countries worldwide to prevent, detect, and respond to infectious disease threats (White House, 2014). The Global Health Security Agenda includes three objectives related to prevention of avoidable epidemics, four objectives related to early detection of outbreaks (including biosurveillance), and two objectives related to rapid and effective response.

Presidential Policy Directive 21: Critical Infrastructure Security and Resilience (2013). This directive, issued by the White House, describes three strategic imperatives to strengthen critical infrastructure security and resilience against physical and cyber threats—unity of effort, information exchange, and data integration and analysis—and six deliverables, including a description of functional relationships within DHS and across the federal government, identification of baseline data and system requirements to enable efficient information exchange, and development of situational awareness capability for critical infrastructure (White House, 2013). The directive also highlights the role of DHS and other federal agencies to lead innovation and R&D as part of the overall effort.

National Strategy for Biosurveillance (2012). This strategy, issued by the White House, encompasses four guiding principles (leveraging existing capacities, whole-of-government approach, added value for all participants, and global perspective); four core functions (scan and discern the environment, identify and integrate essential information, alert and inform decisionmakers, and forecast and advise impacts); and four enablers (integrate capabilities,

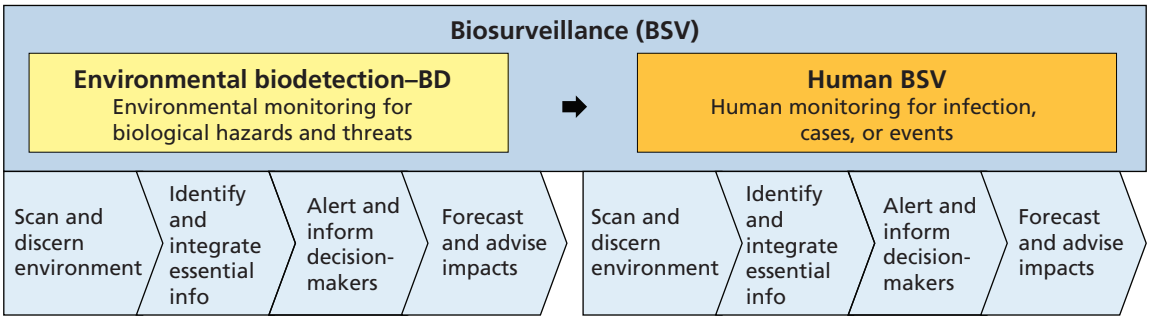
build capacity, foster innovation, strengthen partnerships) (White House, 2012). As specified in the strategy, "The biosurveillance goal is to achieve a well-integrated national biosurveillance enterprise that saves lives by providing *essential information* for better decisionmaking at all levels" (White House, 2012, p. 1). Until a new national biodefense strategy is issued, this strategy and its associated implementation plan remain the government's biosurveillance policy. As such, it suggests conceptual anchors for operational environmental BD and human BSV programs. We situated environmental BD and human BSV in the context of that strategy (Figure 2.1). It is important to note that human biosurveillance does not flow exclusively from environmental sources (i.e., airborne pathogens that are subject to environmental BD). However, as suggested by the arrows in the figure, timely environmental BD can trigger both stepped-up human BSV and actions to alert decisionmakers and prevent extensive disease transmission. Nonetheless, the spectrum of human BSV relevant to DHS—and, thus, this project—extends beyond just airborne biothreats.

National Strategy for Countering Biological Threats (2009). This strategy, issued by the White House in 2009, aims to reduce the risks associated with the intentional or accidental release of a biological agent (White House, 2009). In the context of global interconnectedness and the associated risks of global disease spread, it calls for the federal government to work with domestic and international partners to advance the health security of people worldwide. It focuses on intentional misuse of the life sciences and derivative materials to do harm to people, agriculture, or other critical infrastructure. Under the first of its seven objectives, it calls for building global disease surveillance capacity.

Homeland Security Presidential Directive (HSPD) 21: Public Health and Medical Preparedness (2007). This directive, issued by the White House, establishes a National Strategy for Public Health and Medical Preparedness and lays out four critical components of public health and medical preparedness: biosurveillance, countermeasure distribution, mass-casualty care, and community resilience (White House, 2007a).

HSPD-18: Medical Countermeasures Against Weapons of Mass Destruction (2007). This directive, issued by the White House, builds on the vision and objectives articulated in the 2002 *National Strategy to Combat Weapons of Mass Destruction* and the 2004 *Biodefense for the 21st Century* to ensure that the nation's medical countermeasure R&D and acquisition efforts

Figure 2.1
Environmental Biodetection and Human Biosurveillance Within the Context of the National Strategy for Biosurveillance (2012)



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> target threats that have potential for catastrophic impact on our public health and are subject to medical mitigation; yield a rapidly deployable and flexible capability to address both existing and evolving threats; are part of an integrated WMD [weapons of mass destruction] consequence management approach informed by current risk assessments of threats, vulnerabilities, and capabilities; and include the development of effective, feasible, and pragmatic concepts of operation for responding to and recovering from an attack. (White House, 2007a)

The policy lays out a two-tiered approach for the development and acquisition of medical countermeasures, including focused development of agent-specific countermeasures and the flexible capability for developing new medical countermeasures, such as broad-spectrum approaches to surveillance, diagnostics, prophylactics, and therapeutics.

HSPD-10: Biodefense for the 21st Century (2004). This directive provides a blueprint for the biodefense program based on an evaluation of biological defense capabilities (White House, 2004). It describes four pillars of biodefense (i.e., threat awareness, prevention and protection, surveillance and detection, and response and recovery), objectives for further progress for each pillar, and key roles for federal departments and agencies. The HSPD also calls out cross-cutting functions, including information management and communications; research development and acquisition; creation and maintenance of needed biodefense infrastructure, including the human capital to support it; public preparedness; and strengthened bilateral, multilateral, and international cooperation.

Summary of Policy Landscape

Although each of the policies described here is distinct, they are related in at least five important ways that are relevant to this study. First, the policies all recognize the links between health and security, and several include either title or text with the term *health security*. Second, whether issued by the White House or a federal department, all call for a whole-of-government effort, as distinct from sector- or department-specific effort. Third, they all address biodefense—countering threats from biological agents. Fourth, all except one (relating to medical countermeasures) squarely address biosurveillance. Finally, nearly all of them call for research or innovation related to health security. Thus, although the policy landscape relevant to this study might be complex in terms of the number of extant policies issued over the past several years, they are consistent with one another with respect to health and security (and health security), whole-of-government effort, defense against biological threats, and the prominent roles of biosurveillance, research, and innovation.

Practice Landscape: Operational Programs and Responsibilities of the Department of Homeland Security and Other Federal Agencies

The practice landscape for environmental biodetection and human biosurveillance begins with understanding how these programs are intended to prevent human exposure to biological agents and protect humans from biological threats. Using the core functions outlined in the National Strategy for Biosurveillance as our anchor, we constructed notional logic models that describe the operation of environmental BD and human BSV, shown in Figures 2.2 and 2.3, respectively. Logic models are a way to visually represent a program's or organization's opera-

tions, starting with inputs that drive activities and outputs, which then are given to relevant organizations and decisionmakers and (ideally) lead to intended outcomes (Greenfield, Williams, and Eiseman, 2006). A benefit of constructing a logic model is that it forces an organization to explicitly state how it expects those stakeholders to use the program's outputs to achieve the desired outcomes. In that regard, if the desired outcomes are not being achieved, it provides a road map for diagnosing barriers or identifying flawed assumptions with the conceptional path from inputs to outcomes. Both of the operational logic models shown in Figure 2.2 and Figure 2.3 have the potential to be enabled or enhanced through advances in R&D, represented by the arrow underneath each model. In Chapter Four, we develop more-detailed logic models that display S&T's environmental biodetection and human biosurveillance R&D efforts and desired outcomes. There is good agreement between the types of intermediate outcomes in Figure 2.2 and Figure 2.3 and the types of anticipated outcomes connected with S&T's R&D efforts discussed in Chapter Four.

The practice landscape for environmental biodetection and human biosurveillance also includes the missions and programs of both DHS and other agencies, as highlighted in the following sections.

DHS

DHS has operated two key operational programs related to environmental BD and human BSV, as described next. Figure 2.4 shows the policy landscape described in the previous section and key reports on DHS BD and BSV as described in the sections that follow.

BioWatch

The BioWatch program is the federal government's principal environmental BD program (i.e., for bioaerosol threat monitoring). The system has air monitoring collectors with filter paper samples that must be collected manually and are tested daily by local public health laboratories. The system has been placed in outdoor and indoor locations in approximately 30 (urban) jurisdictions. The pathogens included are not specified in publicly available documents. Between 2003 and 2016, more than 2 million BioWatch samples were tested; these generated 160 BioWatch actionable results, none of which were false positives and none of which were ascribed to intentional release (NAS, 2016).

A need for environmental BD research arose from preparations for Operation Iraqi Freedom in early 2003 to enable timely postexposure prophylaxis, if needed. President George W. Bush articulated the mission of what was to become BioWatch in his 2003 State of the Union address: "Provide, maintain and support a continuous aerosol bioterrorism monitoring capability in selected metropolitan areas" (Office of the Press Secretary, 2003). As noted historically by the first DHS chief medical officer, BioWatch progressed from concept to deployment in 30 days, principally by modifying commercially available products used by EPA to enable biological detection (Runge, undated). However, the BD products themselves were available only because of previous R&D activities, highlighting the importance of research. Speed was crucial in terms of determining sensor placement, pathogens to be monitored, and understanding of local wind dynamics as they relate to pathogen spread. However, one result was a top-down, rather than consultative, buy-in process manifested by resistance from some local jurisdictions and inconsistent CONOPS across relevant response sectors.

The program was initially led by the White House Office of Homeland Security but was moved into the new DHS in early 2003, founded just months earlier in November 2002.

Figure 2.2
Operational Logic Model for Environmental Biodetection Affecting Humans

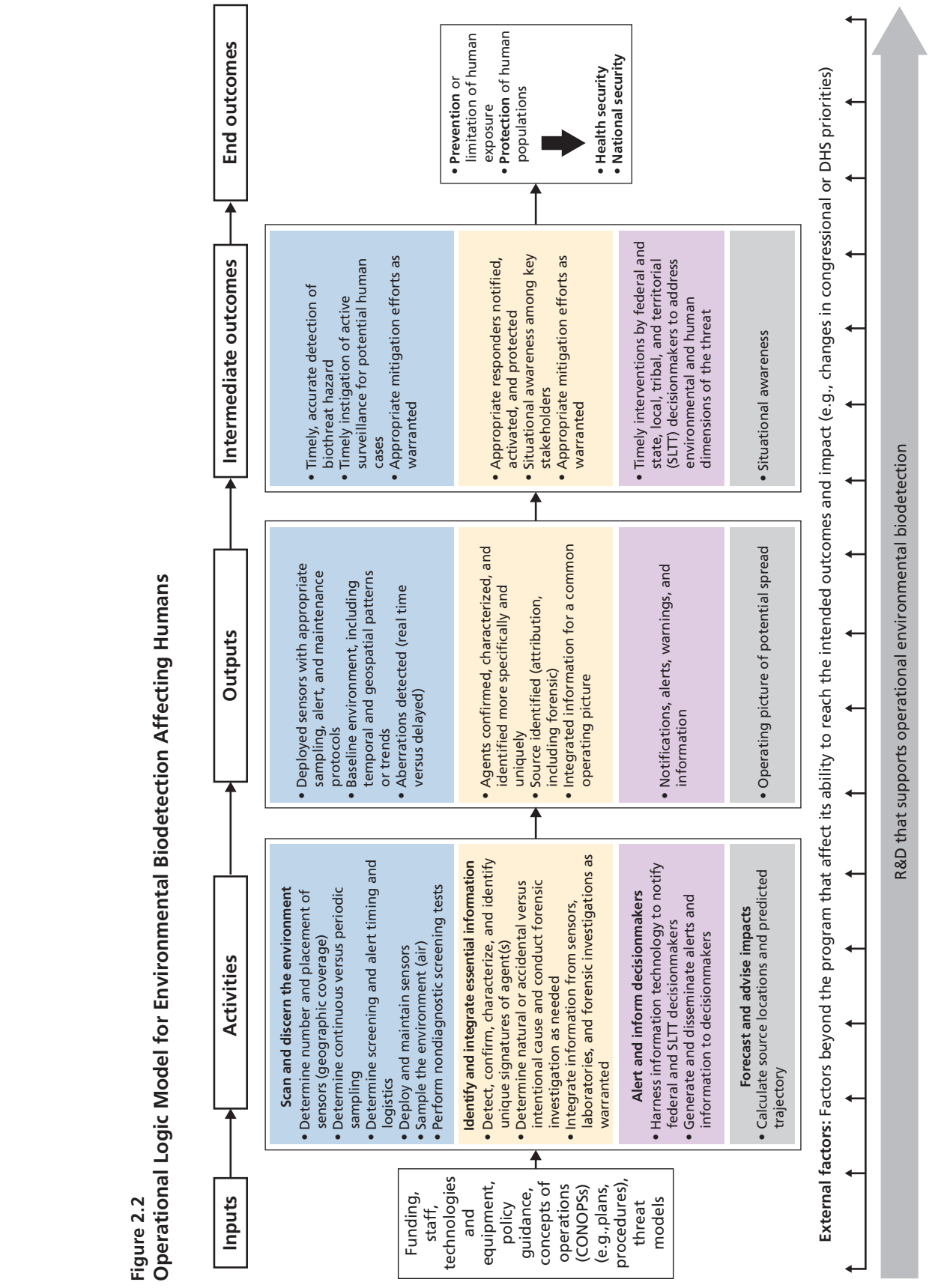

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Figure 2.3
Operational Logic Model for Human Biosurveillance

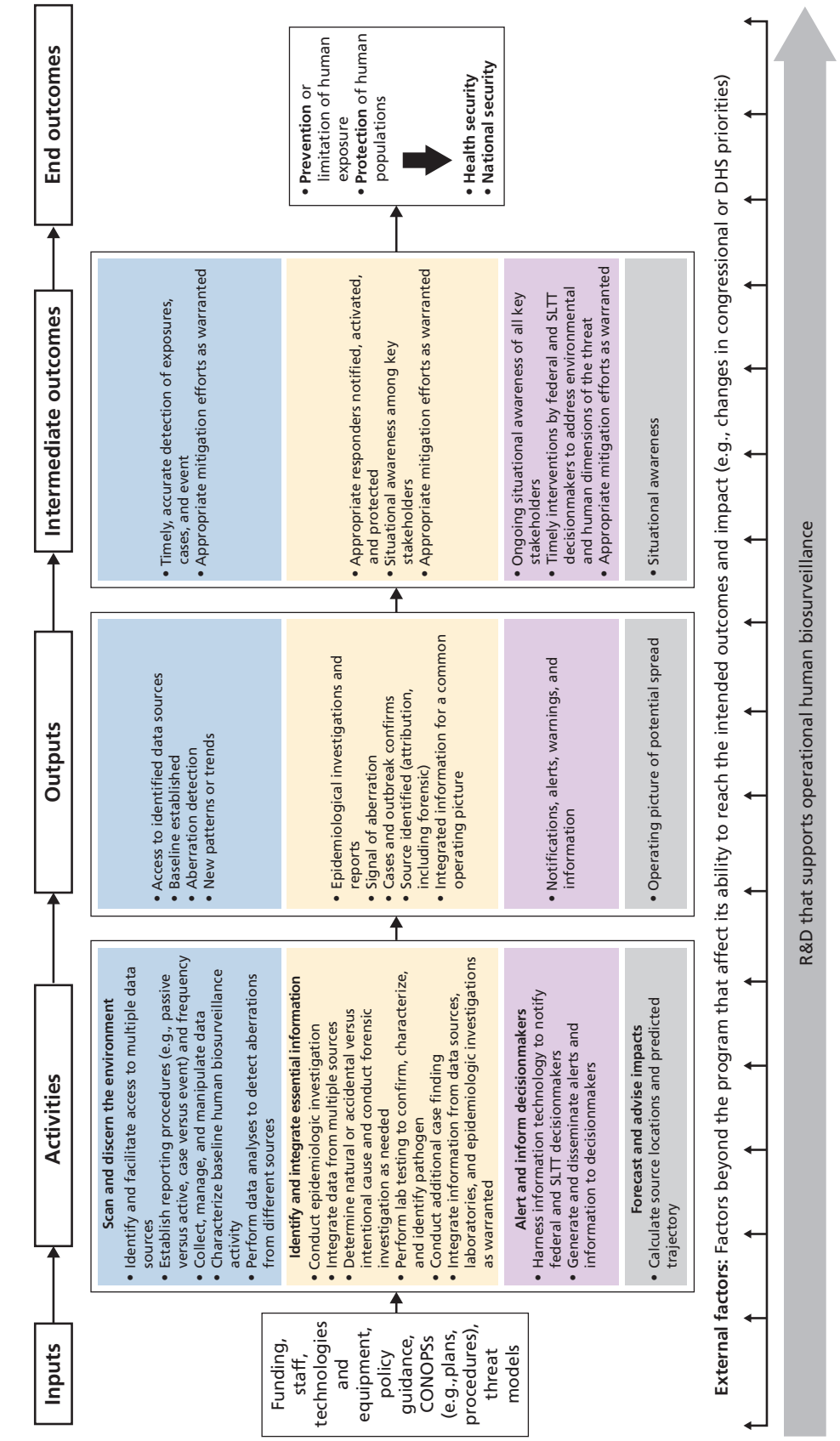
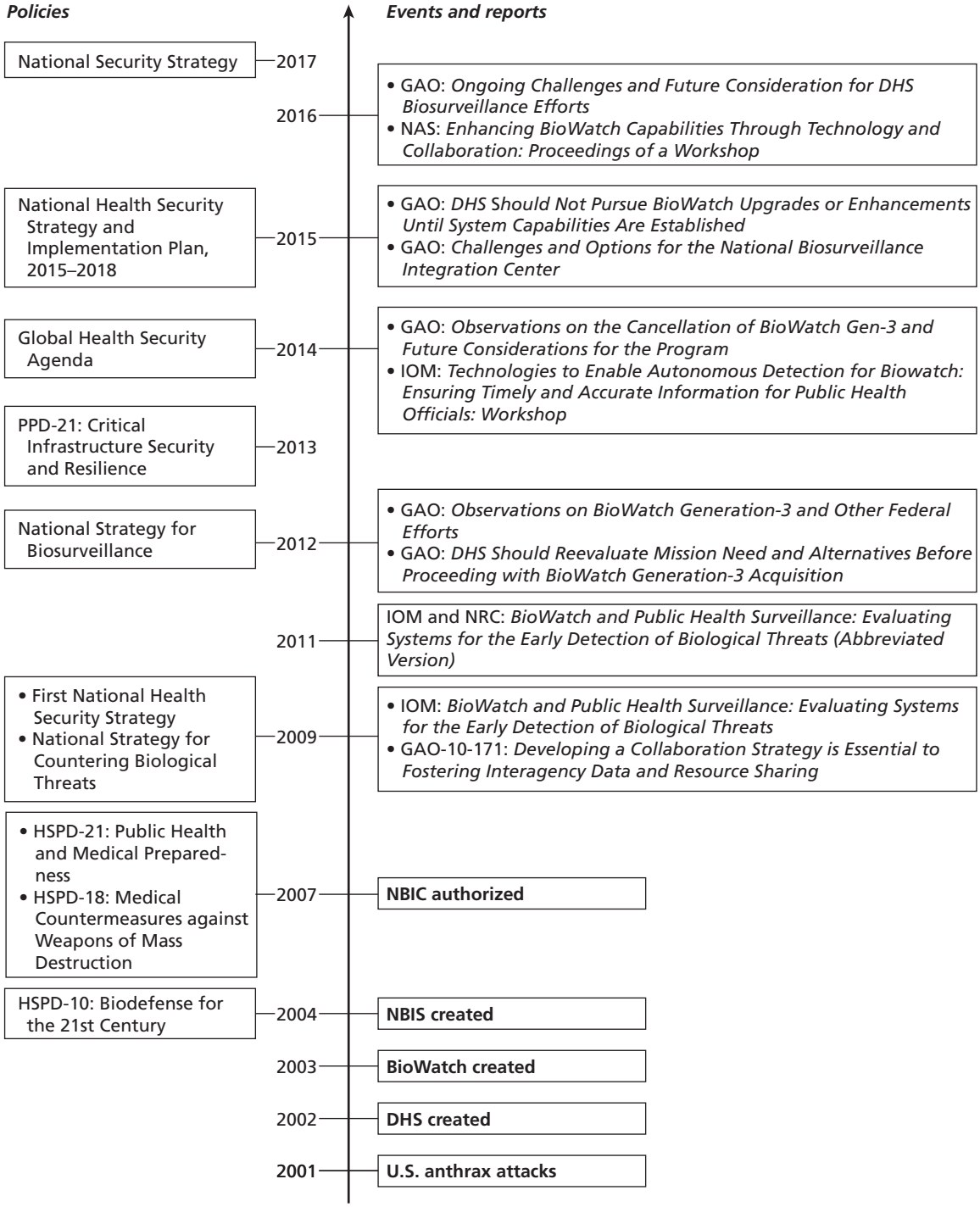


Figure 2.4
Critical Events, Reports, and Policies Relevant to DHS Biodetection and Biosurveillance



NOTE: NAS = National Academy of Sciences[but see the reference-list entry]. GAO = U.S. Government Accountability Office. IOM = Institute of Medicine. NRC = National Research Council. NBIC = National Biosurveillance Integration Center.

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Within DHS, BioWatch was first placed in S&T (2003 to 2007) and was later moved to the Office of Health Affairs (OHA) (2007 to 2017); in December 2017, the DHS Secretary moved it into the new Countering Weapons of Mass Destruction Office.

BioWatch technical requirements have not been defined, and the technology and CONOPS used for BioWatch have not evolved significantly since its establishment in 2003. Program leaders had advanced a proposal for transition from Generation 2 to a Gen-3 system in 2010, which would be autonomous, speedier, and targeted to a broader range of pathogens. Congress commissioned a series of studies by the NAS and GAO to assess the current and proposed new generation BioWatch system, which was ultimately never approved. IOM identified "serious technical and operational challenges and costs" of BioWatch, including its insufficient technical and operational testing for effectiveness, inadequate collaboration with the public health sector to enhance its usefulness, and limited reach (sensors must be in the city and location of pathogen release and included among the lab assays tested) (IOM and NRC, 2011). The title of a 2012 GAO report signals its main conclusion: *DHS Should Reevaluate Mission Need and Alternatives Before Proceeding with BioWatch Generation-3 Acquisition* (GAO, 2012a). Another GAO report underscores DHS's failure to follow its own Acquisition Lifecycle Framework[1] in not having established a mission need before embarking on acquisition and not having systematically analyzed performance or alternatives (GAO, 2012b). A 2013 IOM workshop discussed four alternative technologies—nucleic acid signatures, protein signatures, genomic sequencing, and mass spectrometry—that could be ready for testing within the following three years, seven years, or more than seven years, but the workshop was not designed to offer recommendations (IOM and NRC, 2014). In December 2013, an analysis of alternatives prepared for BioWatch Gen-3 was issued, and in April 2014, DHS canceled Gen-3 acquisition, mostly for cost-effectiveness reasons (GAO, 2014). A 2015 GAO report notes five challenges of an autonomous BD system that could inform the development of performance requirements and recommends the development and testing of such requirements: sensitivity (minimize false negatives), specificity (minimize false positives), secure networked communications, data management and interpretation, and operational maintenance over time (GAO, 2015a). A 2016 GAO report reiterates that technical performance *requirements* have never been established for BioWatch and recommends that such requirements be established to address a specified operational objective and that performance be assessed against these before the system is upgraded (GAO, 2016).

National Biosurveillance Integration Center

NBIS was organized and coordinated by DHS in 2004 but was formally codified in 2007 as NBIC, which is DHS's principal operational biosurveillance program. Congress authorized NBIC in 2007's Public Law 110-53 to help meet the HSPD-10 call for creating "a national bioawareness system that will permit the recognition of a biological attack at the earliest possible moment" (DHS, 2012; White House, 2004). It was designed to actively and passively collect data from a wide variety of sources and integrate them, then, together with analysts from across relevant federal agencies, develop a common situational awareness.

Intended as a whole-of-government effort, the mission of NBIS is to "enable early warning and shared situational awareness of acute biological events and support better decisions

[1] For information on DHS's Acquisition Lifecycle Framework, see Acquisition Management Directive 102-01 (DHS, 2015b, p. 4).

through rapid identification, characterization, localization, and tracking" (DHS, 2015a). According to a 2015 fact sheet on DHS's current website, the center incorporates thousands of data sources, integrates and analyzes data, and makes daily reports available to 900 federal and 1,500 state and local officials (DHS, 2015a). The fact sheet indicates that it is staffed by cross-disciplinary subject-matter experts and has the ability to leverage expertise across multiple federal departments and agencies.

Since 2009, GAO has issued reports that have highlighted critical shortcomings. A December 2009 GAO report noted that DHS did not have the data and personnel it needed and had failed to garner collaborative buy-in from partner agencies (GAO, 2009). GAO recommended development of an interagency collaboration strategy. In 2012, the same year that the White House issued the National Strategy for Biosurveillance, DHS issued an NBIC strategic plan, to be achieved over the ensuing five years (DHS, 2012). The plan's three chapters include an overview of biosurveillance, daily operations of NBIC, and the goals and objectives of the plan, described as having been developed through a "deliberative process that includes views of biosurveillance stakeholders." The goals and objectives derived from the congressional authorization rather than from the stakeholder group. Three years later, GAO issued a follow-up plan that again raised concerns about NBIC challenges in meeting its core functions of data analysis, coordination, and innovation (GAO, 2015b). As before, NBIC had not fully met expectations for data and collaboration from federal partners. Based on a 2014 DHS survey of stakeholders and a GAO survey of those agencies in 2015, only five of 19 federal partners said they shared their data with NBIC; eight of 11 partners stated that NBIC outputs helped their agencies identify biological events to little or no extent; and only three of 19 agencies had provided NBIC with agency liaisons. Several federal partners expressed skepticism about the feasibility of NBIC's integration role. GAO offered five options and described the benefits and limitations of each but did not recommend any option over another. The options included strengthening each of the three core functions, continuing implementation of the 2012 plan, and repeal of the NBIC statute. In short, after seven years of implementation (since 2008), NBIC had not succeeded in garnering the data and collaboration needed to serve as an effective integrator and innovator of federal biosurveillance.

Other Federal Agencies

Other federal agencies also have missions and responsibilities related to health security and the environment, including R&D, environmental BD, and human, animal, or plant BSV (Table 2.1). As indicated in the table, DHS has a unique niche for environmental BD of aerosolized biothreat agents, whereas HHS and DoD also have significant human BSV missions and programming.

Summary

The policy landscape relevant to environmental biodetection and human biosurveillance is complex, with multiple national strategies addressing different aspects of health security and national security. These are inherently whole-of-government functions, with each relevant agency contributing in different ways based on its mission. Based on independent academic and government reviews, the two key DHS operational programs for environmental biodetection and human biosurveillance—BioWatch and NBIC—have not fully achieved their

intended missions, including innovation in BD and BSV and needed collaborations with federal partners. Yet, each of these programs fills a unique niche not presently covered by any other agency—BioWatch for air monitoring for biothreat agents and NBIC for government-wide data integration and creation of value-added biosurveillance information.

Table 2.1
Biodetection- and Biosurveillance-Related Missions of Selected Federal Agencies

Department	Relevant Mission	Biodetection Programming	Biosurveillance Programming
DHS	• Continuous aerosol monitoring for bioterrorism in selected metropolitan areas • Enable rapid early detection and shared situational awareness of biological events, in support of decisionmaking	• BioWatch • New York City test bed	• NBIC
HHS	• Office of the Assistant Secretary for Preparedness and Response (ASPR): lead the nation in preventing, preparing for, and responding to the adverse health effects of public health emergencies and disasters[a] • CDC: increase U.S. health security[b]	None	• ASPR: emergency operations center • CDC: public health surveillance (United States, global)
DoD	• Provide the (healthy, ready) military forces needed to deter war and to protect the security of the country[c] • Integrate biosurveillance for DoD[d]	• Defense Occupational and Environmental Health Readiness System—Industrial Hygiene[e] • S&T program[f]	• Armed Forces Health Surveillance Branch:[g] military health surveillance (U.S., outside the continental United States), global disease surveillance
DoE	• Ensure U.S. security and prosperity by addressing its energy, environmental, and nuclear challenges through transformative science and technology solutions[h] • National laboratories as centers of science and innovation	None	None
USDA	• Food safety as one of eight mission areas (Food Safety and Inspection Service)[i] • Animal biosurveillance (Animal and Plant Health Inspection Service)[j]	None	Animal and plant biosurveillance; no human biosurveillance
EPA	• Protect human health and the environment[h]	None for aerosolized pathogens	No human BSV

[a] See HHS, ASPR, 2018.

[b] See CDC, 2014.

[c] See DoD, 2017.

[d] See Military Health System, undated-c

[e] See Military Health System, undated-b.

[f] See Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Programs, undated.

[g] See Military Health System, undated-a.

[h] See DoE, undated.

I See USDA, undated.

J See USDA, APHIS, undated.

CHAPTER THREE

Non-S&T R&D Landscape

Although the primary focus of this study was to examine the S&T portfolio and assess the current and potential future contributions of S&T-supported R&D to environmental biodetection and human biosurveillance, we wanted to examine the nature and breadth of non-S&T R&D to determine whether S&T does or can fill gaps and whether S&T could, in principle, adapt early phase R&D supported by other funding sources to meet DHS needs. Therefore, we conducted searches of various sites, as described in Chapter One, to identify R&D directly or potentially relevant to environmental BD or human BSV. Our searches were wide-ranging and intended to be illustrative of the nature and breadth of activity rather than exhaustive. After eliminating duplicates and applying retention and exclusion criteria, we analyzed an inventory of 152 R&D activities relevant to environmental BD and 282 relevant to human BSV. The majority of these (106, 70 percent for BD; 268, 85 percent for BSV) represented funded projects identified through searches of the two large federal databases; the remainder, in roughly equal proportions, were identified through searches of published papers and federal agency websites. As noted in the earlier description of methods, we used counts of activities as the most feasible surrogate of level of R&D effort, because we were interested primarily in identifying a broad range of relevant R&D activity and chose to include journal publications and agency websites among our sources, although most did not include funding amounts. The distribution of R&D activity based on funding would likely be different from the patterns described in this chapter. Also, if some activities, such as high TRL R&D projects, have unusually large financial investments or some funders invest more in each activity on average than others, then analyses based on the level of financial investment could be substantially different from those based on the number of activities. Nonetheless, our surrogate measure of activities accomplishes our aim of identifying areas in which R&D is being carried out and where there might be gaps.

This chapter describes how we approached analysis of non-S&T R&D and our detailed findings from these analyses. It concludes with a brief summary of our findings.

Organizing R&D Activities for Analysis

We aimed to examine the source and nature of non-S&T R&D related to environmental BD and human BSV. Specifically, we captured information on the funding source, level of maturity of the R&D (TRL) as gleaned from reading project or published abstracts, and whether the R&D specified any security orientation (i.e., addressed biothreat agents or a context of health security); we note that the last of these was not a specific criterion for inclusion of R&D

activities in our inventories. We also wanted an idea about the topic addressed by the research. To do so, we created and applied a taxonomy for environmental BD and another for human BSV. We created initial taxonomies based on review of our early search results and technology areas discussed during an IOM and NRC workshop (IOM and NRC, 2014) and updated them as the inventories grew. All projects were categorized at the most general (Tier 1) level and, when feasible, into a more specific subtheme within that (Tier 2) using our final taxonomies. Each project was binned into single Tier 1 and Tier 2 levels.

Tables 3.1 and 3.2 present our final taxonomies. The taxonomy for environmental biodetection includes sample collection and processing, sample testing, system configuration, and CONOPS, with different Tier 2 elements within most of these. The taxonomy for human biosurveillance includes data sources and reporting biological diagnostic test R&D, data analysis, system configuration, and CONOPS, again with multiple Tier 2 categories within them.

Representativeness of the BD and BSV Inventories

Our inventory of biodetection and biosurveillance research efforts included primarily activities identified in the NIH and Federal RePORTER databases (70 percent of biodetection activities and 85 percent for biosurveillance). These records describe projects funded since FY 2013, some of which are likely still active. To better understand the degree to which our inventory of biodetection and biosurveillance activities was representative of the overall universe of biodetection and biosurveillance R&D, we conducted a supplemental analysis of relevant research papers indexed in Web of Science. To focus on the current patterns and to arrive at a manageable set of results, we limited our search to research articles published in 2017 (e.g., excluding review papers, proceedings papers). Guided by our taxonomies and the queries we used to search the NIH and Federal RePORTER databases, we constructed an analogous set of queries for Web of Science. Although we did not manually review the resulting papers

Table 3.1
Taxonomy for Environmental Biodetection

Tier 1	Tier 2
Sample collection and processing	Air handling
	Collection
	Transport
	Extraction
Sample testing: primary detection, confirmation, characterization	Real-time detection
	Nucleic acids
	Proteins
	Other
	Whole-of-agent properties
	Enabling technologies
System configuration	Number, location, and type of sensors
	Assay complement selection
CONOPS	None

Table 3.2
Taxonomy for Human Biosurveillance

Tier 1	Tier 2
Data sources and reporting	Clinical providers: physician's offices, hospitals, and clinics
	Emergency providers: emergency departments and poison control
	Work or school absenteeism
	Laboratories
	General public
	Traditional media
	Social media
	Digital evidence from human behavior (e.g., internet search patterns, online shopping behavior, pharmacy purchase or sales data, changes in travel habits)
	Standoff/portal monitors
	Device-based detection
Biological diagnostic testing R&D	Nucleic acids
	Proteins
	Other
	Whole-of-agent properties
	Enabling technologies
	Presyndromic detection
Data analysis	Establishment of baseline
	Anomaly detection
	Determination of natural versus synthetic origin
	Integration of data from different sources
	Projected trajectory of current outbreak
	Forecasting of future disease events
System configuration	Choice of data types and reporting frequency and procedures
	Communications network and infrastructure
CONOPS	Strategies and processes for reporting, deploying diagnostic tests
	Strategies and processes for data analysis, integration
	Strategies and processes for sharing situational awareness, alerting

for relevance, we did determine that the distribution of papers among the Tier 1 taxonomy items was qualitatively similar to that in our inventories (e.g., test development is heavily represented and there is little research on system configuration or CONOPS). We also noted several Tier 2 taxonomy items, such as the use of social media as a biosurveillance data source, that were more prevalent among the supplementary Web of Science results than in the original inventory. The supplemental Web of Science search results also reflected a broader range of

funders than our inventory did. This might be indicative of the diversity of funders supporting work on biodetection and biosurveillance, in addition to the federal funding organizations reflected in the NIH and Federal RePORTER databases that contributed about 80 percent of our inventory items.

Findings

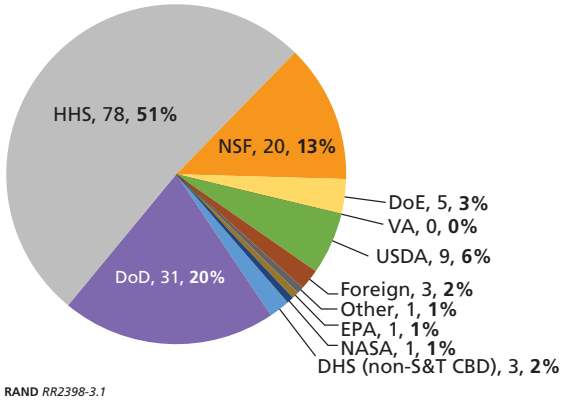
Environmental Biodetection

Our sample of non-S&T R&D included 152 distinct R&D activities related to environmental BD. Some sources of these activities (e.g., published papers, websites) did not include funding levels. Therefore, we used the number of activities rather than funding or other quantitative measures as a surrogate for R&D activities. Most of these (106, 70 percent) were identified through searches of the two large federal databases (NIH or Federal RePORTER), and we identified the remainder through targeted searches of agency websites or databases of published papers. A total of about 82 percent of the 152 activities were funded by HHS (51 percent), DoD (20 percent), or NSF (13 percent) (Figure 3.1).

The largest proportion of non-S&T BD R&D in our inventory addressed sample testing—development of tests for primary detection, confirmation, or characterization of pathogens (Figure 3.2).

We also examined R&D activity for the Tier 2 elements within each major (Tier 1) category (Table 3.3). Although we recognize that our sample of R&D activity is illustrative and not exhaustive, it is likely broadly indicative of Tier 2 areas that are relatively well covered or less well covered and therefore informative for purposes of this study.

Figure 3.1
Funding Sources for Non-S&T Environmental Biodetection R&D Activities



RAND *RR2398-3.1*

Figure 3.2
Non-S&T Environmental Biodetection R&D Activities, by Taxonomy Tier 1 Category

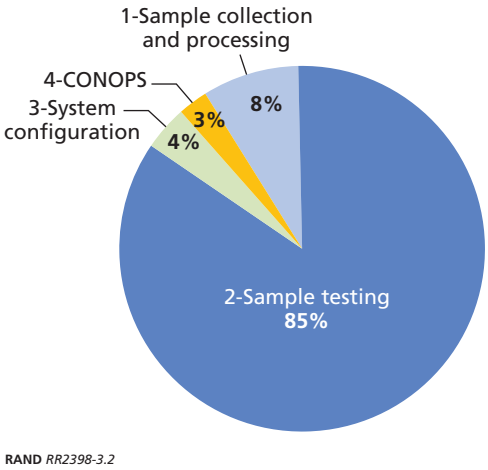


Table 3.3
Distribution of Non-S&T Environmental Biodetection Activity R&D, by Tier 1 and Tier 2 Category

Tier 1	Tier 2	Number
Sample collection and processing	Air handling	6
	Collection	7
	Transport	0
	Extraction	0
Sample testing: primary detection, confirmation, characterization	Real-time detection	29
	Nucleic acids	39
	Proteins	19
	Other	1
	Whole-of-agent properties	8
	Enabling technologies	33
System configuration	Number, location, and type of sensors	5
	Assay complement selection	1
CONOPS	(none)	4

We identified at least one project within each of the Tier 2 taxonomy categories associated with sample testing:

- **Real-time detection** included work for standoff detectors intended to distinguish biological and nonbiological substances, as well as efforts working to characterize single cells rapidly.

  - Efforts sought to use both infrared sensors and visible, ultraviolet, and terahertz lasers to detect biological aerosols at a distance.
  - Technologies analyzing single cells with the long-term potential for application to environmental BD included Raman spectroscopy, including surface-enhanced Raman spectroscopy (SERS) and Single Particle Aerosol Mass Spectrometry.[1]

- **Nucleic acids** included efforts to identify a biothreat agent based on its deoxyribonucleic acid or ribonucleic acid (RNA). Projects in this category used a range of technologies:
  - **Polymerase chain reaction (PCR)** included digital PCR and quantitative PCR. Many of the efforts sought to reduce the testing time or increase the ability to quantify small sample amounts.
  - **Sequencing** included projects to adapt metagenomic sequencing approaches, as well as efforts that first amplified and then sequenced target genomic regions.
  - **Other** technologies included projects hybridizing the sample nucleic acids to an array or beads and projects using loop-mediated isothermal amplification approaches that enrich target sequences without the time- and equipment-intensive temperature cycling used by PCR.

- **Proteins** included activities identifying bioagents based on their protein composition.
  - Many projects used **antibodies or aptamers** to bind to proteins of interest.
  - Others used **spectrometry** techniques, particularly matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS), to detect protein or peptide profiles characteristic of biological agents, as well as profiles characteristic of specific phenotypes, such as antibiotic resistance.[2] The spectrometry techniques described common concentrated samples, such as a bacterial colony, as would be appropriate for a confirmation or characterization test.

- **Other** included a single project that used protein abundance to distinguish laboratory-adapted strains from those recently isolated from nature.
- **Whole-of-agent properties** included projects that worked to understand pathogenicity, aerosol properties, and agent/host interactions, as well as efforts that used microscale cultures to assay for antibiotic susceptibility.
- **Enabling technologies** included efforts developing cross-cutting technologies.
  - Some projects developed **microfluidics** to automate detection or confirmation while reducing sample and reagent requirements. The tests used a range of approaches including loop-mediated isothermal amplification and SERS for detection and fluorescent in situ hybridization of probes to infected cells for confirmation. Many of the approaches are amenable to multiplexing.
  - Others worked to develop improved **readout techniques**. Examples include droplet-on-thermocouple silhouette quantitative PCR systems that promise to be faster or more sensitive; concatemers of fluorescent protein-binding aptamer approaches that seek to

[1] We placed projects using Single Particle Aerosol Mass Spectrometry with real-time detection. We placed projects using other spectrometry techniques, which could not easily be adapted for real-time use, in the proteins category.

[2] We placed a single project using MALDI-TOF-MS to analyze both protein and lipid composition in the protein category.

make binding events detectable to the naked eye; and bacteriophage with thousands of coat proteins engineered to bind to biological agents, amplifying the signal.
  - Additional projects sought to develop single-cell assays,[3] detect single molecules, design compact flow cytometers, or create smartphone-based detection systems.

We identified smaller numbers of projects in each of the other three Tier 1 taxonomy categories:

- **Sample collection and processing** included projects to improve air handling (including particle characterization), viable and nonviable sample collection both with and without filters, sample integrity during transport (for systems in which collection and analysis occur at different locations), and methods for extracting the component of the biological agent to be characterized from the sampling device (including the filter, if present). Examples include efforts studying pathogen viability in aerosols and creating devices—including wearable monitors—for counting, collecting, and measuring aerosol particles.
- **System configuration** included projects studying the number, locations, and types of sensors to include in an environmental detection system, as well as projects considering what biological agents to detect.
- **CONOPS** included projects developing strategies and protocols for relaying the outputs of an environmental biodetection system to decisionmakers.

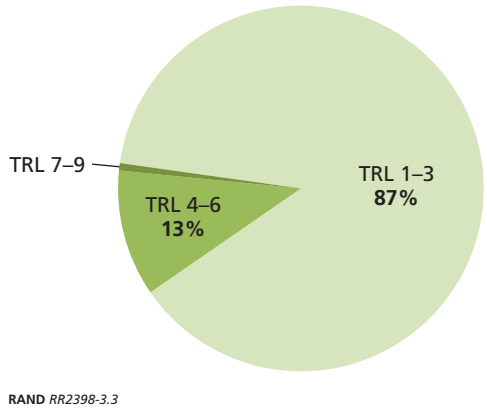
We also examined the technical maturity of each identified activity (which we assigned based on review of the abstracts) with respect to the application of environmental BD of aerosols, the DHS mission.

- High TRL (7–9) projects included a full system prototype (at least) in an operational environment, including those undergoing test and evaluation. The system needed to include both collection and detection of biothreat agent(s) in indoor or outdoor environmental aerosols. The collection and detection could occur at different locations consistent with the final system concept.
- Medium TRL (4–6) projects included efforts directly working to detect biological agents—not necessarily biothreat agents—in environmental aerosols. Testing and evaluating components or subsystems in a laboratory environment (at least) that simulated integration of technology elements using a realistic sample background was sufficient.
- Low TRL (1–3) projects included efforts that would typically precede and fit neither the TRLs 4–6 nor 7–9 definition above. This category included projects working on basic principles or on a single component of an aerosol environmental detection system in isolation. It also included more-mature activities that, although developing technologies relevant to environmental aerosol BD, focused on other applications.

The great majority of non-S&T BD R&D in our inventory—87 percent—was at an early stage of maturity—TRLs 1–3 (Figure 3.3). Only one of the 152 activities, a DoD operational demonstration for U.S. Forces Korea, was at a late stage of maturity—i.e., close to ready for

[3] We placed SERS efforts not intended to operate in real time in the enabling technologies category. In contrast, we placed SERS projects developing real-time detection capabilities in the real-time detection category.

Figure 3.3
TRLs of Non-S&T Environmental Biodetection R&D Activities



application.[4] This preponderance of early stage R&D was found across all funding sources and was greater than for human BSV (see below).

The highest proportion of more-mature R&D in our inventory (TRLs 4–6 and 7–9) was supported by DoD—19 percent of the 31 activities (Figure 3.4). Only 9 percent of BD R&D supported by HHS was beyond TRLs 1–3.

The preponderance of early stage R&D in our inventory (TRLs 1–3) was especially prominent for activity related to sample testing, with relatively higher proportions—albeit of small numbers—of midstage maturity (TRLs 4–6) for R&D addressing sample collection and processing, system configuration and CONOPS (Figure 3.5).

Within our sample of R&D activities, only DoD has sponsored BD R&D across all taxonomy categories. In addition to DoD, only USDA has sponsored R&D addressing system configuration, and only HHS has sponsored activity addressing CONOPS.

The preponderance of early stage (TRLs 1–3) R&D in our inventory was reflected in the observation that only about one-fifth of environmental BD R&D was directly related to *aerosol* samples (Figure 3.6). We included for analysis many undifferentiated early stage R&D activities that were potentially relevant to aerosol BD. In contrast, we included only R&D that addressed aerosol applications for later stage research and research related to system configuration or CONOPS.

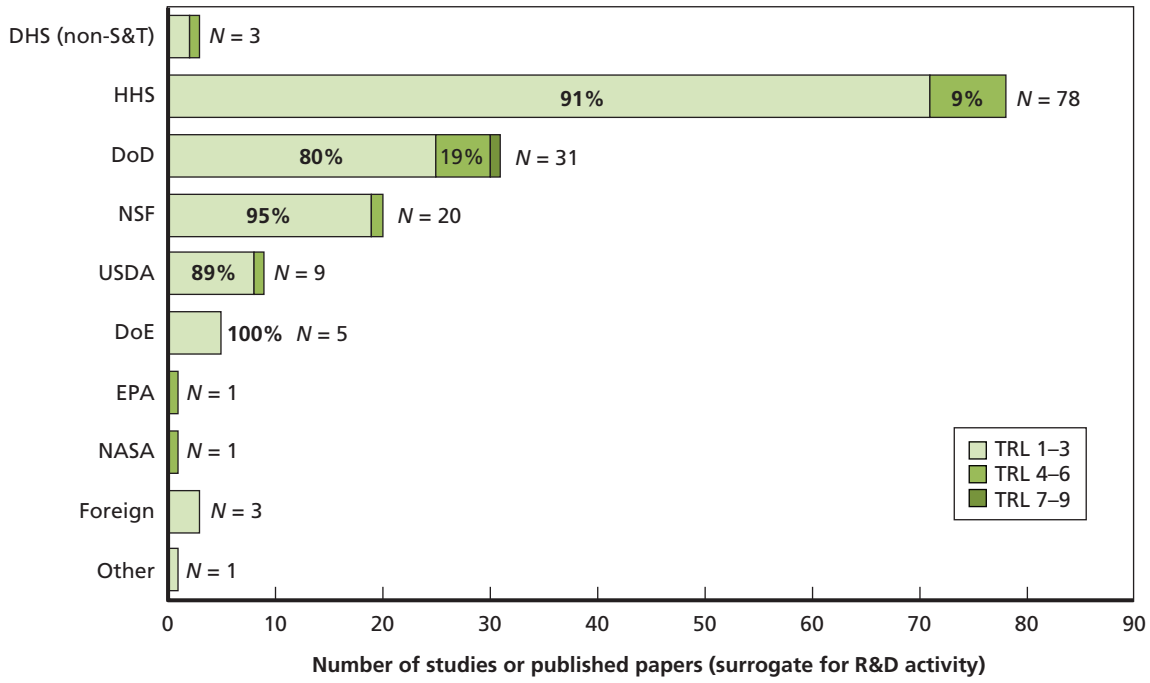
We were also interested in R&D that addressed security concerns, which we gleaned from reading or automatically searching abstracts for mentions of select agents, viral hemorrhagic fever, or a health security context (e.g., mention of "threat" or "bioterror"). Nineteen percent of environmental BD R&D in our inventory addressed such concerns (Figure 3.7).

Human Biosurveillance

Our sample of non-S&T R&D also included 282 distinct R&D activities related to human BSV. Most of these (239, 85 percent) were funded projects captured in one of the large federal databases (NIH or Federal RePORTER). Nearly 90 percent of R&D in our biosurveillance inventory was funded by HHS (66 percent) or NSF (21 percent) (Figure 3.8).

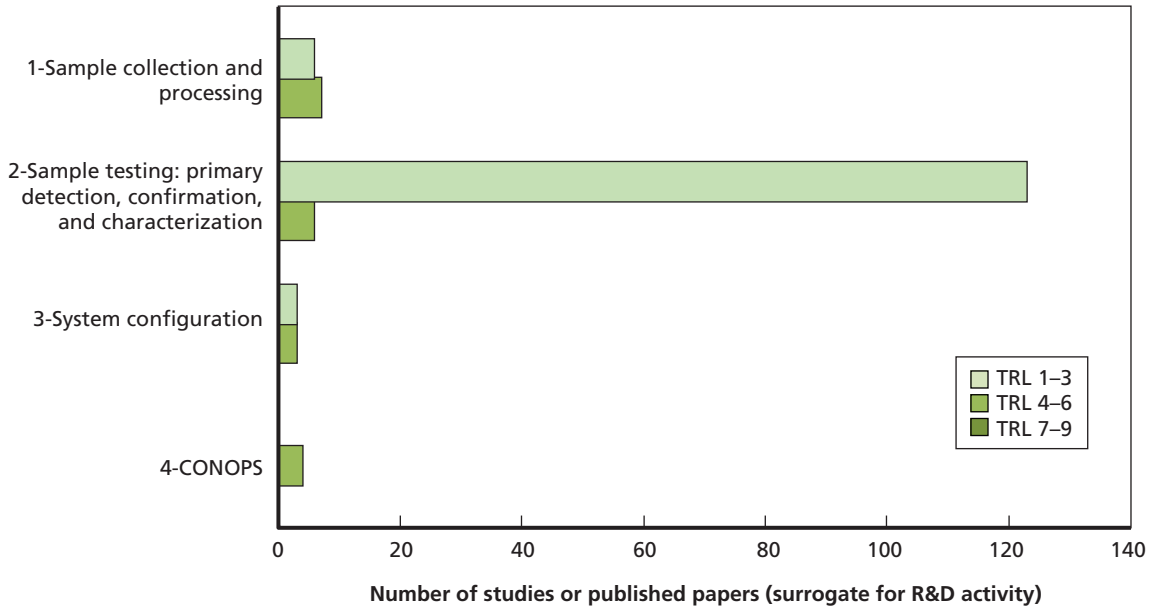
[4] DoD likely would consider this project, which used Advanced Technology Development (Budget Activity 3) money, at TRLs 4–6. For consistency, we based our assessment on the project description and our TRL definitions.

Figure 3.4
Non-S&T Environmental Biodetection R&D Activities, by Sponsor and TRL



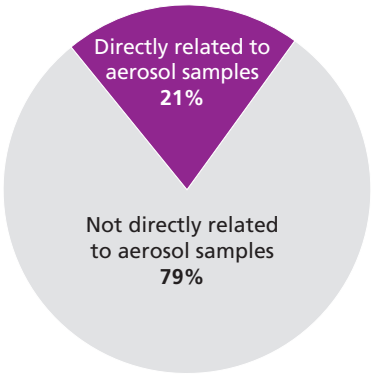
RAND *RR2398-3.4*

Figure 3.5
Non-S&T Environmental Biodetection R&D Activities, by Taxonomy and TRL



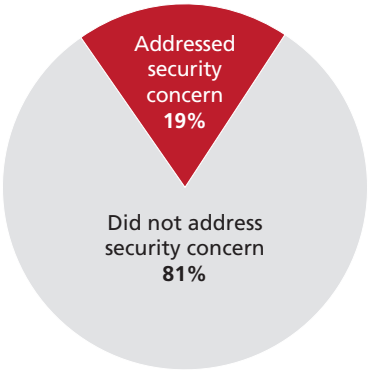
RAND *RR2398-3.5*

Figure 3.6
Non-S&T Environmental Biodetection R&D Activities as Relevant to Aerosol Samples



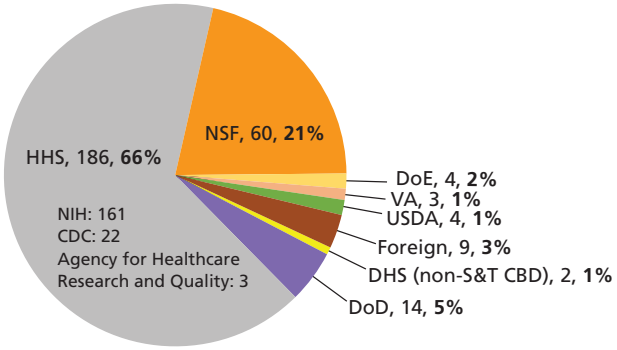
RAND *RR2398-3.6*

Figure 3.7
Non-S&T Environmental Biodetection R&D Activities Addressing Security Concerns



RAND *RR2398-3.7*

Figure 3.8
Funding Source for Non-S&T Human Biosurveillance R&D Activities

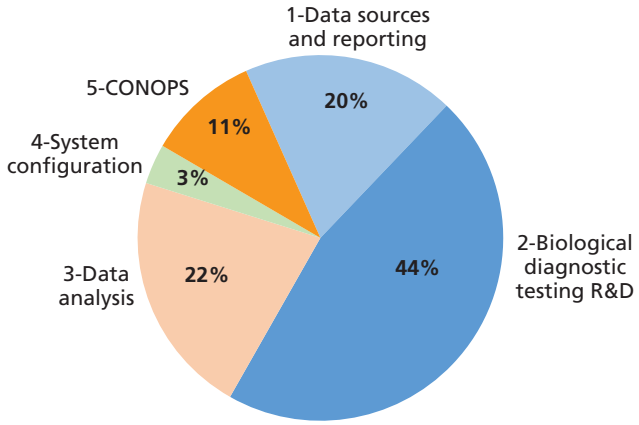


NOTE: AHRQ = Agency for Healthcare Research and Quality.

RAND *RR2398-3.8*

Nearly half of BSV R&D—44 percent—addressed biological diagnostic testing (Figure 3.9). Another 42 percent, split relatively evenly, covered BSV sources and reporting or data analysis.

Figure 3.9
Non-S&T Human Biosurveillance R&D Activities, by Taxonomy Tier 1 Category



The distribution of non-S&T BSV R&D by both Tier 1 and more-detailed Tier 2 taxonomy category (if specified) is shown in Table 3.4. As noted in the previous section under environmental biodetection, we consider our sample of R&D activity to be illustrative (not exhaustive) and broadly indicative of Tier 2 areas that are relatively well covered or less well covered; as such, we consider this level of detail to be informative for purposes of this study. As shown, most R&D addressing data sources and reporting was related to clinical providers or laboratories; none was related to data reported by the general public or through traditional media; and very little addressed social media, device-based detection, or standoff/portal monitors. R&D addressing biological diagnostic test development spanned tests based on nucleic acids to proteins to whole of agent or other, mostly in the context of point-of-care test development; none addressed detection of pathogens during the incubation period (presyndromic). The largest volume of R&D addressing data analysis related to data integration from across multiple sources and forecasting of current or future outbreaks. Relatively little R&D addressed BSV system configuration or CONOPS.

The largest number of R&D activities in our inventory fell into the first three Tier 1 categories. We identified R&D within most, but not all, of the Tier 2 categories related to the first Tier 1 category (data sources and reporting). Our sample included no activities in the Tier 2 categories of surveillance reporting by the general public or traditional media. Details about these Tier 2 categories are as follows:

- **Clinical providers**, including physician's offices, hospitals, and clinics, included BSV from these sources on syndromic reporting, use of electronic health records, claims data, data sources (e.g., nursing homes; hospital patient and emergency rooms; VA and DoD patients), and specific diseases or conditions.

Table 3.4
Distribution of Non-S&T Human Biosurveillance R&D, by Tier 1 and Tier 2 Category

Tier 1	Tier 2	Number
Data sources and reporting	Clinical providers: physician's offices, hospitals, and clinics	15
	Emergency providers: emergency departments and poison control	5
	Work or school absenteeism	3
	Laboratories	12
	General public	0
	Traditional media	0
	Social media	4
	Digital evidence from human behavior	6
	Standoff/portal monitors	1
	Device-based detection	5
	(No Tier 2 classification)	2
Biological diagnostic testing R&D	Nucleic acids	47
	Proteins	36
	Other	10
	Whole-of-agent properties	9
	Enabling technologies	27
	Presyndromic detection	0
	(No Tier 2 classification)	1
Data analysis	Establishment of baseline	5
	Anomaly detection	7
	Determination of natural versus synthetic origin	0
	Integration of data from different sources	21
	Projected trajectory of current outbreak	12
	Forecasting of future disease events	16
System configuration	Choice of data types and reporting frequency and procedures	8
	Communications network and infrastructure	2
CONOPS	Strategies and processes for reporting, deploying diagnostic tests	6
	Strategies and processes for data analysis, integration	11
	Strategies and processes for sharing situational awareness, alerting	11

- **Emergency providers** included surveillance from this source on specific syndromes or diseases—gastroenteritis, acute respiratory infections, vaccine-preventable diseases, and emerging infectious diseases.
- **Work or school absenteeism** activities focused mostly on influenza and acute respiratory infections in school-age children.
- **Laboratory-based surveillance** focused on a range that included specific pathogens or diseases (e.g., gastroenteritis, acute respiratory infections, vector-borne diseases, acute febrile illnesses) or methods (e.g., pooled samples, testing in asymptomatic patients, or laboratory-based surveillance in general).
- **Social media** research included natural language processing, use of social media for crisis mapping and modeling, and monitoring of specific diseases (e.g., Ebola, foodborne illness).
- **Digital evidence of human behavior** activities included monitoring of human mobility patterns, wearable and other medical monitoring sensors, and monitoring of behavioral and environmental exposures.
- **Standoff/portal monitors** included just one activity related to monitoring migratory animals in the aerosphere.
- **Device-based detection** included office-based technologies and smartphone reporting, near-real-time internet-based reporting, and point-of-care diagnosis for influenza linked to smartphone reporting.

The second Tier 1 category, related to development of diagnostic biological tests, had the largest number of BSV R&D activities. Our sample included activities within each Tier 2 category except for presyndromic diagnostic tests.[5] Our inventory did, however, include projects that monitored asymptomatic carriers. Details about these Tier 2 categories are as follows:

- **Nucleic acid–based tests** consisted mostly of projects focusing on specific pathogens, such as select agents, filoviruses, mosquito-borne arboviruses (e.g., dengue, chikungunya, Zika), RNA viruses in general, pertussis, tuberculosis, leptospirosis, and emerging infectious diseases, as well as pathogens defined in terms of clinical syndromes, such as meningitis and encephalitis, viral hemorrhagic fevers, gastroenteritis, or febrile illness in general; one project focused on nucleic acid–based testing for vector capacity (e.g., ticks in Lyme disease).
- **Protein-based tests** included projects targeting viral hemorrhagic fever pathogens (such as Lassa, Ebola, and Marburg), flaviviruses (such as dengue and Zika), influenza, the virus causing Middle East respiratory syndrome, pathogens causing sepsis, anthrax, filariasis, the pathogen causing Lyme disease (*B. burgdorfeii*), cholera, tuberculosis, leptospirosis, pertussis, carbapenem-resistant Enterobacteriaceae, coccidiomycosis, and the pathogen causing trachoma (*C. trachomatis*); one project used this methodology to monitor and verify vaccination.

[5] We searched for research on point-of-care tests and rapid diagnostics as part of our human BSV exploration. Multiple environmental BD searches returned similar or, in some cases, identical projects. When we considered the technologies underlying those projects relevant to environmental BD, we included the results in our set of BD projects. Consequently, some projects appear in both the BSV and BD sets.

- **Other** types of tests targeted *Clostridium difficile* (a common and particularly problematic hospital-associated infection), intensive care unit infections, malaria, and tinea capitis. Rather than detecting proteins or nucleic acids, tests in this category analyzed a range of metabolites, including cell-wall polysaccharides, hemozoin, and volatile small molecules from breath or stool samples.
- **Whole-of-agent tests** detected phenotypic properties of a bioagent (e.g., antibiotic resistance); used such tools as electron microscopy or hyperspectral imaging to characterize a complete bioagent; analyzed patterns of gene and protein expression (rather than detecting the presence or absence of specific genes or proteins); and reacted to the presence of a complete biothreat agent, such as a test that genetically modified a yeast to change color in response to cholera pathogen. The tests targeted urinary tract infections, diarrheal diseases, bacteria in poultry and pathogens and toxins in food products more broadly, Ebola, and arboviruses.
- **Enabling technologies** included new technologies for detecting emerging infections, intentional use of threat agents, and dengue viruses; specific technologies mentioned included plastic chips, novel capture technologies, cellular immune function assays, novel optical cavity biosensors, portable biosensors, plasmonic sensors, magnetic sensing technologies, wearable textile biosystems, lab-on-a-chip programming and computational tools, translation of nanoscale bioelectronics, magnetic tags, optofluidic and microfluidic platforms, and bacteria-powered batteries for testing in remote areas.

Within the third Tier 1 category, associated with data analysis, our sample included R&D activity in all Tier 2 categories except one (determination of natural versus synthetic origin). Although the absence of projects on distinguishing between natural and intentional events within our small sample does not imply the complete absence of work on this topic, the area is considered a gap in the field (Chen, Chughtai, and MacIntyre, 2017). Details about these Tier 2 categories are as follows:

- **Establishment of baseline** included projects addressing human and animal influenzas and influenza C, influenza vaccine effectiveness, and Eastern equine encephalitis.
- **Anomaly detection** included projects related to development, testing, and comparisons of detection algorithms, and setting detection thresholds to maximize detection and minimize false signals
- **Integration of data from different sources** included specific data portals (e.g., DoD's Global Biosurveillance Portal and DoD Biosurveillance Ecosystem [BSVE]), integration of structured and unstructured data (such as text data), use of Big Data, incorporation of new data (e.g., electronic health records, satellite remote sensing, climate and infectious diseases, social media), data integration tool sets, and data focusing on specific diseases or problems (e.g., vaccine-preventable diseases, acute respiratory infections, antimicrobial resistance).
- **Projected trajectory of current outbreak** included projects related to specific pathogens or diseases—influenza, cholera, arboviruses (dengue, Zika, chikungunya) West Nile virus, vector-borne and zoonotic diseases in Uganda, severe acute respiratory syndrome, tuberculosis, malaria, and cutaneous leishmaniasis; one project focused on modeling and machine learning more broadly (i.e., not targeting a specific pathogen).

- **Forecasting of future disease events** included projects focusing on pathogens (e.g., zoonotic pathogens, influenza, trachoma, bioterrorism agents, viral genomes); such methods as Bayesian modeling of specific pathogens (e.g., influenza, anthrax, new pathogens, hand-foot-and-mouth disease, enterovirus-71, Coxsackie virus A16, human immunodeficiency virus (HIV), hepatitis C, animal foot-and-mouth disease); or strictly on methods (e.g., forecastability, spread of viral genomes).

The fourth Tier 1 category, related to system configuration, has only two Tier 2 categories and less R&D activity:

- **Choice of data types** included projects on pathogen metadata, Data Core data for dengue, and multimedia data.
- **Communications networks and infrastructure** included projects on censorship-free smartphone-to-smartphone communications and mobile robots self-engineering communications networks to improve distributed algorithms for response team coordination.

The fifth Tier 1 category, related to CONOPS, has three Tier 2 categories and also relatively little R&D activity:

- **Strategies and processes for reporting and deploying diagnostic tests** included projects on laboratory-based surveillance, strategic timing of specimen collection and availability of laboratory results, and optimal clinic sites for tuberculosis testing.
- **Strategies and processes for data analysis and integration** included projects on integrating human behaviors; integrating medical, environmental, and incident management data; merging viral genetics for zoonotic infections (e.g., influenza, rabies, West Nile virus); decision-support models; the Biosurveillance Data Stream Framework; and mathematical modeling (e.g., of disease, course-of-action analysis, response).
- **Strategies and processes for sharing situational awareness and alerting** includes projects on the Early Alerting and Reporting project, data-sharing across New York State, software platforms, communications across noisy data links, sharing local disease and antimicrobial resistance data, and balancing the advantages of mobile technologies (wearables and personal technologies) against privacy and ethical concerns.

We also examined the TRLs of projects (again, which we assigned based on our review of the abstracts) with respect to the application to the DHS mission of integrated BSV:

- High TRL (7–9) projects included a full system prototype (at least) in an operational environment, including those undergoing test and evaluation. The system needed to address scanning and discerning the environment, integrating and analyzing information, or alerting decisionmakers. The system needed to be applicable for disease caused by biothreat agents but could have broader applications.
- Medium TRL (4–6) projects should, at a minimum, assemble, test, and/or evaluate all pieces of a system that collects or scans relevant information, identifies and integrates essential information, and/or alerts or informs decisionmakers. Systems were not typically integrated fully into current operations or operational plans, but planning for integration needed to be incorporated.

- Low TRL (1–3) projects included efforts that would typically precede and not fit the definitions for TRLs 4–6 or 7–9 described earlier. This category included projects working on just one element or subsystem of a larger integrated BSV system, such as a detection algorithm or data collection for purposes of establishing a baseline for anomaly detection.

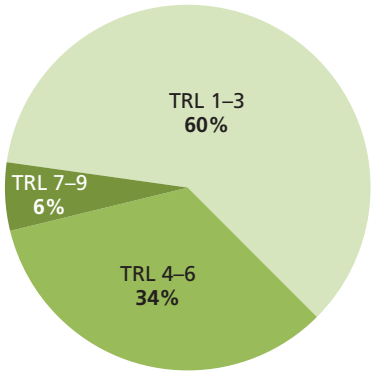
Sixty percent of BSV R&D activity in our inventory was at early stage of maturity (TRLs 1–3) (Figure 3.10), especially that funded by NSF (74 percent, not shown). Another third was at midstage maturity (TRLs 4–6), and very little—6 percent—was at a high stage of maturity (i.e., close to real-world use).

HHS sponsored a higher proportion of more-mature R&D (TRLs 4–6 and 7–9)—41 percent—than the other major sponsor of BSV R&D, NSF (13 percent) (Figure 3.11).

Non-S&T BSV R&D in our inventory spanned early to late stage TRLs across all five taxonomy categories, with more early stage research addressing biological diagnostic test development and more-mature research in the areas of BSV sources and reporting, data analytics, and CONOPS (Figure 3.12). Midstage and later stage R&D constituted a larger share of human BSV R&D than of environmental BD. The heavy weighting toward early stage R&D reflects a natural progression; not all basic research leads to deployed systems. Finally, as mentioned previously, we used counts of R&D activities as a surrogate for level of effort because funding amounts were not available for many of the R&D activities we identified. Distribution based on funding could be significantly different. Additionally, the high incidence of grant-funded projects, which tend to be at lower TRLs, present in our data sources coupled with the absence of industry projects supported by non-SIBR/STTR funding, which tend to be at medium to high TRLs, might also have affected the TRL distribution.

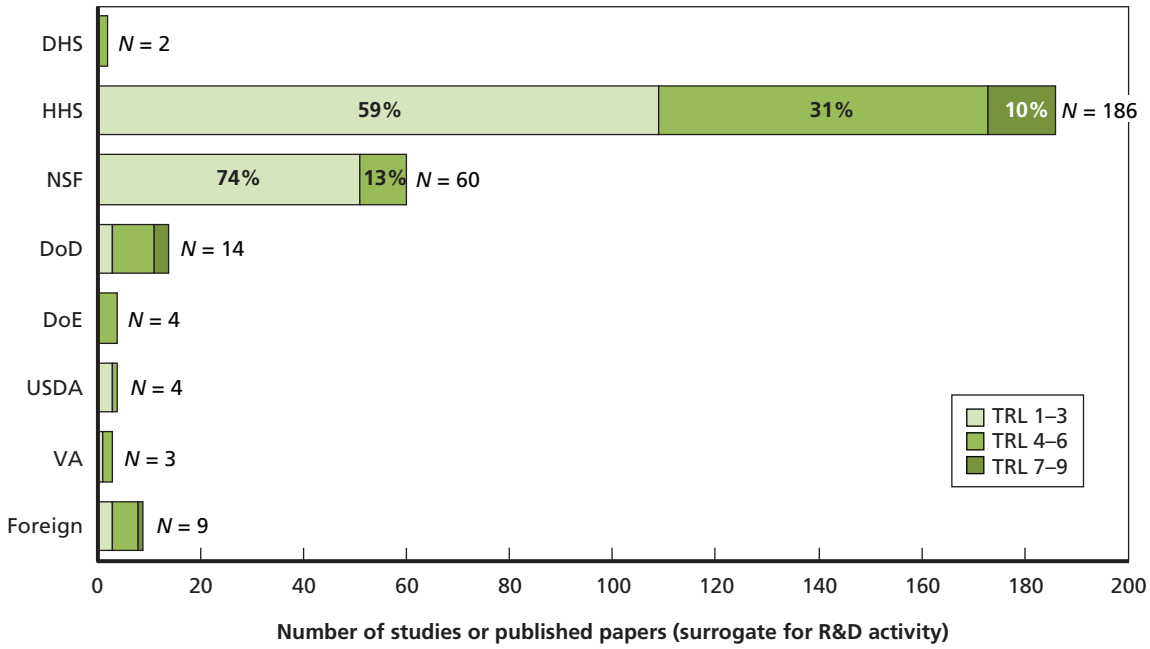
HHS and NHS have sponsored BSV R&D across all taxonomy categories, particularly related to biological diagnostic test development. HHS has sponsored a higher percentage of R&D addressing data sources and reporting and data analytics than other funding sources have. Although only HHS, NSF, and foreign sources have funded R&D in our inventory related to BSV system configuration, all funding sources have sponsored R&D addressing BSV CONOPS—although the volume of R&D in both categories is relatively low.

Figure 3.10
TRLs of Non-S&T Human Biosurveillance R&D Activities



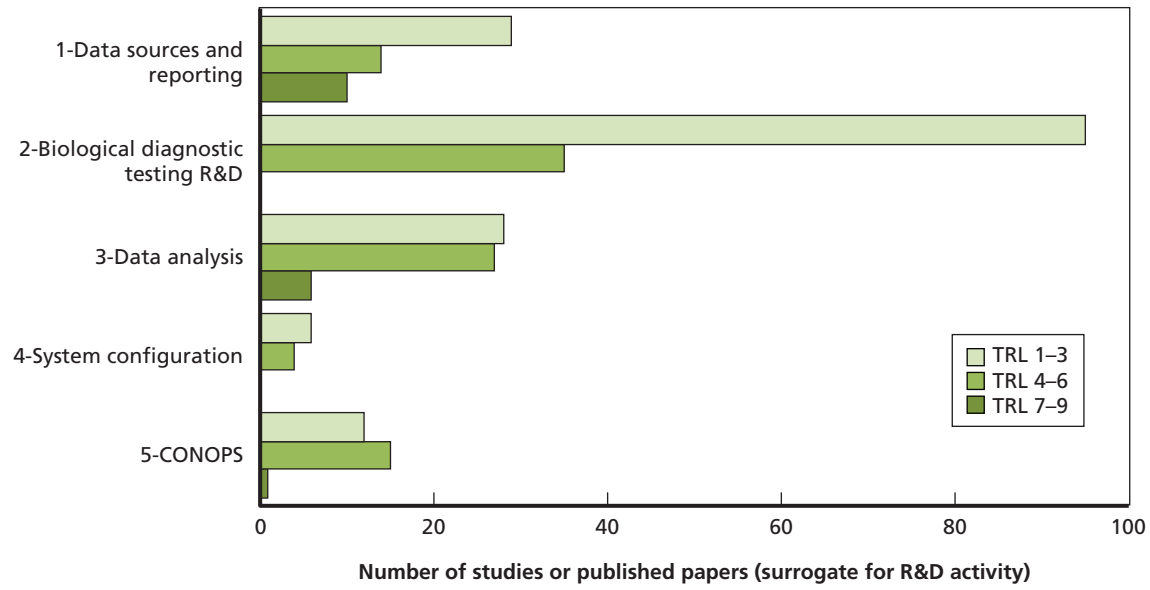
RAND *RR2398-3.10*

Figure 3.11
Non-S&T Human Biosurveillance R&D Activities, by Sponsor and TRL



RAND *RR2398-3.11*

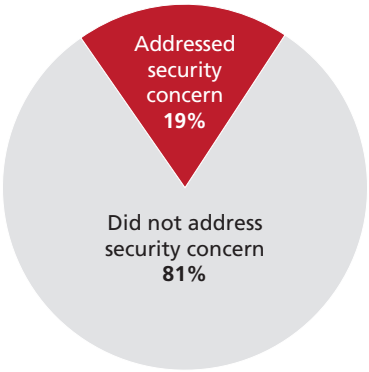
Figure 3.12
Non-S&T Human Biosurveillance R&D Activities, by Taxonomy and TRL



RAND *RR2398-3.12*

We were also interested in human BSV R&D addressing security concerns because of the potential for DHS to adapt outputs from others' early stage research to meet DHS system needs. As with BD R&D, 19 percent of non-S&T BSV R&D in our inventory addressed such security concerns (Figure 3.13).

Figure 3.13
Non-S&T Human Biosurveillance R&D Addressing Security Concerns



RAND *RR2398-3.13*

Summary

In summary, our sample included 152 distinct non-S&T R&D activities related to environmental BD and 282 related to human biosurveillance. These are all within the realm of biosurveillance writ large and thus ultimately support the national policies described in Chapter Two, including the foundational element of biosurveillance, as well as focus on biological threat agents and R&D. Most of the BD R&D has been supported by HHS, DoD, and NSF; most BSV activity has been supported by HHS and NSF. Most of the R&D for both BD and BSV is at early stage of maturity (TRLs 1–3) and addresses test development; very little addresses system configuration or CONOPS, but about one-fifth of both BD and BSV R&D addresses security concerns. These findings suggest areas for which DHS could potentially adapt outputs from some early stage research supported by others rather than supporting all types of such (early stage, basic) research itself: Several relevant areas of R&D—test development, in particular—are already being well covered by non-S&T funders, and some of the non-S&T R&D addresses security concerns that are also of interest to DHS. The findings also suggest gaps that could be priorities for DHS R&D—for example, addressing system configuration and especially CONOPS, which must be established for each department based on its mission. The distribution of R&D activities within Tier 2 categories in our sample provides a slightly more granular qualitative sense as to areas that are relatively well covered versus less well covered by recent or current R&D and thus might inform S&T R&D priorities.

CHAPTER FOUR

S&T R&D

The primary interest of this study was to examine the S&T CBD R&D portfolio and identify areas of value added and potential priorities for future investments. Now that we have described the landscape of policy, practice, and R&D relevant to environmental biodetection and human biosurveillance supported by other agencies, this chapter examines the S&T R&D portfolio in more detail.

Organizing R&D Activities for Analysis

We used our taxonomies to characterize S&T R&D and captured information from the sponsor about targeted customers and the timeline for each project or program. We used the taxonomies to compare S&T and non-S&T R&D. Unlike the non-S&T R&D activities that we assigned only to a single taxonomy category, we assigned some S&T R&D activities to multiple taxonomy categories. We did this because most of the non-S&T R&D activities represented single projects, whereas some S&T R&D reflected programs with diverse activities. We used the TRL or TRL range provided by the sponsor.

We also grouped all S&T CBD activities into specific themes for purposes of both complementary analysis and the development of coherent S&T R&D logic models for environmental BD and human BSV. The themes were not intended to map to the taxonomies used to compare S&T with non-S&T R&D. The four themes include

- developing tests for environmental detection
- evaluating technologies and system concepts
- performing research on biothreats and attribution of bioattacks
- providing resources, expertise, and facilities.

We added a fifth theme to reflect the activities and work that S&T does as part of the broader interagency community related to biodefense and biosecurity:

- facilitating collaboration and maintaining capabilities.

For human biosurveillance, the four S&T-specific themes were

- developing tests for detection in humans
- creating software, prototypes, and tools to aggregate, analyze, and display information and provide decision support

- evaluating technologies and system concepts and conduct feasibility assessments
- engaging the public.

Findings

Environmental Biodetection

The majority of S&T's CBD R&D addresses environmental biodetection. These activities span all four BD taxonomy categories, S&T-specific themes, and stages of maturity (Table 4.1). Within our taxonomy, S&T supports the greatest number of activities related to sample testing (test development) and system configuration and fewer related to sample collection and processing or CONOPS. Most S&T BD R&D aims to serve both DHS and non-DHS customers. Although some programs are, in principle, funded only into FY 2018 or FY 2019, several are due to be funded through FY 2020 or are considered enduring capabilities to be funded into the longer term (Figure 4.1).

Table 4.1
S&T Environmental Biodetection Portfolio, by S&T-Specific Theme, Taxonomy Classification, TRL, and Customer

Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
Develop tests or technologies for environmental detection						
1	Bioassays (environmental component)	Sample collection and processing	Collection	U.S. Secret Service (USSS), S&T, Ag/Bio-Terror Countermeasures		2
		Sample testing	Nucleic acids; proteins; whole-of-agent properties; enabling technologies			
2	Triggered mass spectroscopy for environmental surveillance	Sample testing	Real-time detection	OHA/BioWatch, Center for Domestic Preparedness (CDP), U.S. Coast Guard (USCG), Transportation Security Administration (TSA)		3
3	Autonomous presumptive screening of biothreat aerosols	Sample collection and processing	No second tier	DHS components, OHA	DoD, SLTT law enforcement, public health	3–4
		Sample testing	Enabling technologies			
4	SpinDx	Sample testing	Proteins; enabling technologies	USSS		4
5	Rapid diagnostics (environmental component)	Sample testing	Proteins	USSS		4–5
6	Orthogonal biothreat detection systems	System configuration	Number, location, and type of sensors	DHS components, OHA	DoD, SLTT law enforcement, public health	4–5
7	Viable Aerosol Collection Utility Unit Man-Portable (VACUUM)	Sample collection and processing	Collection; extraction	USSS		5
Evaluate technologies and system concepts						
8	Studies to support orthogonal technologies for BSV Apex	Sample testing	Nucleic acids; whole-of-agent properties	OHA	DoD, HHS/CDC, SLTT law enforcement, public health	Model: 4; other: N/A
		System configuration	Number, location, and type of sensors			

Table 4.1—Continued

Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
9	Utility assessment of non-traditional sensor technologies	Sample collection and processing	No second tier	Operational components, OHA	DoD, HHS/CDC, SLTT emergency medical services (EMS), law enforcement, public health	4–5
		Sample testing	No second tier			
		System configuration	Number, location, and type of sensors			
		CONOPS	No second tier			
10	Field-based biological assessment	System configuration	Number, location, and type of sensors; assay complement selection	Operational components, OHA	DoD, SLTT law enforcement, public health, first responders	5
11	Biodetection technology enhancements	Sample testing	Nucleic acids	OHA/BioWatch		6–7
12	National Environmental Biothreat Detection Architecture	System configuration	Number, location, and type of sensors; assay complement selection	Operational components (U.S. Citizenship and Immigration Services, Federal Emergency Management Agency [FEMA], Immigration and Customs Enforcement [ICE], OHA, Office of Intelligence and Analysis [OI&A], National Protection Programs Directorate, TSA, USCG, USSS)		N/A
		CONOPS	No second tier			
Perform research on biothreats and attribution[a] of bioattacks						
13	Biological Terrorism Risk Assessment	System configuration	Assay complement selection	FEMA, OI&A, Domestic Nuclear Detection Office (DNDO), policy	Executive Office of the President (EOP) (National Security Council [NSC], Office of Science and Technology Policy [OSTP]), Office of Management and Budget (OMB), HSE	Assessment areas: 1–4; agroterrorism: 3–4; tailored assessments: N/A

Table 4.1—Continued

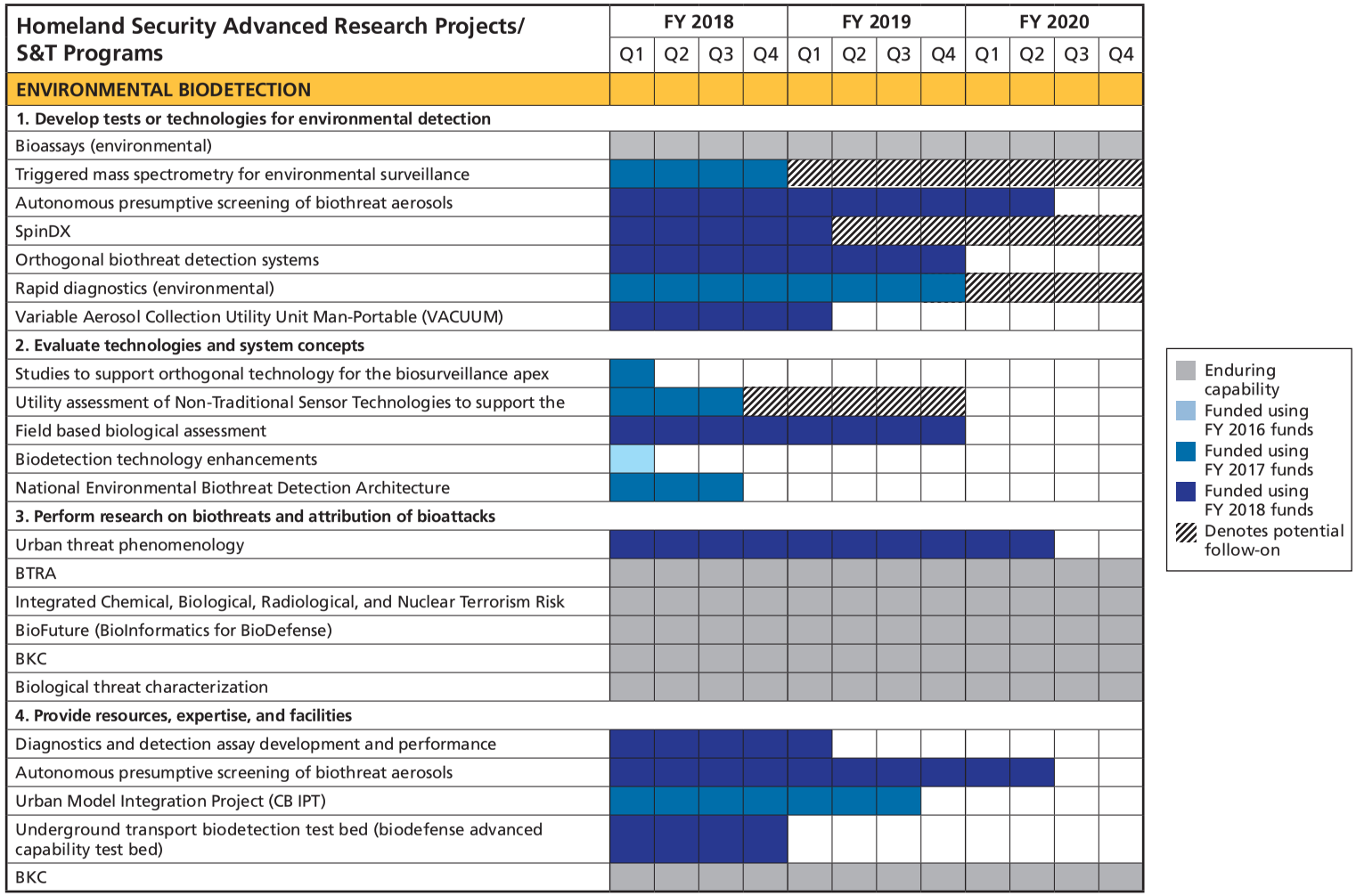
Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
14	Urban threat phenomenology	System configuration	Number, location, and type of sensors; assay complement selection	OHA	SLTT emergency response and recovery managers	2–3
		CONOPS	No second tier			
15	Integrated chemical, biological, radiological, or nuclear (CBRN) terrorism-risk assessment	System configuration	Assay complement selection	FEMA, OI&A, DNDO, policy	EOP (NSC, OSTP), OMB, HSE	Multiple, depending on product; from 4–7 or N/A
16	Biofutures (bioinformatics for biodefense)	System configuration	Assay complement selection	Policy, National Bio and Agro-Defense Facility	Drug Enforcement Administration, DoD (Intelligence Advanced Research Projects Agency [IARPA]), genomic sequencing industry, U.S. Department of Commerce, EOP, Office of National Drug Control Policy	Genetic sequences of interest: 7; others: N/A
17	Biodefense Knowledge Center (BKC)	System configuration	Number, location, and type of sensors; assay complement selection	S&T, Office of Legislative Affairs (OLA)	DoD, DoE	Database: 8; research: 2
18	Biothreat characterization	System configuration	Number, location, and type of sensors; assay complement selection	Operational components		N/A
Provide resources, expertise, and facilities						
19	Diagnostics and detection assay development and performance determination	Sample testing	Whole-of-agent properties	USSS		2
20	Autonomous presumptive screening of biothreat aerosols	Sample collection and processing	No Tier 2	Operational components, OHA	DoD, SLTT law enforcement, public health	3–4
		Sample testing	Real-time detection			

Table 4.1—Continued

Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
21	Underground transport BD test bed	System configuration	Number, location, and type of sensors; Assay complement selection		Metropolitan Transportation Authority of New York City Transit	Technology to be tested: 3–5
22	Urban Model Integration Project (chemical and biological integrated project team)	System configuration	Number, location, and type of sensors; assay complement selection	OHA		3–5
23	BKC	System configuration	Number, location, and type of sensors; assay complement selection	S&T, OLA	DoD, DoE	Database: 8; research: 2

NOTE: N/A = not applicable.
[a] In this assessment, attribution refers to activities other than forensics, the latter of which was beyond the scope of this study.

Figure 4.1
Funding Timetable for S&T Environmental Biodetection R&D Activities



SOURCE: Timeline data provided by sponsor.

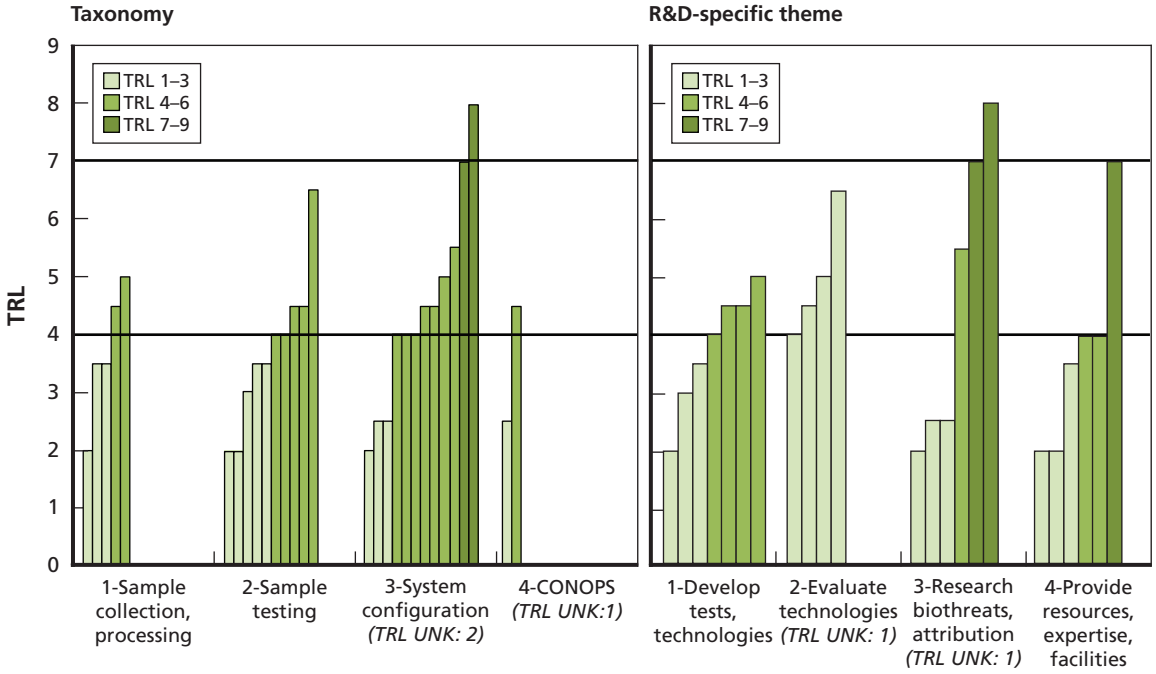
RAND *RR2398-4.1*

The TRL levels of S&T BD activities across taxonomy categories and S&T-specific themes are shown in Figure 4.2.

S&T environmental BD R&D activities span all four taxonomy categories:

- S&T efforts on **sample collection and processing** address issues unique to the environmental BD mission, including extraction of samples from filters and collection of viable samples. Only 1 in 13 non-S&T sample collection and processing efforts had a security focus.
- S&T's **sample testing** work is spread across the Tier 2 taxonomy categories. Although many other organizations (such as DoD, NSF, and HHS) also sponsor a broad range of sample testing projects, the S&T activities—even those at low TRLs—exhibited a much clearer idea than those other projects of how an effort's outputs might fit into an environmental BD system. Although non-S&T sample testing projects favored clinical samples (e.g., blood), S&T sample testing efforts used environmental samples, including aerosol samples. Because clinical and environmental samples have different backgrounds, outputs of non-S&T projects would likely need further development before being used for DHS applications.
- S&T has a particularly rich portfolio of **BD system configuration** activities. S&T sponsors multiple CBD-related R&D activities (listed in Table 4.1 with a Tier 2 category of "assay complement selection") from formal risk assessments to laboratory research that help system designers prioritize the biothreat agents a system should detect. S&T also examines design options for environmental BD in both outdoor and indoor environ-

Figure 4.2
TRLs for S&T Biodetection R&D Activities, by Taxonomy Category and R&D-Specific Theme



NOTES: Each bar represents a single R&D project or activity For projects where the sponsor provided a TRL range for the activity component, we show the average. UNK = unknown.

RAND *RR2398-4.2*

ments, as well as such specialized locations as ports of entry and subways (activities in Table 4.1 with a Tier 2 category of "number, location, and type of sensors"). Although DoD also funds a moderate number of system configuration efforts, USDA was the only other organization we identified as funding any work in the area.

- Across both the S&T and non-S&T portfolios, **CONOPS** was the least populated Tier 1 category, with DoD being the main non-S&T funder.

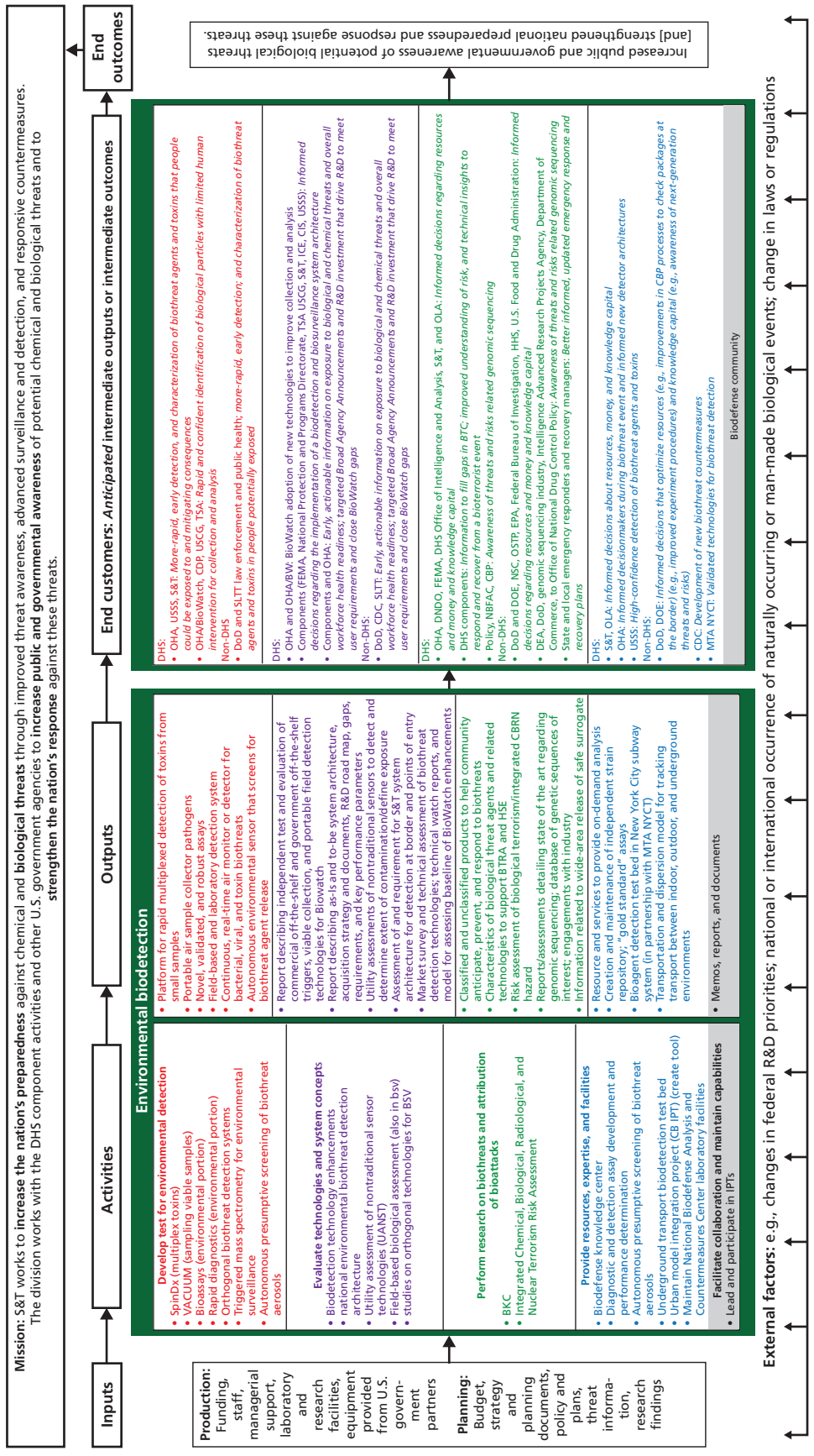
Each of the Tier 1 taxonomy categories included activities that targeted BioWatch as a customer. In contrast, none of the non-S&T efforts identified mentioned BioWatch by name. Nonetheless, outputs from some of this R&D could be relevant for adaptation for BioWatch.

We also developed a logic model to describe S&T BD R&D activities and intended benefits. As mentioned in Chapter Two, logic models can be used to generate a simplified way of visually representing how a program's operations, starting with inputs, proceed to activities and outputs, then ultimately to customers and intended outcomes. In particular, a logic model can be a useful tool for articulating how R&D activities and outputs have contributed or are anticipated to contribute to outcomes consistent with the sponsoring organization's mission or intended societal benefits (Williams et al., 2009; Landree, Miyake, and Greenfield, 2015). For example, specific R&D activities can produce direct, tangible outputs, which, in turn, aim to achieve or contribute to intermediate outcomes (e.g., within operational programs) and, ultimately, contribute to larger and longer-term effects. We reviewed the collection of current S&T R&D activities and then organized them into general themes or streams as a way to depict how collections of similar work might be intended to contribute to desired outcomes and benefits. Each theme is assigned a different color in the logic model, shown in Figure 4.3. To give an example of how to think through our specific R&D logic models, seven S&T environmental BD projects aim to develop tests for environmental detection. Expected outputs from these projects include new platforms, collectors, assays, autonomous sensors, field-based systems, and continuous air monitoring for pathogens of interest. Collectively, the desired intermediate outcomes, targeting both DHS and non-DHS customers, include more-rapid and early detection and identification and characterization of pathogens in air. Ultimately, these will contribute to timely situational awareness and better preparedness.

The collection of activities under each theme has a corresponding set of outputs of similar type. Using information provided to us by S&T, we then identified the customers within DHS and customers external to DHS for each theme and the *anticipated* intermediate and end outcomes. We did not consult with individual customers as to whether or how they already use or intend to use S&T's BD outputs. Consequently, the S&T BD logic model in Figure 4.3 should be considered the anticipated path between S&T's research effort and the desired outcomes or societal benefits from that research. Nonetheless, Figure 4.3 does provide a useful visual description of how S&T's R&D activities align to and support S&T's mission to

> increase the nation's preparedness against chemical and biological threats through improved threat awareness, advanced surveillance and detection, and responsive countermeasures. The division works with DHS component activities and other U.S. government agencies to increase public and governmental awareness of potential chemical and biological threats and to strengthen the nation's response against these threats. (DHS, undated-d)

Figure 4.3
Logic Model for Biodetection R&D



RAND *RR2398-4.3*

Human Biosurveillance

Compared with environmental BD, S&T supports fewer R&D activities addressing human BSV. These activities span most of the five BSV taxonomy categories, are mostly at early stage to midstage of maturity, and aim to serve both DHS and non-DHS customers (Table 4.2). However, most were envisaged to end during FY 2018 or FY 2019 (Figure 4.4).

S&T's BSV R&D covers four of our five taxonomy categories, albeit sparsely.

S&T activities related to **data sources and reporting** address such sources as trade and travel databases and nontraditional sources, such as wearable technologies. The latter (Utility Assessment of Non-Traditional Sensor Technologies) is a short-term project that aims to assess current and emerging BSV and detection technologies, including wearable technologies; demonstrate relevant ones within DHS; and determine whether wearable technologies are relevant to the DHS mission space. Non-S&T R&D in this taxonomy category has focused on different modalities for reporting by clinical and emergency services and laboratories and use of sensor technologies to expand the depth and rapidity of BSV reporting. Just a small handful of projects aim to examine wearable technologies.

All three of S&T's **test development** activities were due to end in FY 2018 or FY 2019. Two of them are in the early stage of R&D: one to develop a small, handheld platform that could test biological samples for multiple biothreat agents and deliver results in less than ten minutes and another to investigate genetic coding that enables antimicrobial resistance of biothreat pathogens, especially those with medical countermeasures in the Strategic National Stockpile managed by HHS. The large volume of non-S&T test development R&D is focused on point-of-care diagnostics using various approaches (e.g., nucleic acids, proteins, whole of agent) and enabling technologies (e.g., laboratory on a chip, mobile phone–based diagnostic testing and reporting).

Four of the five S&T **data analytics** activities were due to end in FY 2018, including development of tools to aggregate data from different sources to detect, track, or investigate outbreaks or integrate data for NBIC; the Biosurveillance Prize, also funded only through FY 2018, aims to support early stage research to develop large data analytics for NBIC to enable rapid detection of biothreat events. Non-S&T R&D in this taxonomy category focuses on establishing baseline patterns, developing algorithms to detect anomalies, and developing models to predict the trajectory of a current outbreak or forecast (mostly naturally occurring) future disease events. Beyond S&T, multiple other agencies—HHS, in particular—fund R&D focusing on integration of data from different sources.

Two S&T activities address BSV **system configuration**. One was due to end in FY 2018; the other, envisaged with a longer time frame, aims to provide decision-support tools for city planners to plan for and respond to biological events. Non-S&T R&D related to system configuration is typically narrow—confined to a specific disease or reporting stream rather than configuration of entire systems run by an agency, such as CDC; some addresses the underlying BSV communications infrastructure.

S&T does not support R&D addressing BSV **CONOPS**. Non-S&T R&D in this area varies widely by funding source and focus. Nearly all agencies, including foreign entities, are represented, and they incorporate modeling, emerging technologies, and both prospective and retrospective examination of BSV operations. In principle, CONOPS R&D addresses a specific BSV topic or system and is less likely than the more readily adaptable R&D associated with diagnostic biological test development to be directly transferable to other agencies.

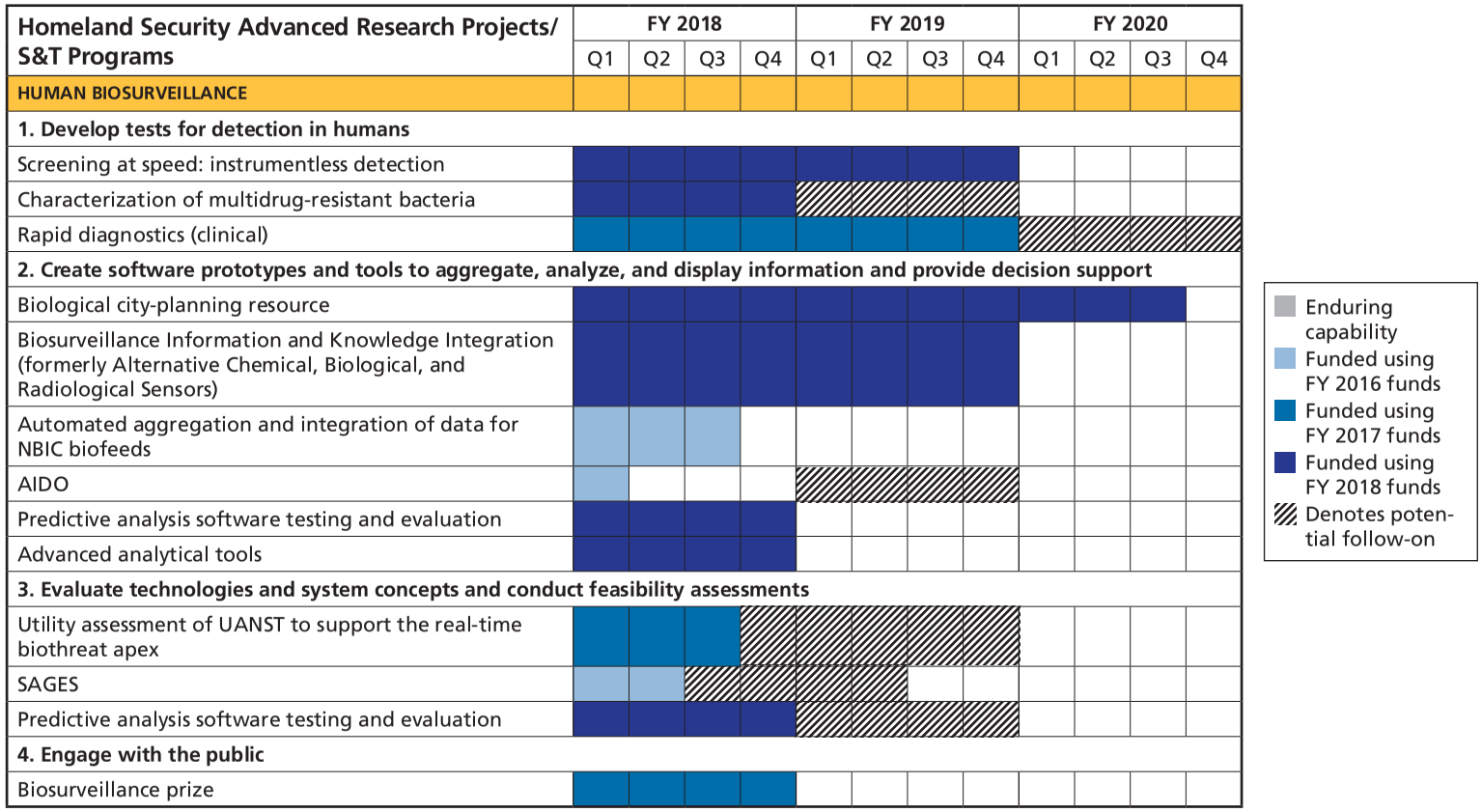
Table 4.2
S&T Human Biosurveillance Projects, by S&T-Specific Theme, Taxonomy Classification, TRL, Customer, and Timeline

Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
Develop tests for detection in humans						
1	Screening at speed: instrumentless detection	Biological diagnostic testing R&D	Enabling technologies	USSS		2
2	Characterization of multidrug-resistant bacteria	Biological diagnostic testing R&D	Nucleic acids	USSS		2
3	Rapid diagnostics integrated product team (clinical)	Biological diagnostic testing R&D	Proteins	USSS		4–5
Create software prototypes and tools to aggregate, analyze, and display information and provide decision support						
4	Biological city planning resource	System configuration	No second tier	FEMA	EPA	3–4
5	Biosurveillance Information and Knowledge Integration (formerly Alternative Chemical, Biological, and Radiological Sensors)	Data analysis	Integration of information from different sources	OHA	SLTT EMS, law enforcement, public health	4–5
6	Automated aggregation and integration of data for NBIC biofeeds	Data analysis	Integration of information from different sources	OHA	DoD; other federal agency NBIS partners	4–5
7	Analytics for Investigation of Disease Outbreaks (AIDO)	Data analysis	Determination of natural versus synthetic origin	OHA/NBIC	DoD DTRA, BSVE users	5–6
8	Predictive analysis software testing and evaluation	Data sources and reporting	Other: trade and travel databases	not specified	not specified	unknown
9	Advanced analytical tools	System configuration	No second tier	not specified	not specified	unknown
Evaluate technologies and system concepts and conduct feasibility assessments						
10	Utility assessment of non-traditional sensor technologies (postexposure, preclinical)	Data sources and reporting	Standoff/portal monitors	Components; OHA	DoD; HHS/CDC; SLTT EMS, law enforcement, public health	4–5 (field demo of wearable technologies)
11	Predictive analysis software testing and evaluation	Data sources and reporting	No second tier	not specified	not specified	unknown

Table 4.2—Continued

Number	Description	Taxonomy Tier 1	Taxonomy Tier 2	DHS Customer	Other Customer	TRL
12	Suite for Automated Global Electronic bioSurveillance	Data analysis	Projected trajectory of ongoing outbreak	FEMA, ICE, S&T, USCG, OHA	DoD; SLTT EMS, public health	N/A
Engage with the public						
13	Biosurveillance prize	Data analysis	Anomaly detection	OHA	DoD; HHS (ASPR/ Biomedical Advanced Research and Development Authority); SLTT EMS, law enforcement, public health	1

Figure 4.4
Funding Timetable for S&T Human Biosurveillance R&D Activities



SOURCE: Timeline data provided by sponsor.

RAND *RR2398-4.4*

The TRL levels of S&T BSV activities across taxonomy categories and S&T-specific themes are shown in Figure 4.5. As shown in both the table and figure, about half of S&T's BSV biosurveillance R&D is at early maturity (TRLs 1–3) and half is at midstage of maturity (TRLs 4–6). S&T supports no work addressing BSV CONOPS (any such research would likely be supported by another part of DHS—in which the operational program, NBIC, is housed—rather than the S&T Directorate).

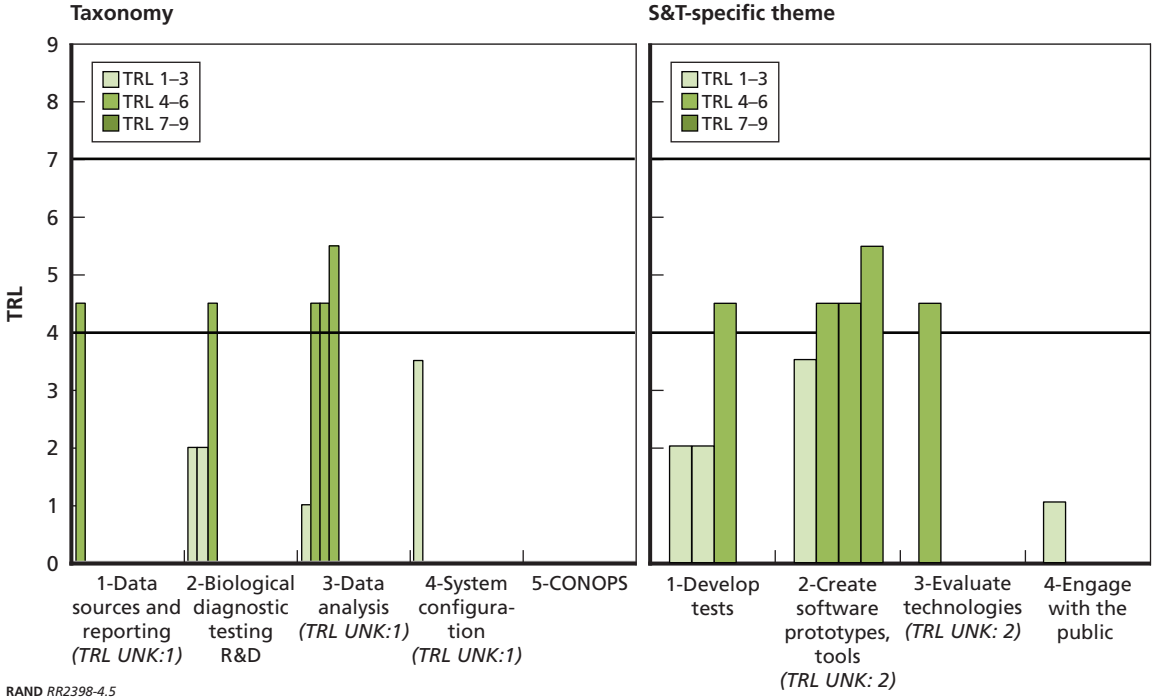
We used the same process used to create the S&T BD logic model shown in Figure 4.3 to create a logic model to represent S&T's BSV R&D, shown in Figure 4.6.

Like in Figure 4.3, for each theme, there is a corresponding set of activities, outputs, customers (internal to DHS and external to DHS), and anticipated intermediate outputs and intermediate outcomes that support the S&T mission. The intermediate outputs and intermediate outcomes are described as being "anticipated" because there has not been contact with S&T's customers to validate what has been done to date with S&T's outputs or how they anticipate using them. The items listed under the "End Customer: Anticipated Intermediate Outputs or Intermediate Outcomes" heading is based on information provided to us by S&T.

Summary

S&T supports a greater number of R&D activities addressing environmental BD than human BSV. R&D in both areas aims to serve the needs of both internal (DHS) and external (non-DHS) customers, though systematic assessment of customer use or satisfaction has not been undertaken to verify the extent to which targeted customers use S&T R&D outputs.

Figure 4.5
TRLs for S&T Biosurveillance R&D, by Taxonomy Category and S&T-Specific Theme



RAND *RR2398-4.5*

S&T's BD research is largely in the areas of test development and system configuration and spans all maturity levels. Its BSV research addresses development of diagnostic tests, software, prototypes, or tools and data analysis; it spans early and midstage maturity levels (i.e., no testing of systems approaching readiness for deployment).

The R&D logic models visually depict similar types of activities across both environmental BD and human BSV and identify specific customers both within DHS and external to DHS. It should be noted that the intermediate outputs and intermediate outcomes shown in Figure 4.3 and Figure 4.6 are described as *anticipated* because we did not speak with any S&T customers to validate their use or intended use of S&T's outputs. Contacting S&T customers was beyond the scope of this project, but it is a potentially useful activity for DHS to consider going forward. Engaging with customers can provide both evidence and data to help document and measure how R&D outputs are contributing to desired outcomes.[1] It can also be useful to document other anticipated paths that lead to outcomes or identify barriers or obstructions preventing S&T's R&D from reaching its intended purpose. Such information also can inform strategic planning and assist leadership with identifying which R&D activities show evidence of achieving outcomes and allow for informed decisions to address identified barriers or rebalance the research portfolio.

In broad terms, S&T's environmental biodetection and human biosurveillance R&D is trying to achieve its mission through enabling desired intermediate outcomes. These intermediate outcomes include earlier, more-rapid, and more-precise detection of biological agents in the environment or in people and more information for decisionmakers so that they can make better-informed decisions about initiating appropriate mitigation actions more rapidly.

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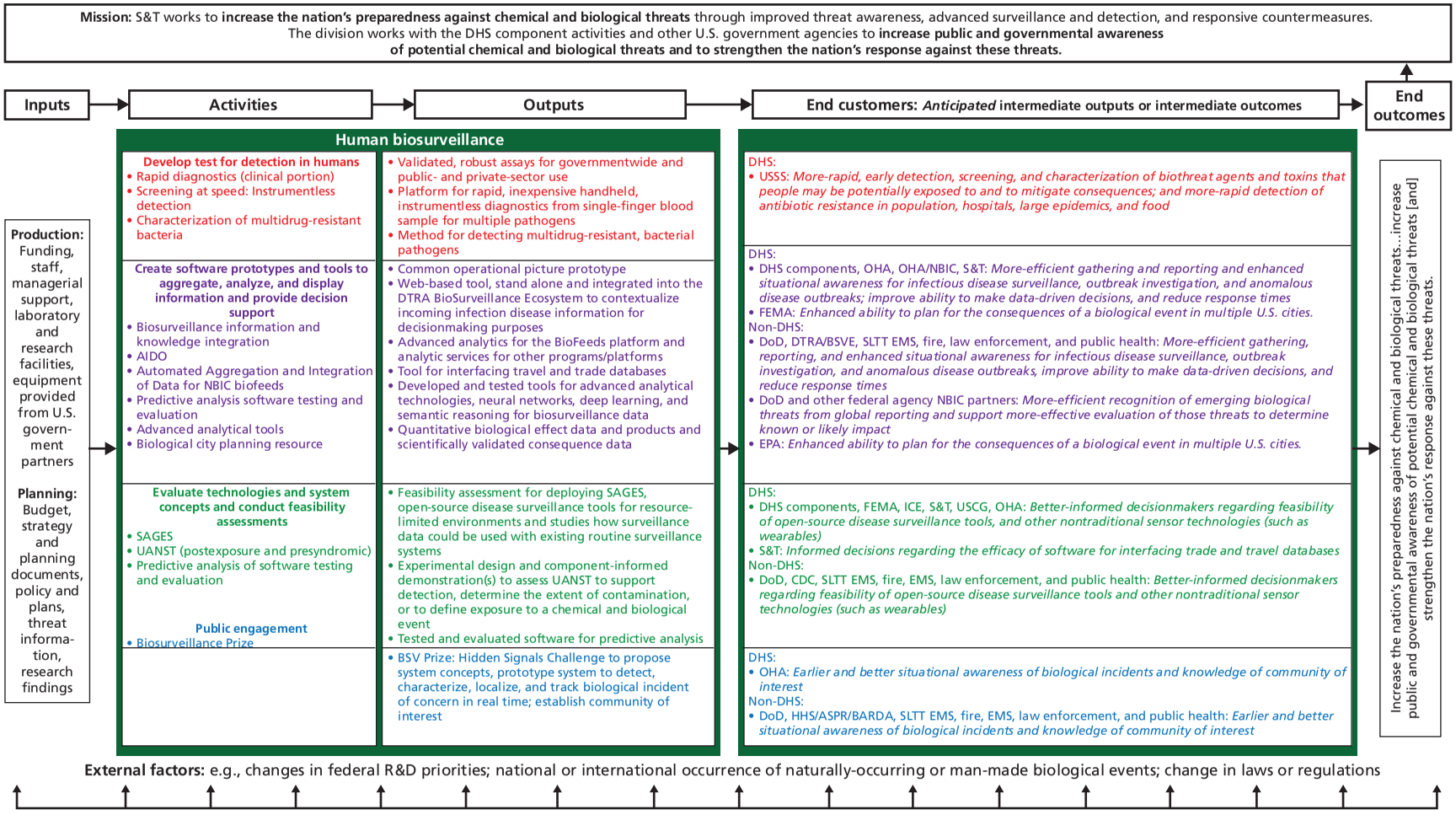
[1] A more detailed description of how to use logic models to develop measures of successful technology transfers is contained in Landree and Silberglitt (2018).

Figure 4.6
Logic Model for Biosurveillance R&D



CHAPTER FIVE

Opportunities and Recommendations

An understanding of the policy and practice landscape, non-S&T R&D relevant to environmental biodetection and human biosurveillance, and S&T's R&D portfolio provide the basis for our analysis of opportunities for future S&T investment. This chapter discusses such opportunities and offers recommendations.

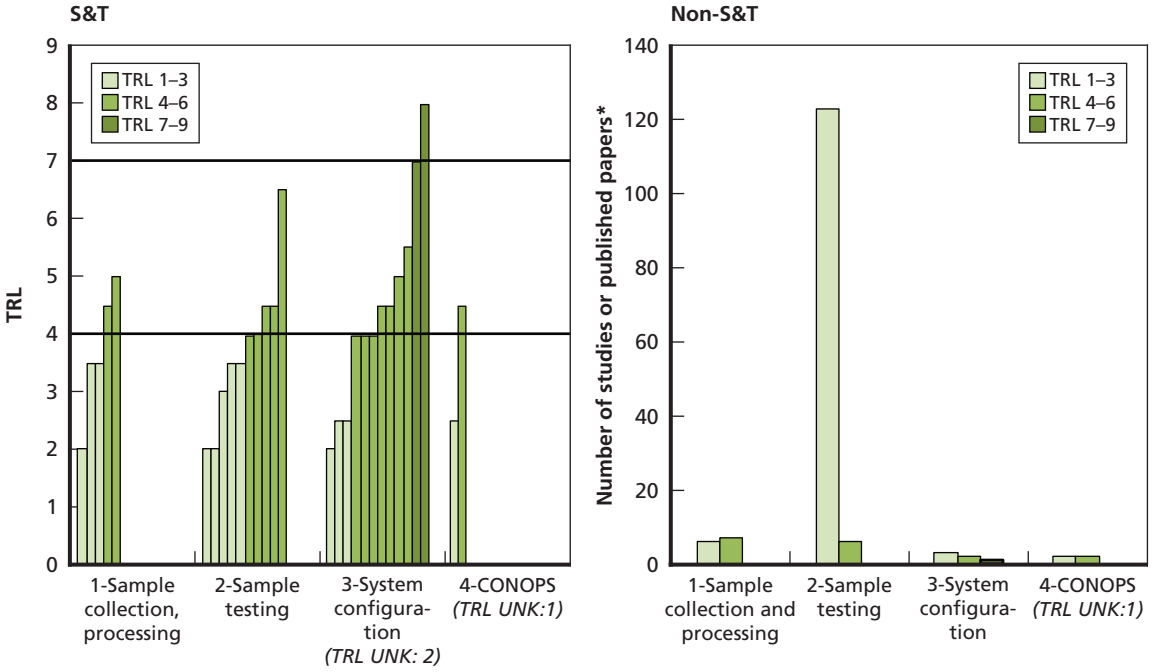
Opportunities

As noted in Chapter Two, DHS has a unique niche within the federal government in the area of **environmental BD** for the civilian population—detection of biothreat agents in air. Although none of the policy documents described in Chapter Two addresses environmental BD specifically, it is generally understood to be subsumed within BSV more broadly. Moreover, these policy-level documents describe the "what" and not the "who" in terms of agency responsibilities. Nonetheless, no other federal agency has current programming for environmental biodetection in civilian populations. S&T's heavy orientation toward R&D in this area reflects the department's role, yet the DHS operational program—BioWatch—remains under scrutiny. Its technology has advanced little since its inception in 2003. Efforts to transition to a next-generation technology (autonomous collection and testing equipment) were hampered by lack of defined technical and operational requirements, performance measurement against those requirements, and justification of cost-effectiveness.

Both S&T and other funding agencies support BD test development, with non-S&T BD R&D more prominently oriented toward test development than other taxonomy Tier 1 categories of sample collection and processing, system configuration, or CONOPS are (Figure 5.1). Moreover, S&T BD test development R&D encompasses early stage research (TRLs 1–3), as does non-S&T R&D. Our sample included non-S&T R&D activity across all Tier 2 categories for BD except two—specimen transport and extraction. Given the illustrative (rather than exhaustive) nature of our sample, these potential gaps might not be significant enough to warrant special attention by S&T. Otherwise, S&T can monitor outputs from early stage research funded by others and adapt those outputs to meet DHS needs, particularly in the area of BD test development while investing selectively in R&D (at all levels of maturity) that is very specific to DHS needs.

In contrast to resources for environmental BD, several federal agencies—including DHS—have missions and programming for **human BSV**. Perhaps because of this, other agencies support human BSV R&D addressing test development to a greater extent than S&T does (Figure 5.2). Because DHS is not a primary BSV data collection agency, it should (and does)

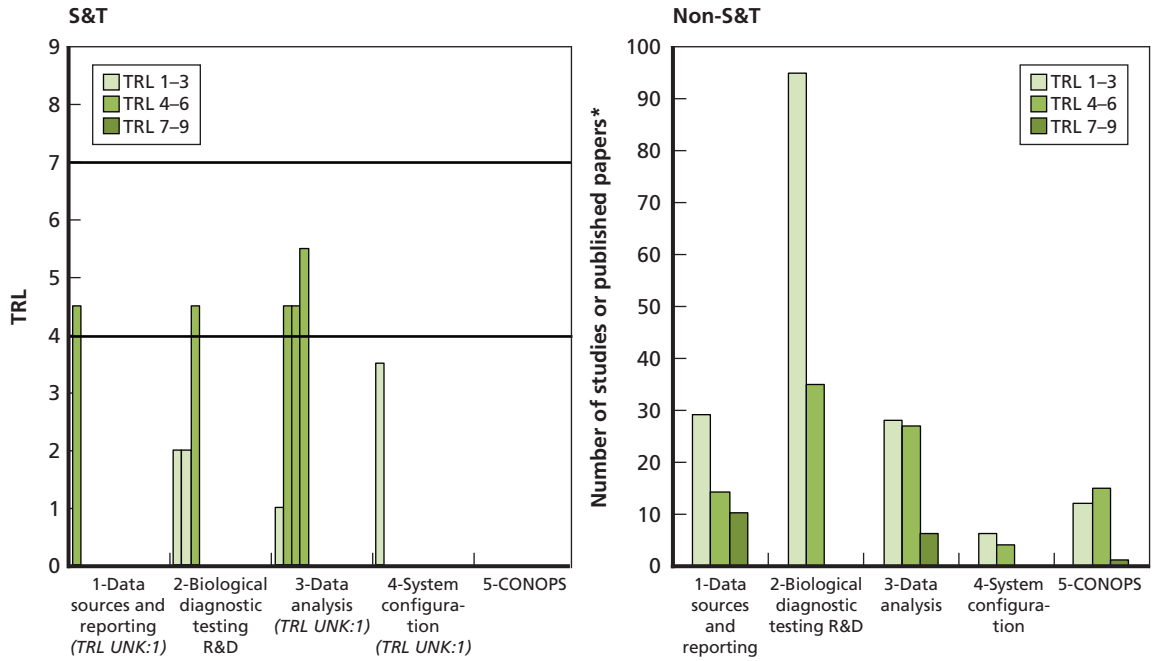
Figure 5.1
Comparison of S&T and Non-S&T Biodetection R&D Activity, by TRL



* Surrogate for R&D activity.

RAND *RR2398-5.1*

Figure 5.2
Comparison of S&T and Non-S&T Biosurveillance R&D Activity, by TRL



* Surrogate for R&D activity.

RAND *RR2398-5.2*

not emphasize R&D related to data sources and reporting. However, it also supports little to no R&D addressing BSV system configuration or CONOPS or more-mature R&D that is closer to ready for application, all of which would be relevant to NBIC.

Recommendations

The discussion of opportunities in this chapter leads to our five recommendations related to directions for future S&T R&D investments. These are conditional on DHS's decisions regarding continued department programming related to environmental BD and human BSV and are as follows:

1. Develop a DHS strategic plan for environmental biodetection and human biosurveillance R&D that is consistent with DHS's role in national biodefense.
2. Prioritize biodetection R&D over biosurveillance R&D, given DHS's unique federal government role in this area.
3. Prioritize R&D addressing CONOPS, given the relative lack of R&D in this area by either S&T or other agencies and the shorter-term potential for real-world application.
4. Actively monitor R&D (at all stages of maturity) supported by other agencies, and adapt relevant outputs to meet DHS needs—for example, addressing biodetection and biosurveillance test development and biodetection aerosol applications.
5. Prioritize midstage and later stage R&D (TRLs 6–9) to complement or balance the current predominantly earlier stage research (TRLs 1–3).

A DHS strategic plan should lay out clear desired intermediate and end outcomes consistent with DHS's role in national biodefense, then construct a program of R&D and other activities aligned to help achieve them. A set of methods (e.g., R&D logic models) can then be used as a planning tool to help guide future investments and to develop metrics for monitoring progress toward defined outcomes.

These recommendations help focus future directions for DHS R&D investments in the areas of environmental BD and human BSV. Again, they depend (at least in part) on the future of DHS's current operational programs in these areas—BioWatch and NBIC. To the extent that they remain as department (and federal) priorities and housed within DHS, there are clear needs for R&D to help improve both of these programs, as highlighted in particular in Chapter Two. Also, DHS components (e.g., USSS, USCG) must be able to access and use the products of R&D to help them ensure their capabilities to carry out their missions.

Potential next steps could include consultation with internal (DHS) and external (non-DHS) customers currently or potentially to be engaged by S&T R&D to verify needs and uses of R&D in furtherance of their respective missions, use of logic models or other planning tools to develop a strategic R&D plan for addressing BD or BSV needs, and development and implementation of measures for tracking uptake and use of S&T R&D outputs and progress toward the intermediate objectives shown in our R&D logic models.

APPENDIX

Details of Non-S&T R&D Search Terms

We searched the NIH RePORTER and Federal RePORTER databases to identify projects relevant to environmental BD or human BSV. Tables A.1, A.2, A.3, and A.4 show the search queries used, including several of note that did not return results. The two databases had different search functionalities, so we modified the queries accordingly.

In NIH RePORTER, we searched for projects from FY 2013 through FY 2018; in Federal RePORTER, we search from FY 2013 through FY 2016, the most recent year available. For multiyear projects, we retained only a single record. In contrast, to capture the range of entities engaged in the work, when investigators from different institutions received separate awards for a single project, we retained multiple records.

We manually reviewed the search results and excluded records with low relevance. To manage the number of records requiring manually review, we used computer scripts to remove results with specified words (second column of Table A.1) or added exclusion terms directly to the search query. In order to identify work that might be applied to environmental BD, we retained projects working to detect or characterize biological agents using novel technologies even if the work did not use aerosol samples. For example, we retained projects using SERS to characterize single eukaryotic cells because the underlying technology, with further development, might be relevant to real-time BD applications. In other cases, such as the use of well-established antibody technology, we searched only for environmental detection projects working directly with aerosols. We captured many other antibody projects when searching for point-of-care tests relevant for human BSV.

Table A.1
Search Terms Used to Identify Non-S&T BD R&D in the NIH RePORTER Database

Search Terms[a]	Exclusion Terms
raman and spectr% and (surface-enhanced or "surface enhanced")	Arsenic, cocaine, marijuana, alcohol, drug abuse, drug testing, angiogenesis, esophagus, uranium, pancreas, pollutant, pesticide
(raman spectr%) and (single-cell or cytometry) not surface-enhanced	N/A
%forensic%	Mental depression, alcohol, imprisonment, recidivism, child abuse, patient, Alzheimer, abuse victim, hereditary disease, human rights, motor cortex, cohort, cocaine, child, heroin, acquired immunodeficiency syndrome, automobile, illicit drug, Superfund, sexual, schizophrenia, borderline personality disorder, mental health
single and particle and aerosol and mass and spectr%	N/A
"air sampling" or "air monitoring"	Clinical, acquired immunodeficiency syndrome, AIDS prevention, placebos, blood alcohol level measurement, sexually transmitted diseases, antismoking, cigarette, nicotine replacement, urinary tract infection, training programs, teaching assistant, autoimmune, implant, vaccine, pregnancy, pregnant, fetal development, leukemia, primary health care, vanadium, pesticide, urine, welding, flame retardants, trichloroethylene, occupational hazard, familial Alzheimer disease, breast feeding, arsenic, chromium, pollution, environmental toxicology, radon, metal poisoning, occupational health, pollutant, lead poisoning, occupational exposure, polychlorinated biphenyls, heavy metals, seafood, diabetes
laminar and flow and condensation	N/A
"digital PCR" or dPCR	clinic
"loop mediated isothermal amplification" or "loop-mediated isothermal amplification" or "rolling circle amplification"	cancer
("matrix-assisted laser desorption" or MALDI) and spectr% and (species or organism) and identif%	Cancer, acquired immunodeficiency syndrome, adipocytes, retina, fossil fuels, Alzheimer's disease, enamel, vascular, cornea, bone, arthritis, lens protein, cocaine, neuron, glioma, zebrafish
Hamilton and Sundstrand and mass and spectrometry[b]	N/A
wetted and wall and cyclone[b]	N/A
aerosol and filter	N/A
Microfluidic and aerosol	N/A
aerosol and (capture or character% or scatter% or absorb% or fluoresce%	Cigarette, drug delivery, macrophage, tobacco, nebulizer, lesion, nicotine, urine, chemotherapy, malaria, vaccine, Alzheimer, greenhouse, cell physiology, nerve, drug formulations, pharmaceutical preparations
unbiased and pathogen and detection	N/A
("quantitative PCR" or qPCR) and (detect% or diagnos%) and biodefense and multiple	N/A
hybridization and detection and biodefense	N/A
"single-molecule field-effect transistor"	N/A
antibod% and biodefense and detection and (aerosol or airborne)	N/A

[a] Percent sign (%) is a wild card.

[b] Search did not return any records.

Table A.2
Search Terms Used to Identify Non-S&T BSV R&D in the NIH RePORTER Database

Search Terms[a]
(absences or absenteeism) and surveillance and infect% not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
"active surveillance" not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
(presyndromic or asymptomatic) and surveillance and infect% not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
automated and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV)
"big data" and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV)
surveillance and biodefense and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
"data analysis" and surveillance and infect% not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
"data integration" and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
"data mining" and surveillance and infect% not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
"electronic health record" and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation)
emergency and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
"epidemiological modeling" and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
forecasting and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
internet and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
mobile and surveillance and infect% not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
("notifiable diseases" or "routine case reporting") not (occupational or chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or tobacco or postoperative)
poison and surveillance not (occupational or chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
"population surveillance" and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
"social media" and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or "HIV")
wearable and surveillance and infect% not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)[b]
biosurveillance

Table A.2—Continued

Search Terms[a]
surveillance and bioterrorism not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
surveillance and (Abrin or "Bacillus cereus" or "Botulinum" or "Conotoxin" or "Coxiella burnetii" or "Crimean-Congo hemorrhagic fever" or "Diacetoxyscirpenol" or "Eastern Equine Encephalitis" or Ebola or "Francisella tularensis" or "Lassa fever" or "Lujo" or "Marburg" or "Monkeypox" or "1918 Influenza virus" or Ricin or "Rickettsia prowazekii" or "Severe Acute Respiratory Syndrome" or Saxitoxin or "South American Hemorrhagic Fever" or Chapare or Guanarito or Junin or Machupo or Sabia or "Staphylococcal enterotoxin" or "T-2 toxin" or Tetrodotoxin or "Tick-borne encephalitis" or "Kyasanur Forest disease" or "Omsk hemorrhagic fever" or smallpox or "Variola major" or "Variola minor" or Alastrim or "Yersinia pestis" or "Bacillus anthracis" or "Brucella abortus" or "Brucella melitensis" or "Brucella suis" or "Burkholderia mallei" or "Burkholderia pseudomallei" or Hendra or Nipah or "Rift Valley fever" or "Venezuelan equine encephalitis" or "African horse sickness" or "African swine fever" or "Avian influenza" or "Classical swine fever" or "Foot-and-mouth disease" or "Goat pox" or "Lumpy skin disease" or "Mycoplasma capricolum" or "Mycoplasma mycoides" or "Newcastle disease" or "Peste des petits ruminants" or Rinderpest or "Sheep pox" or "Swine vesicular disease" or "Peronosclerospora philippinensis" or "Peronosclerospora sacchari" or "Phoma glycinicola" or "Pyrenochaeta glycines" or "Ralstonia solanacearum" or "Rathayibacter toxicus" or "Sclerophthora rayssiae" or "Synchytrium endobioticum" or "Xanthomonas oryzae")
surveillance and (stand-off or standoff or infrared or "thermal scanner" or "non-contact thermometer") not (diabetic or diabetes or chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
surveillance and crowd-sourced
surveillance and smartphone not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or "HIV" or tobacco or stove or postoperative or anemia or melanoma or crashes)
("rapid diagnostics" or "point of care" or "point-of-care" or "point of need" or "point-of-need") not (core or adipose or Hepatitis or hypertension or Phenylketonurias or sickle or cancer or HIV or immunodeficiency or smoking or cigarette or malignant or Alzheimer or diabetes or sleep or Papillomavirus or HPV or "peripheral arterial disease" or "inflammatory bowel disease" or "end-of-life" or mercury or bone or oxytocin or conference or ultrasound or genitourinary or alcohol or sexually or cardiovascular or drug or "traumatic brain" or lithium or MRI or ambulatory or surgical or kidney or asthma or hearing or electroencephalography or metals or Chlamydia or Gonorrhea or stress or neurosurgery or "heart failure" or ophthalmologist or dental or trauma or wound or pancreas or "Acquired Immunodeficiency Syndrome" or postoperative or palliative or language or sarcoma or chronic or anemia or cardiac or neonatal or "chemical exposure" or "vision screening")[c, d]

[a] Percent sign (%) is a wild card.

[b] Search did not return any records.

[c] Search did not behave as expected; we removed records containing any of the terms in the exclusion group in the project abstract, project terms, and project title fields during postprocessing.

[d] We searched for research on point-of-care tests and rapid diagnostics as part of our human BSV exploration. Multiple environmental BD searches returned similar or, in some cases, identical projects. When we considered the technologies underlying those projects relevant to environmental BD, we included the results in our set of BD projects. Consequently, some projects appear in both the BSV and BD sets.

Table A.3
Search Terms Used to Identify Non-S&T BD R&D in the Federal RePORTER Database

Search Terms[a]
raman and (surface-enhanced or "surface enhanced")
raman and (single-cell or cytometry) not surface-enhanced
forensic and micro
single and particle and aerosol and mass and spectroscopy[b]
"air sampling" or "air monitoring"
laminar and flow and condensation
"digital PCR" or "dPCR"
"loop mediated isothermal amplification" or "loop-mediated isothermal amplification" or "rolling circle amplification"
Hamilton and Sundstrand and mass and spectrometry[b]
wetted and wall and cyclone[b]
aerosol and filter not pollution
Microfluidic and aerosol
unbiased and pathogen and detection
("quantitative PCR" or qPCR) and (detect or diagnose or diagnostic)
(hybridization and detect) not cancer not brain
"single-molecule field-effect transistor"[b]
phage and detect not cancer
"matrix-assisted laser desorption" or MALDI
aerosol and (capture or characterize or scatter or absorb or fluoresce) and (micro or virus or pathogen or agent or toxin)
(antibody or antibodies) and biodefense and detection and (aerosol or airborne)[b]

[a] Percent sign (%) is a wild card.
[b] Search did not return any results.

Table A.4
Search Terms Used to Identify Non-S&T BSV R&D in the Federal RePORTER Database

Search Terms[a]
"active surveillance" not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
(presyndromic or asymptomatic) and surveillance not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
automated and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV)
"big data" and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or crop)
"data analysis" and surveillance not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers or algal or "traumatic brain" or ionosphere)
"data mining" and surveillance not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
emergency and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative or livestock or surgery or autism)
"epidemiological modeling" not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
forecasting and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
internet and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative or silicon)
mobile and surveillance not (occupational or chronic or cancer or "mental health" or obesity or alcohol or HIV or "genetic disorder" or transplantation or tobacco or postoperative or cancers)
"social media" and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or "HIV")
wearable and surveillance not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or HIV or tobacco or postoperative)
Biosurveillance
surveillance and (Abrin or "Bacillus cereus" or "Botulinum" or "Conotoxin" or "Coxiella burnetii" or "Crimean-Congo hemorrhagic fever" or "Diacetoxyscirpenol" or "Eastern Equine Encephalitis" or Ebola or "Francisella tularensis" or "Lassa fever" or "Lujo" or"Marburg" or "Monkeypox" or "1918 Influenza virus" or Ricin or "Rickettsia prowazekii" or "Severe Acute Respiratory Syndrome" or Saxitoxin or "South American Hemorrhagic Fever" or Chapare or Guanarito or Junin or Machupo or Sabia or "Staphylococcal enterotoxin" or "T-2 toxin" or Tetrodotoxin or "Tick-borne encephalitis" or "Kyasanur Forest disease" or "Omsk hemorrhagic fever" or smallpox or "Variola major" or "Variola minor" or Alastrim or "Yersinia pestis" or "Bacillus anthracis" or "Brucella abortus" or "Brucella melitensis" or "Brucella suis" or "Burkholderia mallei" or "Burkholderia pseudomallei" or Hendra or Nipah or "Rift Valley fever" or "Venezuelan equine encephalitis" or "African horse sickness" or "African swine fever" or "Avian influenza" or "Classical swine fever" or "Foot-and-mouth disease" or "Goat pox" or "Lumpy skin disease" or "Mycoplasma capricolum" or "Mycoplasma mycoides" or "Newcastle disease" or "Peste des petits ruminants" or Rinderpest or "Sheep pox" or "Swine vesicular disease" or "Peronosclerospora philippinensis" or "Peronosclerospora sacchari" or "Phoma glycinicola" or "Pyrenochaeta glycines" or "Ralstonia solanacearum" or "Rathayibacter toxicus" or "Sclerophthora rayssiae" or "Synchytrium endobioticum" or "Xanthomonas oryzae")
surveillance and (stand-off or standoff or infrared or "thermal scanner" or "non-contact thermometer") not lightning
surveillance and (crowd-source or crowd-sourced)
surveillance and smartphone not (chronic or cancer or "mental health" or obesity or alcohol or "genetic disorder" or transplantation or "HIV" or tobacco or stove or postoperative or anemia or melanoma or crashes)

Table A.4—Continued

Search Terms[a]
(“rapid diagnostics” or “point of care” or “point-of-care” or “point of need” or “point-of-need”) not (core or adipose or Hepatitis or hypertension or Phenylketonurias or sickle or cancer or HIV or immunodeficiency or smoking or cigarette or malignant or Alzheimer or diabetes or sleep or Papillomavirus or HPV or “peripheral arterial disease” or “inflammatory bowel disease” or “end-of-life” or mercury or bone or oxytocin or conference or ultrasound or genitourinary or alcohol or sexually or cardiovascular or drug or “traumatic brain” or lithium or MRI or ambulatory or surgical or kidney or asthma or hearing or electroencephalography or metals or Chlamydia or Gonorrhea or stress or neurosurgery or “heart failure” or ophthalmologist or dental or trauma or wound or pancreas or “Acquired Immunodeficiency Syndrome” or postoperative or palliative or language or sarcoma or chronic or anemia or cardiac or neonatal or “chemical exposure” or “vision screening”)[b]
surveillance and biodefense not (chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or HIV or tobacco or postoperative)[c]
(absences or absenteeism) and surveillance not (occupational or chronic or cancer or “mental health” or obesity or alcohol or HIV or “genetic disorder” or transplantation or tobacco or postoperative or cancers) [c]
“data integration” and surveillance not (chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or HIV or tobacco or postoperative)[c]
“electronic health record” and surveillance not (chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation)[c]
(“notifiable diseases” or “routine case reporting”) not (occupational or chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or tobacco or postoperative)[c]
poison and surveillance not (occupational or chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or HIV or tobacco or postoperative)[c]
population surveillance not (chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or HIV or tobacco or postoperative)[c]
surveillance and bioterrorism not (chronic or cancer or “mental health” or obesity or alcohol or “genetic disorder” or transplantation or HIV or tobacco or postoperative)[c]

[a] Percent sign (%) is a wild card.
[b] We searched for research on point-of-care tests and rapid diagnostics as part of our human BSV searches. Multiple environmental BD searches returned similar or, in some cases, identical projects. When we considered the technologies underlying those projects relevant to environmental BD, we included the results in our set of BD projects. Consequently, some projects appear in both the BSV and BD sets.
[c] Search did not return any results.

References

Blue Ribbon Study Panel on Biodefense, *A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts*, Washington, D.C.: Hudson Institute, October 28, 2015. As of February 14, 2018: http://www.biodefensestudy.org/a-national-blueprint-for-biodefense

CDC—*See* Centers for Disease Control and Prevention.

Centers for Disease Control and Prevention, "Mission, Role, and Pledge," webpage, last updated April 14, 2014. As of May 15, 2018: https://www.cdc.gov/about/organization/mission.htm

Chen, Xin, Abrar Ahmad Chughtai, and C. Raina MacIntyre, "A Systematic Review of Risk Analysis Tools for Differentiating Unnatural from Natural Epidemics," *Military Medicine*, Vol. 182, No. 11–12, 2017, pp. e1827–e1835.

Clarivate, "Web of Science Core Collection," database, undated. As of May 15, 2018: http://webofknowledge.com

DoD—*See* U.S. Department of Defense.

DoE—*See* U.S. Department of Energy.

Federal Select Agent Program, "Select Agents and Toxins List," webpage, undated. As of February 13, 2018: https://www.selectagents.gov/selectagentsandtoxinslist.html

GAO—*See* U.S. Government Accountability Office.

Greenfield, Victoria A., Valerie L. Williams, and Elisa Eiseman, *Using Logic Models for Strategic Planning and Evaluation: Application to the National Center for Injury Prevention and Control*, Santa Monica, Calif.: RAND Corporation, TR-370-NCIPC, 2006. As of March 21, 2018: https://www.rand.org/pubs/technical_reports/TR370.html

HHS—*See* U.S. Department of Health and Human Services.

HHS, ASPR—*See* U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response.

Institute of Medicine and National Research Council, *BioWatch and Public Health Surveillance: Evaluating Systems for the Early Detection of Biological Threats (Abbreviated Version)*, Washington, D.C.: National Academies Press, 2011.

———, *Technologies to Enable Autonomous Detection for BioWatch: Ensuring Timely and Accurate Information for Public Health Officials: Workshop Summary*, Washington, D.C.: National Academies Press, 2014.

IOM and NRC—*See* Institute of Medicine and National Research Council.

Jones, K. E., N. G. Patel, M. A. Levy, B. D. Storeygard, J. L. Gittleman, P. Daszak, "Global Trends in Emerging Infectious Diseases," *Nature*, Vol. 451, February 21, 2008, pp. 990–993. As of May 17, 2018: https://www.nature.com/articles/nature06536

Landree, Eric, Hirokazu Miyake, and Victoria Greenfield, *Nanomaterial Safety in the Workplace: Pilot Project for Assessing the Impact of the NIOSH Nanotechnology Research Center*, Santa Monica, Calif.: RAND Corporation, RR-1108-NIOSH, 2015. As of March 14, 2018: https://www.rand.org/pubs/research_reports/RR1108.html

Landree, Eric, and Richard Silberglitt, *Application of Logic Models to Facilitate DoD Laboratory Technology Transfer*, Santa Monica, Calif.: RAND Corporation, RR-2122-OSD, 2018. As of March 20, 2018: https://www.rand.org/pubs/research_reports/RR2122.html

Military Health System, "Armed Forces Health Surveillance Branch," webpage, undated-a. As of May 15, 2018: https://health.mil/Military-Health-Topics/Health-Readiness/Armed-Forces-Health-Surveillance-Branch

———, "Defense Occupational and Environmental Health Readiness System—Industrial Hygiene," webpage, undated-b.

———, "Integrated Biosurveillance," webpage, undated-c. As of May 15, 2018: https://health.mil/Military-Health-Topics/Health-Readiness/Armed-Forces-Health-Surveillance-Branch/Integrated-Biosurveillance?type=Policies

NAS—*See* National Academies of Sciences, Engineering, and Medicine.

National Academies of Sciences, Engineering, and Medicine, *Enhancing BioWatch Capabilities Through Technology and Collaboration: Proceedings of a Workshop*, Washington, D.C.: National Academies Press, 2016. As of May 17, 2018: https://doi.org/10.17226/23687

National Public Radio, *Timeline: How the Anthrax Terror Unfolded*, February 15, 2011. As of March 15, 2018: https://www.npr.org/2011/02/15/93170200/timeline-how-the-anthrax-terror-unfolded

Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Programs, homepage, undated.

Office of the Press Secretary, "The 2003 State of the Union Address: Complete Transcript of President Bush's Speech to Congress and the Nation," Washington, D.C.: White House, January 28, 2003. As of May 25, 2018: http://whitehouse.georgewbush.org/news/2003/012803-SOTU.asp

Runge, Jeffrey W., "BioWatch: An Abbreviated History," presentation slides, Chertoff Group, undated. As of May 25, 2018: http://www.nationalacademies.org/hmd/~/media/E78F1D3F52D14408B68CFE9ADBB87A50.ashx

U.S. Code, Title 6, Section 104, National Biodefense Strategy. As of February 14, 2018: http://uscode.house.gov/view.xhtml?req=granuleid:USC-prelim-title6-section104&num=0&edition=prelim

USDA—*See* U.S. Department of Agriculture.

USDA, APHIS—*See* U.S. Department of Agriculture, Animal and Plant Health Inspection Service.

U.S. Department of Agriculture, "Mission Areas," webpage, undated. As of May 15, 2018: https://www.usda.gov/our-agency/about-usda/mission-areas

U.S. Department of Agriculture, Animal and Plant Health Inspection Service, "Participation and Partnerships," webpage, last updated December 6, 2016. As of May 15, 2018: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/sa-epidemiology-animalhealth-ceah/sa-general-ceah/ct_activities

U.S. Department of Defense, "About the Department of Defense (DoD)," webpage, last updated January 27, 2017.

U.S. Department of Energy, "About Us," webpage, undated. As of May 15, 2018: https://www.energy.gov/about-us

U.S. Department of Health and Human Services, *National Health Security Strategy of the United States of America*, Washington, D.C., December 2009.

———, *National Health Security Strategy and Implementation Plan: 2015–2018*, Assistant Secretary of Health and Human Services for Preparedness and Response, Washington, D.C., 2015.

U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response, "Saving Lives and Protecting Americans from 21st Century Health Security Threats," webpage, last updated April 26, 2018. As of May 15, 2018:
http://www.phe.gov/about/aspr/Pages/default.aspx

U.S. Department of Homeland Security, "Mission," undated-a. As of March 2, 2018:
https://www.dhs.gov/mission

———, "National Biosurveillance Integration Center," webpage, undated-b. As of March 2, 2018:
https://www.dhs.gov/national-biosurveillance-integration-center

———, *Product Realization Guide*, undated-c. As of May 1, 2018:
https://www.dhs.gov/sites/default/files/publications/product-realization-guide-partnership-focus-508-1.pdf

———, "S&T CBD," webpage, undated-d. As of March 15, 2018:
https://www.dhs.gov/science-and-technology/st-cbd

———, *National Biosurveillance Integration Center Strategic Plan*, Washington, D.C., November 2012. As of March 5, 2018:

https://www.dhs.gov/sites/default/files/publications/nbic-strategic-plan-public-2012.pdf

———, "National Biosurveillance Integration Center," fact sheet, 2015a. As of March 2, 2018:
https://www.dhs.gov/sites/default/files/publications/2015-Factsheet-NBIC_0.pdf

———, *Acquisition and Management Directive 102-01*, Revision 3, July 28, 2015b. As of May 1, 2018:

https://www.dhs.gov/sites/default/files/publications/01.%20Directive%20102-01%20Acquisition%20Management%20Directive.pdf

U.S. Government Accountability Office, *Developing a Collaboration Strategy Is Essential to Fostering Interagency Data and Resource Sharing*, Washington, D.C., GAO-10-171, December 2009.

———, *DHS Should Reevaluate Mission Need and Alternatives Before Proceeding with BioWatch Generation-3 Acquisition*, Washington, D.C., GAO-12-810, September 2012a.

———, *Observations on BioWatch Generation-3 and Other Federal Efforts*, Washington, D.C., GAO-2012-994T, September 2012b.

———, *Observations on the Cancellation of BioWatch Gen-3 and Future Considerations for the Program*, Washington, D.C., GAO-14-267T, June 2014.

———, *Challenges and Options for the National Biosurveillance Integration Center*, Washington, D.C., GAO-15-793, September 2015a.

———, *DHS Should Not Pursue BioWatch Upgrades or Enhancements Until System Capabilities Are Established*, Washington, D.C., GAO-16-99, October 2015b.

———, *Ongoing Challenges and Future Considerations for DHS Biosurveillance Efforts*, Washington, D.C., GAO-16-413T, February 2016.

White House, *Homeland Security Presidential Directive-10: Biodefense for the 21st Century*, Washington, D.C., April 2004.

———, *National Security Strategy of the United States of America*, Washington, D.C., March 2006.

———, *Homeland Security Presidential Directive-18: Medical Countermeasures Against Weapons of Mass Destruction*, Washington, D.C., January 2007a.

———, *Homeland Security Presidential Directive-21: Public Health and Medical Preparedness*, Washington, D.C., October 2007b.

———, National Strategy for Countering Biological Threats, National Security Council, Washington, D.C., November 2009.

———, *National Security Strategy*, Washington, D.C., May 2010.

———, National Strategy for Biosurveillance, Washington, D.C., July 2012.

———, *Presidential Policy Directive/PPD-21: Critical Infrastructure Security and Resilience*, Washington, D.C., February 2013.

———, *Global Health Security: Vision and Overarching Target*, Washington, D.C., February 2014. As of May 17, 2018:
http://www.cdc.gov/globalhealth/security/pdf/ghs_overarching_target.pdf

———, *National Security Strategy*, Washington, D.C., February 2015.

———, *National Security Strategy of the United States*, Washington, D.C., December 2017. As of February 14, 2018:
https://www.whitehouse.gov/wp-content/uploads/2017/12/NSS-Final-12-18-2017-0905.pdf

WHO—*See* World Health Organization.

Williams, Valerie L., Elisa Eiseman, Eric Landree, and David M. Adamson, *Demonstrating and Communicating Research Impact: Preparing NIOSH Programs for External Review*, Santa Monica, Calif.: RAND Corporation, MG-809-NIOSH, 2009. As of March 14, 2018:
http://www.rand.org/pubs/monographs/MG809.html

World Health Organization, *WHO Research and Development Blueprint: 2018 Annual Review of Diseases Prioritized Under the Research and Development Blueprint*, Geneva, Switzerland, 2018. As of May 17, 2018:
http://www.who.int/emergencies/diseases/2018prioritization-report.pdf?ua=1