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A STRATEGIC VISION FOR BIOLOGICAL THREAT REDUCTION

The U.S. Department of Defense and Beyond

Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs

Committee on International Security and Arms Control

Policy and Global Affairs

A Consensus Study Report of

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

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Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs

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Preface

The Biological Threat Reduction Program (BTRP), part of the U.S. Department of Defense (DOD), today is a product of bold and innovative thinking in the early 1990s by Senators Sam Nunn and Richard Lugar, and a cadre of practical academic thinkers. The broader framework they established, the Cooperative Threat Reduction (CTR) Program, was conceived as a valuable tool to address a particular set of challenges associated with the dissolution of the Soviet Union. The program has since evolved and transformed in scope and mission, engaging more widely in other parts of the globe beyond the former Soviet Union to prevent the proliferation or use of weapons of mass destruction, including by enhancing biosecurity and disease outbreak identification. More recently, the CTR Program has once again focused concern on state-level threats. Throughout the lifetime of the program thus far, biosecurity incidents, both in the United States and abroad, have occurred much less frequently than either biosafety incidents or naturally occurring disease events. But technology, connectivity, and the erosion of norms against the use of unconventional weapons all contribute to making these biological risks and threats ever more complex and the timelines to address them shorter.

Our study committee was asked to recommend a new strategic vision for health security in a setting of rapid changes in biotechnology and geopolitics, by considering which forms of engagement have been successful, what else is needed, and how future work may be more effective. In short, how should BTRP engage partners in the United States and around the world to help make the world safer for the U.S. military forces, for the United States, and thus for other countries; that is, safe from intentional misuse of biological materials, laboratory accidents, natural outbreaks, and technical surprise?

The Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs wrestled with how to advise BTRP with a strategic vision when an effective strategy must include other parts of the U.S. government and, for that matter, other governments and organizations in the United States and abroad. Furthermore, we, the co-chairs, are from distinct professional backgrounds (Keusch from global health and Franz from the military) representing a

broad range of tensions between distinct communities, each of which emphasizes different parts of the same problem set often called global health security. These communities sometimes draw conceptual mission boundaries based on the origin of a threat (accidental, natural, or intentional), which enables them to limit the scope of their work so that while the two may overlap, mission conflict is minimized. This made the study process challenging but ultimately resulted in a stronger report. We see this as a metaphor for BTRP itself. CTR is about building human relationships and capabilities, and opening lines of communication—primarily in the health and research sectors—to reduce risks and threats across the biological space. Public health engagement has also historically reduced threats, but typically not as its first priority, which is to improve health.

To the uniformed military and DOD, it is essential to recognize that the work of BTRP and CTR more broadly is a defense mission, and it requires coordination. Guidance from the White House and from the Secretary of Defense reaffirm the need for coordination within the U.S. government and for partnerships outside of it—coordination is easy to speak about but hard to deliver. Whether for protection of deployed U.S. military forces and U.S. interests overseas, or for protection of the homeland, DOD will only be fulfilling this aspect of its mission if it works with partners to anticipate, prevent, detect, respond to, and recover from biological risks and threats, whatever their origin. We may not know whether an outbreak is a result of intentional, accidental, or natural events during the timeframe in which action must be taken. And DOD needs to recognize that BTRP, if given sufficient flexibility to identify and develop programs on emerging risks, can strengthen each action taken to counter threats and mitigate risks. But it is even more complicated, as the current and ongoing Ebola outbreak in northeastern Democratic Republic of the Congo demonstrates. Like this one, future outbreaks may occur in unstable areas where armed civilian and ideological militias willing to engage in violence against healthcare workers, both domestic and international, where citizen distrust of government and the international community is equally dispensed, and where there may be no support for a foreign military or civilian effort to engage and deliver much-needed infrastructure, diagnostics, therapeutics, vaccines, and other support. BTRP should be strategically suited to systematically build the relationships and community engagement ultimately necessary for acceptance in the country.

For the public health sector, it is essential to recognize that DOD has enormous resources and capabilities, medical and logistical, to prevent and respond to emerging infectious disease. Its logistical reach alone is unmatched, but it can also engage more easily with some governments. In places, public health organizations will be the most effective partner to engage internationally, but in others it will be the military that can provide the entrée. By working within an effective interagency mechanism, BTRP can serve as a bridge between these communities and facilitate their cooperative efforts globally.

In this report, we describe the history of CTR and BTRP as well as the dynamic technological and geopolitical worlds of today so that the reader can better understand what needs to change and where BTRP must go. The middle chapters examine context and cases to illustrate what has been effective, where there are gaps and shortcomings, and what new obstacles might block the way to further success. The committee offers recommendations that we believe will significantly enhance the impact and efficiency of BTRP for the next 5 years and beyond. We conclude that global engagements resulting from relationships of respect and trust between and among professionals are needed—indeed, it may be needed now as much as or more than at any previous time—that BTRP is an essential component of the nation's options for addressing current and future needs, that there are potential improvements to how it is implemented, and that it remains one of the most cost-effective arrows in the quiver of DOD and the U.S. government.

Gerald T. Keusch and David R. Franz, *co-chairs*
Committee on Enhancing Global Health Security through
International Biosecurity and Health Engagement Programs

Acknowledgment of Reviewers

This Consensus Study Report was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the National Academies of Sciences, Engineering, and Medicine in making each published report as sound as possible and to ensure that it meets the institutional standards for quality, objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process.

We thank the following individuals for their review of this report: Ekanem Braide, Federal University of Lafia; Seth Carus, National Defense University; Diane DiEuliis, National Defense University; Jeanne Fair, Los Alamos National Laboratory; Asha George, Bipartisan Commission on Biodefense; Elizabeth George, Environmental Protection Agency; Diane Griffin, Johns Hopkins University; Aamer Ikram, National Institute of Health Pakistan; Bonnie Jenkins, Women of Color Advancing Peace, Security and Conflict Transformation; Kent Kester, Sanofi Pasteur; Margaret Kosal, University of Maryland; Clifford Samuel, Gilead Sciences, Inc.; Christine Uhlenhaut, World Organisation for Animal Health; and Pavlos Vlachos, Purdue University.

Although the reviewers listed above provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations of this report nor did they see the final draft before its release. The review of this report was overseen by Gail Cassell, Harvard University, and Nancy Connell, Johns Hopkins University. They were responsible for making certain that an independent examination of this report was carried out in accordance with the standards of the National Academies and that all review comments were carefully considered. Responsibility for the final content rests entirely with the authoring committee and the National Academies.

Contents

Acronyms

ACESO	Austere Environment Consortium for Enhanced Sepsis Outcomes
AFRIMS	Armed Forces Research Institute of Medical Sciences
AHSC	Alliance for Health Security Cooperation
AIDS	Acquired immunodeficiency syndrome
ASD	Assistant Secretary of Defense
ASF	African swine fever
BEP	Biosecurity Engagement Program
BOHRN	Bat One Health Research Network
BSV	Biosurveillance
BTRP	The Biological Threat Reduction Program
BWC	Biological Weapons Convention
CBEP	Cooperative Biological Engagement Program (former name of BTRP)
CBRN	chemical, biological, radiological, and nuclear
CDC	Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
CISAC	Committee on International Security and Arms Control
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CTR	Cooperative Threat Reduction
DNA	Deoxyribonucleic acid
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOJ	Department of Justice
DOS	Department of State
DRC	Democratic Republic of the Congo
DTRA	Defense Threat Reduction Agency
EVD	Ebola Virus Disease

FAO	Food and Agriculture Organization
FBI	Federal Bureau of Investigation
FMD	Foot and mouth disease
FSU	Former Soviet Union
FY	Fiscal year
GHSA	Global Health Security Agenda
HHS	Department of Health and Human Services
HIV	Human Immunodeficiency Virus
HPAI	Highly pathogenic avian influenza
IAVI	International AIDS Vaccine Initiative
IFBA	International Federation of Biosafety Associations
IHR	International Health Regulations
IOM	Institute of Medicine
ISTC	International Science and Technology Center
JEE	Joint External Evaluation
JMEDICC	Joint Mobile Emerging Disease Intervention Clinical Capability
MERS-CoV	Middle East Respiratory Syndrome coronavirus
MUWRP	Makerere University Walter Reed Project
NAMRU	Naval Medical Research Unit
NAPHS	National Action Plans for Health Security
NAS	National Academy of Sciences
NASEM	National Academies of Sciences, Engineering, and Medicine
NGO	Nongovernmental organization
NRC	National Research Council
NTI	Nuclear Threat Initiative
OIE	World Organization for Animal Health
OSD(P)	Under Secretary of Defense for Policy
PEPFAR	President's Emergency Plan for AIDS Relief
PHEIC	Public Health Emergency of International Concern
RNA	Ribonucleic acid
SARS	Severe acute respiratory syndrome

SARS-CoV	Severe acute respiratory syndrome coronavirus
SO/LIC	Special Operations and Low-Intensity Conflict
STCU	Science and Technology Center-Ukraine
UN	United Nations
USAHA	United States Animal Health Association
USAID	United States Agency for International Development
USAMRU	U.S. Army Medical Research Unit
USDA	United States Department of Agriculture
WAB-NET	Western Asia Bat Research Network
WHO	World Health Organization
WMD	Weapons of mass destruction

Executive Summary

The Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs was asked to articulate a 5-year strategic vision for international health security programs and provide findings and recommendations on how to optimize the impact of the Department of Defense (DOD) Biological Threat Reduction Program (BTRP) in fulfilling its biosafety and biosecurity mission. Because BTRP is just one of several U.S. government programs conducting international health security engagement, both the strategic vision and the success of the program rely on coordinating actions with the U.S. government as a whole and with its international partners.

Ongoing revolutions in the life sciences, ease of access to information, rapid transportation of people, and widespread trade in animals and plants all point toward novel threats from new actors, shorter timelines, and less geographic protection. As a result, there are greater risks now than ever before to deployed U.S. military forces, U.S. interests overseas, and to the homeland. International engagement is one of the most cost-effective tools available to prevent adverse events rather than to respond to them after they occur. BTRP's engagements are a critical component of DOD's mission to protect the United States' national security by reducing the likelihood that a natural, accidental, or intentional outbreak from outside of the United States will cause significant harm to the United States or its allies and interests. BTRP should be given as much geographic and programmatic flexibility as possible to understand and address broadly the biosafety and biosecurity needs of its partner nations as the program serves U.S. interests. Mutually beneficial programs increase the likelihood of adoption and sustained ownership by partners, and if the program builds trusted relationships then communication with U.S. partners may continue even after DOD funding ends.

There are advantages to addressing natural, accidental, and intentional incidents or outbreaks as different manifestations of the same family of challenges. They may have ambiguous origins but the capabilities needed to address them overlap. An integrated view of biological threats also prevents bureaucratic boundaries from interfering with partnerships and progress. Furthermore, the overall mission encompasses anticipation, deterrence, prevention, detection, response, mitigation, and recovery.

Action or intervention is possible at every stage and different components of the U.S. government effort (DOD, Department of State, U.S. Agency for International Development, Centers for Disease Control and Prevention (CDC), and others) have advantages in one or another part of the mission or in different partner countries, and so may be better able to intervene and eliminate, reduce, or mitigate risks at the most opportune and effective stage of development in different contexts. The U.S. government will be most effective and efficient if it identifies and prioritizes the threats it wishes to counter and applies resources through the channels that are best poised to address the associated needs. Strong interagency coordination must drive these prioritization and resource-allocation efforts if the needs are to be effectively addressed.

No U.S. government program currently has or should be expected to have the authority or the capability to act on every aspect of the challenge of global health security. To address that challenge, BTRP and other agencies need to be part of a durable interagency coordination mechanism that addresses the full set of biological threats and risks, wherein the agencies best suited to each task are given the necessary tools. An effective mechanism will provide BTRP with greater geographic and programmatic flexibility, will allow BTRP to demonstrate better awareness, prevention of threat development, and more timely response, and will enhance BTRP's ability to partner effectively within DOD, with other U.S. government agencies, with other nations, as well as with nongovernmental organizations (NGOs), the private sector, and academia.

In this report, the committee (See Appendix A for committee member biographies) provides several recommendations for optimizing BTRP success in its current mission and the wider-looking strategic vision proposed by the committee.

A 5-YEAR VISION

In the next 5 years, BTRP, working with its many DOD partners, should encourage, engage, support, and co-lead the U.S. government's development of a durable interagency mechanism to address the full set of biological threats and risks to deployed U.S. military forces, U.S. interests overseas, and to the homeland. This mechanism should seek to intervene and eliminate, reduce, or mitigate risks at the most opportune and effective stage of development and identify the agency or agencies best suited to engage and advance the mission. An effective interagency mechanism will

provide for: (1) greater geographic flexibility; (2) demonstrably better awareness and prevention of threat development; (3) more timely response; and (4) effective partnerships within DOD, with other U.S. government agencies, with other nations, as well as NGOs, the private sector, and academia. Likewise, an effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies.

Embrace an Integrated View of Biological Threats

There are advantages to addressing natural, accidental, and intentional incidents or outbreaks as different manifestations of the same family of challenges. They have functional similarities and common prevention, detection, response, and recovery initiatives. They may have ambiguous origins but the capabilities needed to address them overlap. Ultimately, needs of force protection and national health and safety may be similar or the same in virtually all cases. An integrated view of biological threats prevents bureaucratic boundaries from interfering with partnerships and progress.

Identify Needs and Opportunities

Effective disease surveillance extends beyond detection of disease outbreaks to noting and responding to the conditions that feed and lead to infectious disease risks and threats. Such risks include inadequate domestic diagnostic laboratory infrastructure or poor domestic disease surveillance and public health capabilities, and inadequate subject-matter expertise to prevent and respond to infectious diseases. Effective disease surveillance must also be paired with input and analysis from the security sector and analysis to evaluate opportunities to intervene.

Select International Partners

Foreign governments (hosts and non-hosts), NGOs, the private sector, academia, international organizations, and networks including the Global Health Security Agenda and the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction provide both resource synergies and information networks vital to preparedness and early warning.

Select Partners in the United States

To enhance efficiencies and leverage scarce human and physical resources, BTRP should draw broadly on CDC, DOD, Department of State, Federal Bureau of Investigation, Department of Health and Human Services, Department of Agriculture, NGOs, private sector, academic partners, and subject-matter experts.

Strengthen Relationships and Build Networks Within the Department of Defense

BTRP must establish working relationships within DOD before they are needed. Particularly, regular open and frank communication must be ongoing between BTRP and combatant commands, Office of the Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict Division, Office of the Assistant Secretary of Defense for Health Affairs, the Office of the Secretary of Defense for Policy, and other relevant DOD partners.

Evaluate and Refine

BTRP should regularly evaluate progress and refine its approaches. It should add or subtract partners, create new networks, and share lessons learned and best practices. It should support and value human relationships between experts within the relevant scientific, technical, and health sectors and thoughtfully terminate unproductive partnerships.

In Remembrance

Dr. David Hamburg, 1925-2019
Senator Richard Lugar, 1932-2019

In April 2019 as this National Academies of Sciences, Engineering, and Medicine committee deliberated about the future of the Biological Threat Reduction Program, Dr. David Hamburg and Senator Richard Lugar, two of the architects of the Cooperative Threat Reduction (CTR) Program, passed away. They were among a select group of individuals who, after the dissolution of the Soviet Union in 1991, sought to address the enormous proliferation threats posed by unemployed scientists and unsecured offensive nuclear and chemical weapons, and later, biological weapons (Ford, C., 2016). Informed by years of scholarship on nuclear security and U.S.–Russia relations—such as the International Peace and Security Program established in 1983 by Dr. Hamburg during his time as President of the Carnegie Corporation of New York—security and foreign policy experts saw a clear need to address a significant emerging nonproliferation challenge. This nonproliferation program laid the foundation for CTR, specifically by supporting the Prevention of Proliferation Task Force that produced the seminal report, *Soviet Nuclear Fission: Control of the Nuclear Arsenal in a Disintegrating Soviet Union* (Campbell, 1991), that ultimately led to the development of the Soviet Nuclear Threat Reduction Act of 1991[1] which was co-sponsored by Senator Lugar and Senator Sam Nunn (Rosenberg, 2004). Three years later, in 1994, the CTR Program evolved to include the former Soviet biological weapons program and a decade later global biological threats and risks more broadly, and evolved to focus on reducing threats through partner-country capability building. The reduction of biological threats via the CTR Program has continued ever since, and now engages partners beyond the originally authorized geographic areas of the former Soviet Union.

[1] Soviet Nuclear Threat Reduction Act of 1991, Pub. L. No. 102-228 (1991).

Along with other eminent figures such as Senator Nunn and Secretary of Defense Ashton B. Carter, Dr. Hamburg's and Senator Lugar's vision and leadership in reducing nuclear, chemical, and biological proliferation threats will be felt for years to come as the world grapples with both old and new threats from state-level programs, naturally occurring and accidentally released pathogens, and scientific and technological advances that exacerbate existing risks and/or present new risks.

This committee is honored to contribute to continuing the efforts initiated by Dr. Hamburg, Senator Lugar, and their partners in ensuring a world secure from harms caused by biological agents and malevolent exploitation of peaceful research.

Summary

The Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs was asked to examine U.S. programs that promote international health security, provide the principles that guide such programs for success, and advise the Department of Defense (DOD) Biological Threat Reduction Program (BTRP) on how to coordinate with other agencies and organizations to achieve established goals and ensure that biosafety and biosecurity remain priorities. The committee was also tasked with identifying the most important unaddressed security risks, explaining the overall mission to help align budget and policy priorities, and articulating a 5-year strategic vision for BTRP operating within the larger health security space. This study was sponsored by BTRP, which is part of the Cooperative Threat Reduction (CTR) Program.

CTR's programs were reexamined by Congress around 2007, to account for the changing security environment after national security efforts had expanded to include countering terrorism much more prominently (Benkert, 2007). In 2009, CTR's programs were given broader geographic scope and authority. This enabled particularly the DOD Cooperative Bioengagement Program (the name of BTRP at that time) to work in many more countries, employing a broader set of capacity-building tools to facilitate, for example, biosurveillance and joint research, and to secure storage of clinical samples from affected individuals. This report is another reexamination of DOD's international health security efforts in the context of further evolution of the broader security environment that now incorporates an emphasis on state-level threats.

DOD international engagement in health-related activities has historically resulted in a direct benefit for the United States by advancing knowledge of infectious disease epidemiology and the development of medical countermeasures as well as fostering good will and trust with international partners. As noted, the threats and risks of state-sponsored activity or terrorist misuse of infectious disease and biology for harm have changed over the past 20 years. Nonetheless, the scientist-to-scientist

engagement approach to threat reduction, opening channels of communication around common technical interests in relevant health challenges, continues to be an effective approach to threat reduction and enhanced security for the U.S. military and the homeland. Indeed, international engagement is one of the most cost-effective tools available to prevent adverse events, and prevention is much more cost-effective than responding to an outbreak. By providing value to host countries' efforts to diminish their risk of serious outbreaks, enhance disease surveillance, and increase the speed of response and averting the varied consequences, bioengagement also reduces the risk to the United States. In this context, the BTRP mission aligns with the National Defense Strategy of 2018, which is the current operating framework for all DOD programs, including programs that address biological threats. Beyond the National Defense Strategy (2018), the National Security Strategy (2019), National Strategy for Countering Weapons of Mass Destruction Terrorism (2018), National Biodefense Strategy (2018), and Global Health Security Strategy (2019) all contribute to BTRP's operating framework for preventing and detecting biological threats. Furthermore, the Global Health Security Strategy outlines roles and responsibilities for DOD, which include scientific engagement and threat reduction. Because of the evolving landscape of biological threats, the broader set of tools used by BTRP is needed now more than ever, especially as BTRP is well suited to promote norms against theft and malicious exploitation of peaceful biological sciences, and against the development of offensive biological weapons capabilities.

AMBIGUITIES AND FUNCTIONAL SIMILARITIES MAKE NATURAL, ACCIDENTAL, AND INTENTIONAL THREATS DIFFERENT MANIFESTATIONS OF THE SAME FAMILY OF CHALLENGES

The National Security Strategy, the National Biodefense Strategy, and the Global Health Security Strategy include within the scope of biological threats naturally occurring, accidental, and intentional biological incidents, and also include the concept of interlinked human, animal, plant, and environmental health (called One Health). BTRP's mission in addressing these threats is difficult because the threats and the social, political, and physical environments in which they arise are increasingly

changing at a faster rate than over the previous decades of the program's history.

Greater global connectivity increases the ease of transmission and broadens the reach of infection, which in turn demands faster, more effective response. Given the speed of travel around the globe, an individual in one country with a highly communicable disease can arrive in any other country in approximately 24 hours or less. Outbreak timelines are being compressed and as a result so is the time available to plan and implement an effective response to an outbreak.

Global trends facilitate potential misuse of biology, including increased access to biological information, new techniques to manipulate pathogens that do not require sophisticated or expensive technology, and willingness to breach norms against misuse. Easier access to relevant knowledge and much more effective tools for previously unimagined biological research and technology capabilities can also set the stage for accidents. Methods for engineering and synthesizing microbial pathogens have already enabled competent molecular biologists to construct viable infectious pathogens simply from genetic sequence information. Digitalization of biology and design of new technologies to manipulate biological materials challenge current biological governance and oversight structures within and outside the United States. Threats are also increasing due to the development of more numerous and effective vectors for pathogen transmission, including in some cases, an increase in the number, type, and composition of vectors and an increase in the number, types, and characteristics of strains that can infect those vectors, as well as reduced time needed to move biological threats across vast geographical areas. The changing climate has, and will continue to have, significant effects on outbreak location, severity, and incidence rate, in part driven by alterations in the habitats and range of insect and animal pathogen vectors and proximity to wildlife. These trends are accelerating as science and modern transportation advance and move at greater speed.

While the threat of intentional use of biological weapons by state or non-state entities has not diminished, the threat from natural events currently dominates the infectious disease landscape. But the origins of outbreaks may be ambiguous. The boundaries between risk and threat continue to blur and converge at a quickening pace. As the National Biodefense Strategy of 2018 states,

> Biological threats originate from multiple sources. The United States will include, within the scope of biodefense, not just countering deliberate biological threats, but also

> the threats that stem from naturally occurring and accidental outbreaks. This approach will allow the United States Government to fully utilize, integrate, and coordinate the biodefense enterprise and ensure the most efficient use of all biodefense assets. (2018, p.3)

This suggests the need for more common strategies to prevent both risks and threats, and to be prepared to act rapidly and effectively when the need arises. The consequences of not doing so can be great, as we have seen in West Africa from 2014 to 2016, and currently in the Democratic Republic of the Congo. Naturally occurring disease can seriously destabilize countries and regions, occurring as a "perfect storm" in settings in which civil society is fragmented, authority is fragile, and resources to address emerging outbreaks are limited. Intentional introduction of disease agents can have a similarly destabilizing effect, and may be even more challenging if they have been deliberately modified to be more destructive and/or to resist existing medical countermeasures.

The committee finds that in addition to having similar consequences, natural, accidental, and intentional incidents or outbreaks have functional similarities and there are advantages to addressing them as different manifestations of the same family of challenges. They may have ambiguous origins but the capabilities needed to address them overlap, including common prevention, detection, response, and recovery initiatives. Ultimately, many of the needs of force protection and national healthcare infrastructure for response to infectious disease threats and safety may be similar or the same in virtually all cases. An integrated view of biological threats also prevents bureaucratic boundaries from interfering with partnerships and progress.

DOD, including the Defense Threat Reduction Agency (DTRA) and BTRP, is aware of these realities. While the existing norms and treaty commitments against the use of biological weapons have not been breached on a large scale in recent decades, there are clear indications that these moderating forces are strained.

How can the United States be prepared to anticipate and respond to the myriad of potential existing and emerging threats? How can the United States and the international community receive early warnings or even be cognizant of developing threats? What parts of the U.S. government, and which department or entity within the multiple components of government, are capable, prepared, and willing to address these threats? The committee believes it will take many U.S. government programs

working together with other governments and nongovernmental partners to address these challenges. DOD has an essential role to play in that effort.

A DIVERSE TEAM OF ORGANIZATIONS IS NEEDED TO ADDRESS THE COMPLEX THREAT LANDSCAPE

The overall mission of addressing biological threats encompasses anticipation, deterrence, prevention, detection, response, mitigation, and recovery. Action or intervention is possible at every stage, and different components of the U.S. government effort have advantages in one or another part of the mission, or in different partner countries, and so may be better able to intervene and eliminate, reduce, or mitigate risks at the most opportune and effective stage of development in different contexts. For example, the Centers for Disease Control and Prevention (CDC), the U.S. Agency for International Development (USAID), military medical units, the World Health Organization, the Global Health Security Agenda (GHSA), the United Nations Food and Agriculture Organization, World Organisation for Animal Health, the African CDC, Pan American Health Organization, and academic researchers each have unique capabilities and relationships. GHSA, which is described in the section beginning on page 39, is a group of countries, international organizations, nongovernmental organizations (NGOs), and private-sector companies that have come together to advance a world safe and secure from infectious disease threats by making new, concrete commitments to elevate global health security as a national level priority (GHSA, 2019). Because the international landscape for addressing biological threats involves many nongovernmental, governmental, and intergovernmental actors, effective coordination and communication are critical to ensuring success of biological threat reduction programs (see Appendix C).

The U.S. government will be most effective and efficient if it identifies and prioritizes the threats it wishes to counter and applies resources through the channels that are best poised to address the associated needs. Strong interagency coordination must drive these prioritization and resource allocation efforts if the needs are to be addressed.

No U.S. government program currently has or should be expected to have the authority or the capability to act on every aspect of the global health security challenge; but today, organizational divisions and boundaries interfere with realizing improvements in efficiency and cost-effectiveness. To address that problem, BTRP needs to be part of a durable

interagency coordination mechanism that addresses the full set of biological threats and risks, wherein the agencies best suited to each task are given the necessary tools. An effective mechanism will have greater geographic and programmatic flexibility and will demonstrate better awareness and prevention of threat development, and more timely response, and will partner effectively within DOD, with other U.S. government agencies, and with other nations, as well as with NGOs, the private sector, and academia. Likewise, an effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies.

DOD Has Unique Capabilities to Address Evolving Biological Threats

As noted, DOD is not the only or even the central mission holder in an integrated effort to address biological threats. However, DOD's programs provide a security focus, while most other U.S. government departments and agencies involved in global health security programs are primarily focused on health and biosafety challenges, and less on biosecurity. Moreover, in contrast to CDC and USAID programs, the mission of DOD's (but not necessarily the principle mission of BTRP's) programs is first and foremost to support deployed U.S. military forces, U.S. interests overseas, and the homeland (Philpott, 2019).

DOD has long held essential, interwoven parts of the bioengagement mission, ranging from force protection to protection of U.S. civilians overseas, to protection of the homeland, to prevention of indirect harm to the United States and its interests that may result from disruption of critical functions, such as transportation and trade. International bioengagement by DOD contributes to military readiness, planning, and force protection important for U.S. national security. For example, the U.S. Army and U.S. Navy overseas laboratories provide important information on endemic and emerging outbreaks and have helped to identify and validate medical countermeasures or prevention strategies, while promoting and sustaining the critical personal relationships of trust where they operate. These relationships are essential for the necessary transparent exchange of information and insight. DOD's efforts can be aided by working with international organizations, networks, consortia, and the public/private sector at times when partner countries are skeptical of the U.S. military presence. In certain areas of the world, and in certain contexts, partner

countries may be more comfortable with United Nations-based agencies or BTRP-type organizations than with DOD directly.

BTRP plays an important role in DOD's engagement to reduce biological threats, and can play an even greater role. BTRP establishes critical lines of communication about biological threats, from any origin, with foreign governments and responsible individuals; supports operational and situational awareness where it can operate; invests in building capacity that improves biosecurity; and generates information that ultimately provides additional security to the United States. The kind of engagement BTRP conducts promotes individual relationships of trust. Understanding and trust between technically competent individuals, particularly over the long term, contributes further to trust and understanding among leaders in ministries and governments. Where trust exists, transparency increases. BTRP is perfectly placed within DOD to engage with global partners to create the necessary common ground to address biosafety and biosecurity priorities. At the same time, for no added cost, cultures of trust help to stabilize nations and regions, making them less welcome areas of operation for sub-state groups or individuals with ill intent. While the important role BTRP plays may be too far in the background to be recognized by higher-level military and political leadership, it is highly effective, particularly relative to its very small portion of the DOD budget.

BTRP cannot do it all. Resources are limited, and BTRP as well as other partners must address the perennial mandate to produce the best outcome as efficiently as possible. Not only is it right to use funds efficiently and effectively, it will also strengthen BTRP. By building sound working relationships with other U.S. government, NGO, and global networks of experts, BTRP can leverage its resources more effectively and be better attuned to threats, risks, and even successes around the world. Common interests with potential partners abroad may include epidemiology, genetic engineering, point-of-care or other field-enabled diagnostic methodologies, and disease surveillance and response. Working together on these common interests may be of direct benefit to the host country (whether those partners are from the country's military or other relevant parts of government) as well as to the United States. Recognizing differing cultural contexts and aligning interests, resources, and outcomes can achieve greater effectiveness for all partners.

THE NEED TO ANTICIPATE, DETECT, AND RESPOND RAPIDLY TO THREATS

To address the family of natural, accidental, and intentional incidents effectively and efficiently, the U.S. government must be able to anticipate, detect, and respond rapidly to these threats. This begins with identifying risk factors, needs, and opportunities. Disease surveillance extends beyond detection of disease outbreaks to noting and responding to the conditions that feed and lead to infectious disease risks and threats. For example, inadequate domestic clinical and research laboratory infrastructure or poor domestic public healthcare infrastructure, and inadequate numbers of subject-matter experts to prevent and respond to infectious diseases may allow an outbreak to occur where it may have otherwise been preventable. Effective disease surveillance must also be paired with sustained analytical efforts, allowing for the identification of opportunities to guide intervention prior to an outbreak.

The size of the global workforce with expertise in enormously powerful new biotech capabilities has increased greatly, raising new concerns regarding individual or small group attempts to create new deadly or drug-resistant strains of pathogens. Advances in science have increased the ability to manipulate virulence and/or create drug- and vaccine resistance in an unsophisticated laboratory environment in almost any country. Timely information on such dangerous pursuits, gained from a network of trusted international partners, is now more valuable than ever.

Cooperative programs are likely to function most effectively when personal engagement has occurred and the people involved from the relevant agencies and organizations know and trust one another before a biological crisis occurs. BTRP's history provides positive examples of such advanced engagement that allowed for rapid response that would otherwise have been unavailable (e.g., early response to the 2014 Ebola outbreak in Guinea) (U.S. DOD, 2015).

Success at anticipating and responding to perceived threats or opportunities is varied and sometimes imprecise. Cases in which it is feasible to anticipate and identify a specific need, and in which one can, in advance of an incident, identify the specific biosecurity consequences of not engaging are rare. However, there are also cases when analysts have reason to believe that an adverse event is likely to emerge in a country or a small region, even if they do not know exactly what it will be and when it will occur. The important counterthreat action in such cases is to

establish a flexible capability to detect and respond quickly when something does arise.

BTRP's resources are relatively small and have been shrinking in recent years (see Appendix B for recent funding levels for BTRP). For this, and other geopolitical and epidemiological reasons, BTRP should not engage an international state or partner just because it can; rather, such engagement should be informed, strategic, and likely to yield benefits. For BTRP to take the "strategic view" will require careful articulation of why engagement is required, where it would be required, and with what resources, including human resources.

THE NEED FOR GEOGRAPHIC AND PROGRAMMATIC FLEXIBILITY

Geographic flexibility is essential for effective and efficient implementation of bioengagement efforts. More rapid evolution and emergence of threats from infectious disease, and increased bureaucratic complexity at DOD, as at any large organization, led the committee to recommend greater geographic and programmatic flexibility for BTRP. This would enable BTRP to engage in a geographic region before a situation becomes critical and a response much more expensive—and sometimes less effective—than it would have been years or even months earlier.

As with the flexibility to engage around the world where biorisks and biothreats currently exist or are anticipated to emerge geographically, BTRP would be well positioned to address the full range of challenges (natural, accidental, intentional) if it also had the programmatic flexibility to address risks that may emerge beyond the boundaries of traditional disciplinary research. Transdisciplinary and interdisciplinary research can generate new scientific findings that are less well understood from the perspective of potential biothreats and biorisks. Because engagements are with humans, not technologies or pathogens, BTRP should be proactively communicating with its counterparts in engaged countries and have the programmatic flexibility to undertake broadly relevant activities in true partnership with their host-country colleagues. This will invariably result in greater relevance of the program with the engaged country and its personnel, and increase the likelihood of success and thus sustainability with domestic personnel and resources. Mutually beneficial programs are the only ones that will be sustainable for the long term.

BTRP evaluates progress in its engagements on a regular basis. If this is part of a larger DOD and interagency evaluation of efforts in a country or region, then these evaluations afford opportunities to refine the approach to engagement. This could mean modifying BTRP staffing needs, reworking the composition of partners, revising their roles, creating new networks, and sharing lessons learned and best practices. It may also prompt the interagency or the programs to thoughtfully terminate unproductive partnerships. Since it is very difficult to scale the success of BTRP's engagements, just hiring contractors and providing a project budget will not necessarily lead to proportional gains in success.

To allow for the greatest return on the investments made with increased flexibility, BTRP would benefit from an increased number of technical experts in the program. With more technical experts, decisions on how to best support countries as they strengthen their capabilities to detect, diagnose, and report on diseases can be more effective. It takes experience to discern what is really required to help a country partner, particularly when there are a variety of requests and solutions offered from multiple directions.

THE IMPORTANCE OF RECRUITING AND RETAINING THE MOST EFFECTIVE BTRP PROFESSIONALS

Connections to people and their institutions are the common thread through all of BTRP's efforts, whether for biosurveillance, establishing norms, building laboratory capacity, strengthening biosafety and biosecurity rules and practices, or enabling rapid and effective response. While cooperative threat reduction programs have focused on technical solutions for the past 30 years, with some significant success, it is also clear that human relationships of trust developed through long-term engagements contribute both directly and indirectly to national security, and can even be deterrents to aberrant behavior.

When an outbreak occurs, such relationships can cut through the chaos of the moment and streamline the rapid implementation of a healthcare and public health response. Further, trusted relationships can help experts who have previously worked together to potentially obtain and secure samples of infectious diseases, making it markedly more likely that clinical research and trials of medical countermeasures or vaccines can be approved and implemented in time to gather sufficient information to assess safety and efficacy of the modality being studied.

Global networks of individuals and organizations with a common interest in biosecurity threats and risk reduction can become powerful tools for communication, thought leadership, security, and stability. Multilateral networks at the intergovernmental level allow people to work together and leverage investments in funding, which, in turn, foster more opportunities for information exchange, development of personal relationships, and appropriate action. One such effort is the successful implementation of the networking concepts under GHSA. BTRP has supported some of the biosafety/biosecurity components of GHSA and thereby has extended the impact of its own resources, expanded its influence, and promoted an improvement in functional capacity of the involved nations in a strategic manner. While less structured, another such effort in which BTRP has been involved is One Health, which encompasses an integrated approach linking human, animal, plant, and environmental health (as described in the section beginning on page 73).

By enabling BTRP to more effectively engage globally and be proactive in relevant activities, BTRP can provide DOD leadership with a perspective on biosecurity and disease threats from the ground level up. To the extent that BTRP can promote such professional networks among military and civilian scientists, public health, animal health, and plant health practitioners from the United States and partner countries, the benefits of engagement will be perceived more rapidly. Protection of U.S. military forces or U.S. citizens in a country at risk of an outbreak is enhanced when collaborations and trained healthcare workers are in place before cases are discovered. This report provides examples of such successes.

Essential linkages between BTRP and partners abroad require greater involvement of BTRP staff rather than through the contract process with non-DOD experts. Understanding and implementing mission-critical initiatives can be difficult to transfer to external contractors. Bringing more human resources into BTRP itself can allow for selection of staff based on critical skills necessary to build relationships. These skills include the ability to listen attentively and understand the needs, thoughts, culture, and history of the partners, even when they differ from U.S. biosecurity perspectives.

THE IMPORTANCE OF BROADER AWARENESS ABOUT BTRP'S EXPERIENCE AND EXPERTISE

As described throughout this report, BTRP has a broad portfolio of bioengagement projects and activities to advance biosecurity across the world as a means of protecting deployed U.S. military forces, U.S. interests overseas, and the homeland. BTRP has gained a great deal of experience and expertise working in a wide range of countries and regions on a host of critical issues. The depth and scope of this experience, however, is not well known within DOD or across the U.S. government, including key congressional committees, and among international partners. Likewise, the range of skills and assets that BTRP can contribute to addressing extant and evolving biorisks and biothreats is also not as well known as it should be. To maximally contribute to U.S. and international efforts to reduce risks from natural, accidental, or intentional outbreaks and other bioincidents, BTRP must be allowed the resources and the platforms to articulate its successes. Further, BTRP must be encouraged to offer its expertise and resources to other partners within and beyond DOD that may be addressing current or anticipated challenges.

BTRP must establish working relationships within DOD before they are needed. Particularly, regular open and frank communication must be ongoing between BTRP and combatant commands; the Office of the Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict; Office of the Assistant Secretary of Defense for Health Affairs; the Office of the Secretary of Defense for Policy; various military medical research and development laboratories (to include sites Outside Contiguous United States); and other relevant DOD partners. If BTRP can establish these partnerships, including by sharing its successes and available expertise more broadly, it will further broaden the base of understanding about BTRP and its mission and programs.

The wide range of people and government, nongovernment, and commercial organizations that are involved in one or more aspect of addressing biosafety and biosecurity requires more diligent awareness of others' programs and initiatives, their areas of geographic and substantive engagement, and where goals and objectives of different groups and organizations may overlap or diverge. As a result, to increase the positive outcomes of its work, BTRP must be present and active at meetings and conferences where other potential partners, especially those from partner countries, are in attendance. Through such outreach and networking, BTRP can grow its awareness and understanding of others' work, and

increase its opportunities for establishing and maintaining trusted relationships.

During the early days of the Nunn-Lugar CTR Program in the former Soviet Union, a small senior advisory group was used very effectively by DTRA, not only to assist with scientific reviews of projects under consideration for U.S. funding, but also, importantly, to advocate for the CTR Program. A group of senior experts, including non-U.S.-based experts with relevant experience, even serving on a volunteer basis, could add a robust foundation to BTRP's efforts, increase the sustainability of proposed approaches, and improve international perceptions and acceptance of BTRP. One potentially important contribution of such a group could be helping to link BTRP professionals, BTRP-supported experts, and other partners together through regional and global networks. Participation in science conferences, introduction of experts across regions and/or areas of scientific expertise, and exchanges of scientific publications and visits may also enhance BTRP's impact.

THE STRATEGIC VISION FOR BTRP

Over the next 5 years, DOD/BTRP should encourage, engage, support, and help drive the U.S. government's development of a durable interagency mechanism that draws on military, medical, diplomatic, and other expertise to address the full set of biological threats and risks (human, animal, plant) to deployed U.S. military forces, U.S. interests abroad, and the homeland, seeking to intervene and eliminate, reduce, or mitigate threats at the most opportune and effective stage of development. An effective mechanism will have greater geographic and programmatic flexibility and communication links; will demonstrate better awareness and prevention of threat development and more timely response; and will partner effectively within DOD, with other U.S. government agencies, as well as with other nations, NGOs, the private sector, and academia. Likewise, an effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies.

With the rapid pace of change in the biosciences, a span of 5 years can seem like an even shorter period. Indeed, anticipation of threats that may emerge from natural occurrences, accidental incidents, or intentional actions may be considered an impossible exercise. Yet, building on two decades of experience and expertise by implementing the pillars of the proposed strategic vision articulated here, DOD's BTRP is well poised to

seize opportunities prior to events and respond efficiently and effectively should an event occur, thereby improving the biosecurity of deployed U.S. service personnel and civilians abroad, and strengthening security of the United States itself.

The committee's recommendations, which are highlighted in Chapter 6 of this report, are as follows:

RECOMMENDATION 1: The Office of the Secretary of Defense for Policy should seek a global determination from Congress, which would give BTRP authority and flexibility to work when and where national biosecurity needs–and diplomatic opportunities–are identified or reasonably anticipated.

RECOMMENDATION 2: DTRA should give BTRP as much programmatic flexibility as possible to understand and broadly address the current and anticipated biosecurity and biosafety needs of each country where it engages. The needs may be underlying biosecurity challenges, so the actions may be one step removed from traditional activities, such as building in-country and regional networks, organizing focused scientific meetings, and developing emerging leaders.

RECOMMENDATION 3: BTRP should select technical engagement professionals to represent the U.S. government in these important engagements with consideration of their communication, interpersonal, and diplomatic skills and, as necessary, provide training in diplomacy and on the political contexts in which they work to supplement their necessary science backgrounds.

RECOMMENDATION 4: The Office of the Secretary of Defense for Policy together with BTRP should monitor and identify likely future potential infectious disease vulnerabilities in the changing threat landscape. As a part of this forward assessment process, BTRP should identify opportunities to bolster local partner countries' capabilities to detect aberrations from the norm early in an event or outbreak in order to better anticipate events through improved disease surveillance and better analytical capacity.

RECOMMENDATION 5: BTRP should focus more attention and emphasis on linking experts inside and outside of BTRP, including leaders in partner countries, into regional and global networks to further BTRP's mission goals and enhance its awareness of technical and epidemiological developments. These include extant threats to political, social, and economic stability and long-term partner government sustainability in the context of outbreaks of emerging infectious diseases in humans, food animals, or crops in order to improve biosecurity broadly in vulnerable and at-risk partner countries.

RECOMMENDATION 6: BTRP should acquire greater scientific expertise on its staff and proactively engage with the broader scientific community to better understand technical and scientific developments in emerging infectious diseases. This engagement can be accomplished by some combination of participating in important scientific meetings, contracting with scientific organizations, establishing a scientific advisory group, and/or working with individual experts. The goal is to access expertise and experience working internationally on topics of biosafety and biosecurity, epidemiology, disease surveillance, security, biotechnology, industry, and related topics. These efforts will strengthen BTRP's ability to meet its responsibilities and obligations, and enhance its effectiveness.

RECOMMENDATION 7a: BTRP should establish closer working relationships with the combatant commands, Army Futures Command, Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict, and the Office of the Assistant Secretary of Defense for Health Affairs for coordination and prioritization of limited resources, and the service laboratories as well as relevant interagency partners such as the Centers for Disease Control and Prevention and the National Institutes of Health, sharing its unique capabilities and insights about biothreats. Through effective synchronization, these entities can assist one another to more effectively protect the force and the nation.

RECOMMENDATION 7b: Over the next 5 years, BTRP, working with its many DOD partners, should encourage,

engage, support, co-lead, and help drive the U.S. government's development of a durable interagency mechanism that draws on medical, military, diplomatic, scientific, and other expertise to address natural, accidental, and intentional biological threats and risks to the deployed force and to the nation. An effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies. Likewise, it will allow for greater geographic flexibility, more effective communication links, and will demonstrate better awareness and prevention of threat development, and more timely response. To enhance overall coordination, BTRP should partner effectively within DOD, with other U.S. government agencies, with other nations, as well as with NGOs, the private sector, and academia.

1

The History of Cooperative Threat Reduction (1991-2018)

KEY MESSAGES

- International engagement in health-related activities by the Department of Defense (DOD) has historically resulted in direct benefit for the United States by advancing knowledge of infectious disease epidemiology and the development of medical countermeasures as well as fostering good will and trust with international partners.
- With the dissolution of the Soviet Union, both its biological weapons infrastructure and its highly experienced scientists working on offensive programs were vulnerable to exploitation by other malevolent nations or terrorist groups. The Nunn-Lugar Cooperative Threat Reduction (CTR) Program, based on scientist-to-scientist technical engagement, reduced the risk of proliferation when political negotiations and inspections failed.
- The threats and risks of state-sponsored or terrorist misuse of biology have changed over the past 20 years, but the scientist-to-scientist engagement approach to threat reduction, opening channels of communication around common technical interests in relevant health challenges, continues to be effective and has enhanced security for the U.S. military forces, U.S. interests overseas, and the homeland.

STUDY BACKGROUND

The National Academies of Sciences, Engineering, and Medicine (NASEM) Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs was tasked with examining the Biological Threat Reduction Program (BTRP), a

component of the CTR Program within DOD's Defense Threat Reduction Agency (DTRA), and other domestic and international efforts with similar health security goals. The committee has explored the history of the CTR Program, often called the Nunn-Lugar Program after the two sponsors of the 1991 legislation that established it, and the evolution of the biological threat reduction component and biological threats of concern. The goal of this exploration was the development of a 5-year strategic vision for BTRP's work within the larger health security space to promote biosafety, biosecurity, disease surveillance, health security, and biorisk management with partner countries, and to make recommendations to ensure this vision can be achieved. (See Box 1-1 for the statement of task guiding the committee's work and note that although it includes "international health security programs and organizations with missions to enhance health security," the sole sponsor of this study was BTRP.) When a federal government sponsor requests a study, the National Academies typically provides recommendations to that sponsor and not other parties, but a strategic vision for BTRP must include its partners in the U.S. government and beyond. The committee therefore makes recommendations primarily to BTRP and notes what the program needs from its partners to succeed.

To carry out the study, the committee held a series of information-gathering meetings, requested data and reports from BTRP, conducted an extensive literature review; sent committee members and staff to others' meetings, including the Fifth Global Health Security Agenda (GHSA) Ministerial Meeting in Bali, Indonesia; and drew on committee members' experience and expertise. At the information-gathering sessions, the committee heard from relevant U.S. government programs—BTRP, the Office of the Under Secretary of Defense for Policy, the Department of State Biosecurity Engagement Program (BEP), the Centers for Disease Control and Prevention (CDC), the Department of Health and Human Services (HHS)—contractors and nongovernmental organizations (NGOs) that work on biosafety and biosecurity and global health security more broadly with other countries, other countries' programs (e.g., the United Kingdom and Finland), international organizations (World Health Organization [WHO], World Organisation for Animal Health [OIE]), and academic experts.

BOX 1-1
Statement of Task

An ad hoc committee will examine international health security programs and organizations with missions to enhance health security by promoting biosafety, biosecurity, disease surveillance, health security, and biorisk management with foreign partner countries. By engaging experts from countries that actively sponsor such work and building on past work that established overall goals (such as Global Health Security Agenda action package 5-year targets), the study committee will address the following questions:

1. What principles guide successful health security programs?

2. How can the programs around the world better coordinate and align actions with established targets to ensure that efforts are not duplicated unnecessarily and opportunities are not missed because of gaps in authorities and program practices?

3. What steps can be taken to ensure that health security programs continue to prioritize biosafety and biosecurity over the next 5 years?

4. What gaps are most important for the international community to address to advance global health security over the next 5 years?

5. How should the overall mission be integrated to make it easier to make budget priorities match policy priorities?

In its report, the study committee will articulate a 5-year strategic vision for health security and provide findings and recommendations to address these questions.

In its discussions, it became clear to the committee that different groups use the same terms differently. Threats and risks, for example, are interchangeable for one group and distinct but related for another. To make our report clearer, we list here several common terms with an explanation of our usage of those terms.

- **Bioengagement**: the engagement of specialists on issues associated with biology, life sciences, biotechnology, and/or any other related field
- **Biothreat**: the use of biology, life sciences, biotechnology, and/or any other related field in a way that is highly likely to cause harm or danger

- **Biorisk**: any aspect of biology, life sciences, biotechnology, and/or any other related field that exposes one to harm or danger
- **Deterrence**: creating a sense of doubt or fear of consequences as a means of discouraging an action or event
- **Dissuasion**: efforts made to persuade an individual (or individuals) not to take a particular course of action
- **Global determination**: the legal provision by Congress to allow BTRP to operate in any country and/or region of the world without additional authorization or approval
- **Health security**: ensuring the safe and secure provision of healthcare for animals and humans
- **Risk**: potential for an outcome that exposes one to harm or danger
- **Threat**: a natural or human-generated occurrence highly likely to cause harm or danger

OVERVIEW OF THE EVOLUTION OF COOPERATIVE THREAT REDUCTION

This chapter provides an overview of the evolution of cooperative threat reduction activities, beginning with programs established to respond to the dissolution of the Soviet Union, continuing to the broader range of today's U.S. programs and related international activities. This report has adopted the following terms to refer to various programs: The Department of Defense Cooperative Threat Reduction Program is referred to as DOD CTR, and the broader U.S. government CTR programs that span multiple departments and agencies are referred to as U.S. government CTR.

The modern U.S. concept of CTR originated in November 1991 with the passing of the Nunn-Lugar Act (the Soviet Nuclear Threat Reduction Act of 1991), with an initial focus on securing and dismantling nuclear weapons and missile technology in the former Soviet Union (FSU).[1] The stated purpose of the act at the time was to secure and dismantle weapons of mass destruction and their associated infrastructure in FSU states (Woolf, 2002). Soon after passage of the Nunn-Lugar Act it was recognized that biological weapons and related components and expertise represented serious threats also in great need of threat reduction programs. The senators' timing was nearly perfect because this new concept and resulting approach to threat reduction, based on building understanding

[1] Soviet Nuclear Threat Reduction Act of 1991, Pub. L. No. 102-228 (1991).

and ultimately openness and trust, were already accepted when the Trilateral Agreement, which was signed in September 1992 by the United States, the United Kingdom, and the Russian Federation in an attempt to cooperatively halt or demilitarize the massive Soviet biological weapons program, failed for lack of cooperation and trust among parties. The Trilateral Agreement was structured around a security-centric approach to identifying treaty contraventions and negotiating the dismantlement of the Russian bioweapons program. The Nunn-Lugar legislation called for a cooperative science-based approach to disarmament. Early efforts in biological threat reduction under the Nunn-Lugar CTR Program intended to redirect scientists to peaceful activities, and to discourage them from moving to other countries along with their lethal technologies and tacit knowledge.

Pre-History of International Cooperative Threat Reduction Engagement History

DOD engaged in bioweapons research from 1943 until 1969 (Carus, 2017), and formally rescinded the program by signing and ratifying the Biological Weapons Convention in 1972 and 1975, respectively (UN, 2020c). DOD had also sponsored very effective small, bilateral, cooperative initiatives targeting the threats of naturally occurring infectious disease around the globe that could affect U.S. military forces serving in these regions but were surely a concern for the host country population as well. These initiatives include several laboratories focused on locally occurring and emerging infectious diseases in various parts of the world supported by the Naval Medical Research Command, and consisting of Naval Medical Research Units (NAMRUs) (U.S. Navy, 2020a):

- Southeast Asia (NAMRU-2, 1944 to present)
- Egypt (NAMRU-3, 1942 to present)
- Ethiopia (NAMRU-5, 1965 to 1977)
- Peru (NAMRU-6, 1983 to present)

The U.S. Army Medical Research and Materiel Command/Walter Reed Army Institute for Research sponsored U.S. Army Medical Research Units (USAMRUs) in the following countries (U.S. Army, 2008, 2019, 2020):

- Kenya (USAMRU-K, 1969 to present)
- Malaysia (USAMRU-M, 1948 to 1989)

- The Republic of Georgia (USAMRU-G, 2014 to present)
- The Armed Forces Research Institute of Medical Sciences in Thailand (1958 to present)

These units have served as valuable training grounds for military medical research as well as military and civilian scientists from the host country, while fostering strong and lasting personal relationships of trust between local scientists and U.S. military and civilian scientists. The infrastructure and sustained focus on communicable diseases has allowed a large cadre of experts to rapidly address emerging infectious diseases as they have become more common and better recognized as threats to human health.

In a 2011 assessment of the scientific contributions of these overseas laboratories, Peake and colleagues noted that these laboratories "bring broad global health benefits beyond their immediate mission of force health protection." Scientists at these labs focus on developing products such as prophylactic and therapeutic drugs, vaccines, diagnostics, and scientific knowledge. Their continued "ability to conduct Phase III clinical trials in indigenous areas result in medical advances that not only save the lives of men and women in uniform, but also have dramatic health benefits for all populations vulnerable to neglected diseases. In many important instances, the DOD laboratories' findings have helped mitigate or eradicate diseases on a global scale, as well as have identified or diagnosed previously unknown pathogens" (Peake et al., 2011, p. 2).

An example of the effectiveness and trusting relationships built through these laboratories is also found in the history of NAMRU-3 when, in 1967, laboratory staff were allowed to stay through Egypt's 1967 Arab–Israeli War with Israel and during a 7-year hiatus in diplomatic relations between Egypt and the United States, while all other similar foreign organizations were forced to leave (Hibbs, 1993). These laboratories have helped establish and stabilize infectious disease research capabilities worldwide and have provided the United States with security-related good will around the globe at relatively very little cost and without making security the focus of their efforts. Important scientific discoveries have emerged from these laboratories as a further return on the investment: for example, the early studies on the treatment of scrub typhus with chloramphenicol in Malaysia in 1948 (U.S. Army, 2008), or the treatment of cholera and the development of oral rehydration therapy at NAMRU-2 in Taiwan (Cash, 1987), and NAMRU-3 in the late 1940s and early 1960s, respectively (U.S. Army, 2008, 2019, 2020).

THE ORIGINS OF THE BIOLOGICAL THREAT REDUCTION PROGRAM (CTR 1.0)

The dissolution of the Soviet Union raised concerns regarding the potential loss and vulnerability of its tens of thousands of nuclear weapons; tens of thousands of metric tons of stockpiled chemical agents; and a massive biological weapons research, development, and production infrastructure. Hence, the initial focus of CTR was to assist newly independent states of the FSU to safely and securely dismantle weapons systems, particularly at sites where nuclear weapons were located. The Nunn-Lugar Act defined three primary objectives:

1. Assist FSU states to destroy nuclear, chemical, and other weapons;
2. Transport, store, disable, and safeguard weapons in connection with their destruction; and
3. Establish verifiable safeguards against the proliferation of such weapons.[2]

In 1992, the mission was expanded to include dismantling delivery systems for these weapons, including missiles and missile launchers, destroying destabilizing conventional weapons, preventing the diversion of weapons-related scientific expertise, facilitating demilitarization of defense industries and converting military capabilities and technologies, and expanding military-to-military and defense contacts (Lederberg et al., 1992; NAS, 2009).[3] The Trilateral Agreement, signed in the same year by

[2] Soviet Nuclear Threat Reduction Act of 1991, Pub. L. No. 102-228 (1991).

[3] Coincidentally, also in 1992, the Institute of Medicine published what has proven to be a ground-breaking report, *Emerging Infectious Diseases: Microbial Threats to Health in the United States*, which documented the increasing frequency of outbreaks due to newly identified pathogens or known pathogens with new properties or outbreak potential (IOM, 1992). A few years later, a Presidential Decision Directive (NSTC-7) was issued and, noting the limited worldwide disease surveillance and preparedness for emerging infectious diseases, called on DOD to improve worldwide emerging infectious disease surveillance and preparedness (NSTC, 1997). The result was the DOD Global Emerging Infections Surveillance and Response System (DOD-GEIS), which expanded the mission of the medical research components of DOD to include global disease surveillance. Over the subsequent two decades, GEIS has coordinated a disease surveillance and response network through collaborations involving the U.S. military overseas laboratories, partners in countries around the world, laboratory capacity-building initiatives, and epidemiologic training

the United States, the United Kingdom, and the Russian Federation, was an attempt to halt the former Soviet biological weapons program through an effort to negotiate, inspect, and ensure that the former Soviet biological weapons program—consisting of three Russian Ministry of Defense laboratories and some 18 Biopreparat laboratories and factories—had ended. However, when the Trilateral Agreement team arrived in Russia in 1994, the Russian Ministry of Defense funding for the biological warfare laboratories and production facilities had ceased and staff salaries were no longer being paid. As a consequence, employees at the multiple former biological weapon facilities operated by Biopreparat, the non-military part of the program, were increasingly desperate to support themselves and their families (ACDA, 1994; Chevrier and Henry, 1998). To provide support to these individuals, the International Science and Technology Center (ISTC) was established in Moscow in 1994 under an agreement with the Russian Federation. ISTC became the interlocutor for the CTR Program and similar programs of several other countries, and was able to provide money for assistance and collaborative civilian technical research and training to these former biological weapons experts, while avoiding taxation by the Russian or other recipient governments. The United States and other governments insisted on the ISTC arrangement so that the Russian government would not withhold a portion of the funds meant to support struggling scientists and engineers. Thousands of Russian life scientists, if they qualified as former weaponeers, participated in joint projects related to laboratory safety, security, and quality enhancement; basic infectious disease research; development of medical countermeasures and diagnostics for endemic and reemerging diseases. In the first 20 years that ISTC was active, more than 70,000 former weapons scientists in more than 760 research institutes spread across the FSU had been engaged in ISTC projects and activities (ISTC, 2020; Nikitin and Woolf, 2014).

DTRA was established in 1998, incorporating the CTR Program within its organization. Under congressional direction, the Secretaries of Defense, State, and Energy agreed to transfer funding responsibility for certain activities from the DOD budget request into the Departments of State and Energy budgets. By 2000, several government departments supported the CTR activities in the Russian Federation, including the Departments of State and Energy; HHS, including the National Institutes of Health and CDC; the National Science Foundation; the U.S. Agency for

endeavors. From the time GEIS was established, it has worked in close coordination with the CTR Program.

International Development; the Environmental Protection Agency, and the Department of Agriculture. Departments and agencies that had traditionally not been engaged in international security efforts were included in this significant program to support the redirection of the massive Soviet biological weapons enterprise.

In a related policy statement, the Clinton administration's National Security Strategy of 1999 stated that "diseases and health risks can no longer be viewed solely as a domestic concern. Like the global economy, the health and well-being of all peoples was becoming increasingly interdependent. With the movement of millions of people per day across international borders and the expansion of international trade, health issues as diverse as importation of dangerous infectious diseases and bioterrorism preparedness profoundly affect our national security" (White House, 1999, p. 13).

TAKING STOCK OF THE FIRST 15 YEARS, AND PLANNING AHEAD TO BIOLOGICAL COOPERATIVE THREAT REDUCTION: CTR 2.0

During the 15 years following the passage of the Nunn-Lugar Act, DOD invested nearly $7 billion in CTR activities (Woolf, 2012). As noted above, under the CTR Program, this funding went to safeguard and dismantle vast stockpiles of nuclear and chemical weapons, and a large biological weapons research and manufacturing enterprise in the FSU, as well as to engage scientists in productive peaceful applications of science. Following the terrorist attacks in the United States on September 11, 2001, and the subsequent mailing of anthrax-laced letters to several news organizations and two U.S. senators (FBI), there were renewed concerns that terrorists were interested in acquiring chemical, biological, radiological, and nuclear weapons, related materials, and knowledge from the FSU (Nikitin and Woolf, 2014). In response, the George W. Bush administration released the National Strategy to Combat Weapons of Mass Destruction (WMD) in 2002, expanding the strategic focus of the CTR Program to also address the threat posed by non-state terrorists, particularly those seeking to acquire WMD capabilities (U.S. DOS, 2009). During this period, international cooperation became more formalized to strengthen CTR programs. For example, in 2002 the Group of Eight, or G8, countries announced the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, committing these countries

to fund a total of $20 billion on nonproliferation projects, with a particular emphasis on the destruction of WMD stockpiles in the FSU, including the destruction of stockpiles of chemical weapons, dismantling decommissioned nuclear submarines, and safeguarding/disposing of fissile material, as well as employing former weapons scientists (NTI, 2018). In the administration's 2004 National Biodefense Strategy, the importance of preventing and reducing future biological weapons threats was emphasized, while mitigating risks from "advances in biotechnology and life sciences—including the spread of expertise to create modified or novel organisms—[that] present the prospect of new toxins, live agents, and bioregulators that would require new detection methods, preventive measures, and treatments" (White House, 2004a). Congress also authorized the spending of DOD CTR funds outside the FSU under Public Law H.R. 1588,[4] the first example being CTR's response to Albania's request for assistance to destroy its stockpile of chemical weapons. This destruction of a chemical stockpile was subsequently achieved through cooperative efforts between the government of Albania and DTRA (Woolf, 2012).

The U.S. Department of State launched its own global biosecurity engagement program (subsequently designated the Biosecurity Engagement Program or BEP) in 2006. Reflective of CTR's expanded geographic scope, initial focus was to ensure the physical security of pathogens, upgrade laboratory biosafety procedures, and improve approaches for combating infectious diseases in South Asia, Southeast Asia, and the Middle East (NRC, 2007). It was also during this period that the revised and enhanced International Health Regulations (IHR) (2005) were adopted as an agreement among 196 countries to build their capacities to detect, assess, and report emerging infectious disease outbreaks, and to provide assistance as needed to respond with healthcare and public health control measures (WHO, 2019d). The latest iteration of IHR entered into force in 2007 (WHO, 2016a), and while there have been enduring issues with the implementation of IHR, DOD, and BTRP as a part of DOD, has made large contributions in support of IHR (2005) implementation efforts. These efforts have included participating in reporting activities and establishing disease surveillance in collaboration with host countries, such as building capacities for monitoring of respiratory diseases. During this era, the U.S. government became particularly focused on a natural, but potentially catastrophic threat to

[4] National Defense Authorization Act, 108th Congress, § 1301 (2004).

national and global health, stability, and ultimately security: pandemic influenza. The spread of the H5N1 influenza virus in poultry populations in 2005, especially in the East Asia and Pacific regions, generated global fears that the virus could mutate to become a potentially catastrophic influenza pandemic along the lines of the pandemic that killed some 40 million people worldwide in 1918 and 1919. President George W. Bush initiated a whole-of-government response. In November 2015, the U.S. Homeland Security Council issued the National Strategy for Pandemic Influenza to guide preparedness and response. The intention was described as "(1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society." (HSC, 2005, p. 2). The federal government planned to use all instruments of national power and leverage global partnerships to address the pandemic threat.

The May 2006 Implementation Plan for the National Strategy for Pandemic Influenza tasked the Department of State with leading the federal government's international engagement, bilateral and multilateral, to promote development of global capacity to address an influenza pandemic. The first priority for DOD support in the event of a pandemic was "to provide sufficient personnel, equipment, facilities, materials, and pharmaceuticals to care for DOD forces, civilian personnel, dependents, and beneficiaries to protect and preserve the operational effectiveness of our forces throughout the globe." DOD, in conjunction with the Departments of State and HHS, would "utilize its existing research centers to strengthen recipient-nation capability for surveillance, early detection, and rapid response to animal and human avian influenza" (HSC, 2006, p. 52).

From 2007 to 2011, negotiations took place at WHO resulting in the *Pandemic Influenza Preparedness Framework*, approved by the World Health Assembly in May 2011. The objective of the framework is to improve pandemic influenza preparedness and response and to strengthen the protection against pandemic influenza by improving and strengthening the renamed WHO Global Influenza Surveillance and Response System. The objective is to have a "fair, transparent, equitable, efficient, effective system for, on an equal footing: the sharing of H5N1 and other influenza viruses with human pandemic potential; and access to vaccines and sharing of other benefits" (WHO, 2011, p. 6). The global focus on

pandemic influenza preparedness and response was a precursor to the broader effort under the rubric of GHSA.

The Past Decade of Biological Threat Reduction: CTR 2.0

The National Defense Authorization Act for Fiscal Year 2008[5] authorized the DOD CTR Program activities to expand partnerships and cooperation agreements to countries beyond the FSU and Europe, namely in the Middle East and Asia, as well as to pursue denuclearization activities in the Democratic People's Republic of Korea. The same law authorized the National Academy of Sciences (NAS) to undertake a review of the DOD CTR Program and recommend ways to strengthen and expand it. The report, *Global Security Engagement: A New Model for Cooperative Threat Reduction,* was released in 2009, and the programmatic modifications described in the report necessary to address the changing international security environment in the future were described as "CTR 2.0." Box 1-2 summarizes the key recommendations of the report.

BOX 1-2
Global Security Engagement: A New Model for Cooperative Threat Reduction

Key Recommendations

- Expand Cooperative Threat Reduction (CTR) programs beyond the former Soviet Union, update their form and function, and support these activities as an active tool of foreign policy.
- Engage a broader range of partners in a variety of roles to enhance global security.
- Situate direction of the Program at the White House through the National Security Council and implementation through the Departments of Defense, State, Energy, Health and Human Services, and Agriculture, and other relevant cabinet secretaries.
- Include a broad group of domestic partners including government, academia, industry, nongovernmental organizations and individuals, and an expanded set of tools, as well as international multilateral partnerships that

[5] National Defense Authorization Act, 110th Congress, § 1301 (2008).

address both country- and region-specific security challenges.

- Recognize the contribution of personal relationships and professional networks developed through CTR programs.
- Structure the legislative framework, funding mechanisms, and program-leveraging opportunities to support more effective threat reduction initiatives across multiple domestic and international partners.

Further geographical expansion of engagements occurred under the Obama administration, largely through BTRP, and programmatic expansion occurred through a shift in emphasis from destroying and securing weapons facilities and diverting activities of former weaponeers to increasing security by strengthening detection/diagnostic and disease surveillance capabilities. The second Presidential Policy Directive and the National Strategy for Countering Biological Threats in late 2009, was very much in agreement with recommendations of the 2009 NAS report, and outlined three important themes relevant to CTR: (1) the inclusion and combination of intentional and natural biological threats; (2) an increased focus on international engagements; and (3) increased efforts to prevent adverse events. DTRA, working primarily in Africa, the Middle East, and Southeast Asia, placed a new emphasis on university-to-university collaborations by soliciting collaborative research proposals from U.S. and partner-country academic institutions. Program leadership added influenza to the list of threat agents authorized for collaboration, because of the security consequences of a major pandemic and the global concern about the potential consequences of such an event, and greatly increased its efforts in global disease surveillance. The National Security Strategy of 2010 also emphasized the need to continue working with international and domestic partners on ways to reduce the risks associated with unintentional as well as deliberate outbreaks of infectious disease and to strengthen resilience across the spectrum of high-consequence biological threats (White House, 2010). From a functional perspective, Congress provided DOD with co-mingling authority, requested in the 2009 NAS report, which allowed the CTR Program to accept funding contributions from appropriate outside organizations and foreign governments.[6] In addition, as requested in the 2009 NAS report, the DOD CTR Program

[6] Authority to carry out Department of Defense Cooperative Threat Reduction Program, U.S. Congress, Pub. L. No. 113-291 § Chapter 48, 50 Stat. (2014).

was given limited notwithstanding authority by allowing the National Defense Fund the use of funds regardless of the restraints of any other law.[7]

It had become clear that the metrics for success of CTR activities (the so-called "Nunn-Lugar Scorecard") could not accurately illustrate the impact and effectiveness of CTR 2.0 programs for biological engagement. While the scorecards could be used to count numbers of nuclear warheads deactivated, submarines decommissioned, ballistic missiles eliminated, and nuclear test tunnels sealed, they did not reflect important activities such as long-term working relationships between scientists and clinicians, crisis prevention, and improvements in biological security and biosafety capabilities.

In 2013, the memorandum of understanding known as the umbrella agreement that established the legal framework for U.S.–Russian collaboration under the CTR Program expired. Russian leadership chose to terminate its support for ISTC in Moscow, originally established to administer grants and manage the transfer of funds from the United States, the European Union, Japan, Norway, and South Korea to support threat reduction projects and facility renovation efforts aimed at redirecting scientists to peaceful activities.

Beginning in early 2014, three important events occurred. First, ISTC moved from Moscow to Nur-Sultan, Republic of Kazakhstan, where it continues to operate under the same name. A similar body, the Science and Technology Center in Ukraine (STCU) was established in 1993 and still exists today. STCU and ISTC provide support for CTR-type activities, indicating that different geographical offices provide the necessary flexibility to serve different needs. Second, GHSA was launched to pursue a multilateral and multisectoral approach to "strengthen both the global capacity and nations' capacity to prevent, detect, and respond to human and animal infectious diseases threats," whether natural, accidental, or intentional (GHSA, 2019). At present 67 countries have signed GHSA membership agreements; this has created new opportunities for global engagement. GHSA has taken on the essential need to advance IHR (2005) capacity by an invigorated effort to assess the state of readiness of countries for disease surveillance, reporting, and response to emerging infectious disease outbreaks through its process of voluntary Joint External Evaluations. Third, in 2014, the U.S. government, including DOD, responded to the West Africa Ebola epidemic at the direction of President Obama, coordinated by the Assistant Secretary of Defense for

[7] Ibid. § 3713.

Special Operations/Low-Intensity Conflict. BTRP was able to provide critical assistance early in the response through its ongoing laboratory engagement program at the Lassa fever study ward at Kenema Hospital in Sierra Leone. BTRP was in place well before the declaration by WHO of a Public Health Emergency of International Concern and a vigorous international response could be organized. Major contributions of BTRP were to convert its established Lassa fever diagnostic platform in Kenema to Ebola diagnostics and to transfer the technology to Liberia as well.

Finally, in September 2017, NASEM held a symposium titled *Cooperative Threat Reduction Programs for the Next Ten Years and Beyond* (NASEM, 2018). The symposium focused not just on biological threat reduction, but also included nuclear and chemical threat reduction as well. Bringing together many current and former government officials and representatives of NGOs who had developed policy for and managed or observed the impacts of CTR programs over the years, the symposium opened with a brief review of history, evolution, and contributions. Speakers then discussed technological, geopolitical, and fiscal realities in 2017, and the way ahead. At the end of the symposium, the co-chairs summarized the meeting with a series of observations taken from the plenary and breakout sessions:

- Cooperation between and among government agencies, NGOs, and the private sector are critical to reducing threats to the United States. The "cooperative" part of CTR makes the concept unique and especially valuable in an increasingly interconnected world.
- It is important for CTR programs to communicate how engagement improves the security of the United States, demonstrating explicitly, through detailed examples, how their work is done and what threats are being reduced. CTR programs can better articulate their value to policy makers by designing and using simple (outcome) metrics, but only where appropriate.
- The United States and the Russian Federation have years of experience working together on arms control and CTR programs, and these efforts have created longstanding positive relationships that could be used to renew technical cooperation and improve transparency and trust between the United States and the Russian Federation. Although expert views differ on the current state of Russia's plans and programs, the relationships established through this engagement can help address concerns that may arise and establish a path forward to reengagement in the future.

- CTR programs will continue to focus on reducing threats and risks but can also support efforts that build relationships and scientific partnerships, which are the foundation of sustainable CTR. Scientific partnerships often lay the foundation for larger cooperative efforts and can eventually lead to more transparency between governments, creating sustainable long-term security.
- Labels are important. Sometimes cooperative efforts stall because the CTR partner country thinks that the United States has deemed the partner a threat. "Global security engagement" or "cooperative risk management" as opposed to "cooperative threat reduction" might be better ways to describe some programs with certain countries.
- The United States can enhance the impact of CTR by creating government–industry collaborations, including flexible arrangements to more easily partner with industry and create incentives for companies to support national and international security goals.
- The United States can do better at engaging and partnering with multilateral organizations like the United Nations (UN), Security Council Committee established pursuant to resolution 1540 (2004), UN Office for Disarmament Affairs, UN Office for Counter-Terrorism, WHO, Food and Agriculture Organization of the UN, International Plant Protection Convention, and OIE to strengthen global and international norms against the acquisition and use of WMD.
- It is important for the United States to maintain robust capabilities to undertake classical CTR-like WMD elimination, as U.S. CTR programs and expertise could be the basis for eliminating WMD abroad if the opportunity arises. In the future, CTR capabilities can also be used to address threats and risks from dual-use technologies like additive manufacturing, process-intensive chemical production, genome editing and synthetic biology, drones, and cyber systems.

The Current Reality: BTRP Poised for CTR 3.0

It was with that backdrop and in that the Committee on Enhancing Global Health Security through International Biosecurity and Health Engagement Programs undertook the deliberations associated with this study, and developed the findings and recommendations described in the following chapters. The committee began its work with a review of the current state of BTRP and CTR (See Box 1-3).

BOX 1-3
Biological Threat Reduction Program Description

NOTE: The following excerpt is from the *Fiscal Year 2020 President's Budget, Operation and Maintenance, Defense-Wide Cooperative Threat Reduction (CTR) Program*. March 2019 (U.S. DOD, 2019a)

Cooperative Threat Reduction

Today's weapons of mass destruction (WMD) threat environment includes state and non-state actors acquiring, developing, or using WMD through readily available knowledge, technologies, and materials. During Congressional testimony in 2017, then Secretary of Defense James Mattis described the Department of Defense (DOD) CTR Program as DOD's most comprehensive and effective tool for working cooperatively with international and interagency partners to mitigate WMD-related threats. Moreover, the program has strong linkages to the National Defense Strategy (Strengthening Alliances and Attracting New Partners) and DOD Geographic Combatant Command (GCC) priorities–namely, building partner capacity to counter the proliferation of WMD. To address these transnational threats and to meet national and DOD/GCC priorities, the CTR Program works with partner nations to build their capacity to prevent the proliferation or use of WMD. With a focus on eliminating, securing, detecting, and interdicting WMD and related systems and materials, the CTR Program takes a layered approach to help its partners address WMD-related threats as close to the source as possible:

- Eliminate. When possible CTR eliminates WMD and related systems or materials.
- Secure. If cooperative elimination is not possible, CTR consolidates, secures, and accounts for WMD and related systems or materials at their source.
- Detect and Interdict. Where the program cannot fully address the threat at the source, it works with partner countries to detect and prevent trafficking, enhance disease detection and surveillance, and cut off proliferation pathways.

The DOD CTR Program consists of the following efforts: Strategic Offensive Arms Elimination, Chemical Weapons Destruction, Global Nuclear Security, the Biological Threat Reduction Program (formerly the Cooperative Biological Engagement Program, an administrative name change to accurately reflect the mission of this effort), the WMD Proliferation Prevention Program, and Other Assessments and Administrative Costs.

The Biological Threat Reduction Program (BTRP)

BTRP (formerly Cooperative Biological Engagement Program) facilitates elimination, safety, and security of especially dangerous pathogens (EDPs) as well as rapid detection and reporting of diseases caused by EDPs. This reduces the risk of EDP holdings, accidental release, or EDPs being used for nefarious purposes. It also reduces the risk of localized outbreaks becoming regional destabilizing events and increases the safety of U.S. forces.

Examples of BTRP Objectives:

- Secure dangerous pathogens and mitigate the risk of illicit proliferation and of non-state terrorist groups and violent extremist organizations from acquiring biological materials, equipment, and expertise; ensure tailored but consistent approaches to training, diagnostic processes, and reporting; enhance regional organizations' biological threat reduction capabilities and infrastructure investment sustainment through regional and international scientific engagements and partnerships; strengthen linkages and facilitate sharing of biosecurity and safety (BS&S) and biosurveillance best practices among BTRP partner nations; enhance partner nations' individual and regional capability to detect, diagnose, and report human and animal EDPs; enhance the region's BS&S capabilities to reduce the risk of accidental or intentional release of EDPs.
- BTRP is currently partnering with the following countries: Armenia, Azerbaijan, Cambodia, Cameroon, Ethiopia, Georgia, Guinea, India, Iraq, Jordan, Kazakhstan, Kenya, Laos, Liberia, Malaysia, Philippines, Senegal, Sierra Leone, South Africa, Tanzania, Thailand, Turkey, Uganda, Ukraine, Uzbekistan, and Vietnam. If the political situation presents opportunities for engagement, additional activities will occur with Pakistan and Indonesia.

2

The Changing Biothreat Landscape

KEY MESSAGES

- The National Security Strategy, National Biodefense Strategy, and Global Health Security Strategy include the following within the scope of biological threats: naturally occurring, accidental, and intentional biological incidents; and One Health.
- The nature of the biothreat is evolving, including the effects of global changes in the biotechnology on Biological Threat Reduction Program (BTRP) initiatives; what actions might BTRP take now to keep pace with these changes?
- Because the international landscape for addressing biological threats involves many nongovernmental, governmental, and intergovernmental actors, effective coordination and communication are critical to ensuring success of biological threat reduction programs.

In recent years, the concept of *biothreat* has continued to evolve to include natural, accidental, and intentional threats and their social, economic, political, and security consequences; exploitation of biotechnologies for malicious and/or military use; and unauthorized access to biological data. This evolution reflects the significant changes that have been observed in human and animal health, the biotechnology landscape, the bio-based economy, and international sample and data-sharing policies. These changes have been enabled by globalization of the biological and biotechnological sciences, Internet-connected facilities and information systems, an influx of new funders and practitioners, and increased investments in biodiversity and environmental scanning.

The U.S. government policy landscape for biodefense and health security focuses on factors and technologies that either enable or prepare strategic plans to respond to natural, accidental, or intentional biothreats. In 2019, the National Security Strategy, National Defense Strategy,

National Biodefense Strategy, Global Health Security Strategy, and U.S. government involvement in the Global Health Security Agenda (GHSA) and associated human and animal health agreements all contributed to the overarching context within which BTRP now finds itself operating. This relatively recent governing framework is built on a nonproliferation foundation, which is promoted by the Biological and Toxin Weapons Convention, United Nations Security Council Resolution 1540, and the legislation and policies governing Cooperative Threat Reduction Programs (CTR). Within this complex policy context, BTRP's efforts to prevent biothreats is further complicated by the influence of threats emanating from cyber-attacks of facilities and information systems, and policies preventing open, transparent sharing of samples and scientific data.

This chapter provides a high-level outlook on the evolving nature of the biothreat, specifically focusing on how global changes in the biotechnology landscape may affect BTRP initiatives and what actions BTRP can take now to keep pace with these changes.

FINDING 2.1: The development of threat-specific prevention and detection approaches can be improved through anticipation of current and future threats presented by natural, accidental, and intentional incidents involving high-consequence pathogens and toxins and by misuse of advances in scientific research, development, and application.

FINDING 6.1: Preparing for and responding to existing and potential biosecurity threats requires an agile ability to consider traditional biological threats and the contributions of new research strategies and tools to understand the pathogenesis and epidemic potential of emerging pathogens.

GLOBAL HEALTH SECURITY

The mailing of anthrax-laced letters just 1 month after the terrorist attacks on September 11, 2001, in the United States (FBI), highlighted several inadequacies in U.S. and international preparedness and response to biological threats. Since that time, the international community has recognized the importance of addressing biological threats whether naturally occurring, accidental, or intentionally-released.

This broader definition of biothreats had developed in the late 1990s with the 1997 emergence of H5N1 influenza virus in humans (Neumann et al., 2010). Several subsequent outbreaks highlighted the need to stengthen capabilities for addressing biological events that could result in significant harm to human, animal, and plant health, economies, and society: the emergence of West Nile virus in the United States in 1999 (Roehrig, 2013); the Amerithrax incidents in 2001; the 2003 outbreak of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) (Denison, 2004); and the 2012 outbreak of Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Coleman and Frieman, 2013).

Indeed, as this report was being finalized in January 2020, an outbreak of a novel coronavirus originating in Wuhan, China, was reported (Wang et al., 2020). Within 1 month of its recognition it had caused more confirmed infections than SARS-CoV over the entire course of that outbreak. The novel coronavirus has resulted in the quarantine of major cities in China with the cessation of air, train, and road traffic, as well as closure of international borders and the implementation of passenger screening at airports around the world for fever or clinical symptoms, and has already been declared by the World Health Organization (WHO) to be a Public Health Emergency of International Concern. With increasingly rapid modern transportation and globalization of commerce, unintentional threats to national security include pathogens that can spread rapidly, spillover from animals to humans, cause severe disease in humans and/or animals, devastate agricultural systems, cause fear and loss of trade and/or tourism, impact the security of the food supply chain, and impose economic harms (Jones et al., 2013).

Investments in biodiversity (i.e., sequencing organisms in different environments), detection of microbial species from different sources, and better diagnostic technologies have revealed the large number and diversity of emerging and re-emerging pathogens that infect humans, animals, and plants. In addition, the intentional contamination of livestock or crops (preharvest or postharvest) has long been considered a potential national security threat, and examples, while relatively few, are quite relevant (Caudle III, 2001; Hugh-Jones and Brown, 2006; Keremidis et al., 2013). These agriculture and food system vulnerabilities were recognized in Homeland Security Presidential Directive/HSPD-9 (White House, 2004b), through which the Departments of Agriculture (USDA) and Health and Human Services (HHS), and the Environmental Protection Agency were directed to work together in conducting disease surveillance and developing response programs to prioritize and mitigate such “disease,

pest, or poisonous agents" threats (White House, 2004b). Furthermore, the rapid and modern distribution of animal and plant products underscores the scale and broader impact of international incidents on the security of nations, such as the accidental contamination by a pathogen or a toxin in complex food products.

Consistent with the broader definition of biothreats, the International Health Regulations (IHR) (2005) and GHSA incorporated a systems-based approach for proactively, rather than reactively, addressing these types of natural, accidental, and intentional biological threats.

International Health Regulations (IHR 2005)

For more than three decades, infectious disease specialists have documented the emergence and re-emergence of pathogens throughout the world. Before 2005, IHR required member states of WHO to report single cases of cholera, plague, or yellow fever; described measures for decontaminating transportation vehicles; and created requirements for health documents for individuals traveling from infected to unaffected areas that confirmed prior vaccination against yellow fever virus (WHO, 1969). In May 2005, the World Health Assembly adopted the revised IHR, an international legal instrument known as IHR (2005), to update the global framework to detect, report, and respond to any infectious diseases, chemical, and radiological incidents causing public health effects of international concern, not just cholera, plague, and yellow fever. The emergence and rapid global spread of SARS-CoV in 2003 emphasized the need for global action and served as an important driver for the approval of the revised IHR (2005) to prevent, protect against, control and respond to the international spread of disease while avoiding unnecessary interference with international traffic and trade. IHR (2005) is also designed to reduce the risk that diseases might spread to other countries via international airports, ports, and ground crossings (WHO, 2009 and 2016a). These threats can include natural and human-made biological, chemical, and radiological incidents. IHR (2005) establishes a set of rules to support the Global Outbreak Alert and Response Network, and requires countries to improve international surveillance and reporting mechanisms for public health events, and strengthen their national surveillance and response capacities.

IHR (2005) officially entered into force in June 2007 and now is binding in 196 countries across the globe, including all WHO member states (WHO, 2017). Every government was obligated to develop,

strengthen, and maintain the capacity to detect, assess, notify, and report events, and to respond to public health threats and emergencies of international concern within 5 years of coming into force, with the possibility of two 2-year extensions (WHO, 1969). However, fewer than 20 percent of countries had achieved full compliance with IHR (2005) by the 2012 deadline (Hamblion et al., 2014). To assist countries in implementing IHR (2005), WHO released a monitoring framework for countries to assess and improve or develop core capacities for preventing, preparing for, and controlling public health emergencies of international concern (WHO, 2018). The core capabilities cover laboratory capacity (which includes biosafety and biosecurity) and disease surveillance (Refaey, 2011), both of which fall within BTRP's current initiatives. Unfortunately, resources available to WHO and within individual countries to upgrade national capacity are limited, preventing many countries from fully achieving the IHR (2005) core capabilities.

FINDING 4.1: The International Health Regulations (2005) require all countries to achieve minimum core competency to detect, assess, report, and respond to public health, plant, and animal health risks and emergencies of national and international concern. Not all countries have met these requirements, in significant part because of inadequate resources to implement assessment and capacity strengthening support at the country level.

The Global Health Security Agenda

The challenges that many countries faced in implementing IHR (2005) led the United States, WHO, the United Nations (UN) Food and Agriculture Organization (FAO), World Organisation for Animal Health (OIE), and 18 countries to launch GHSA in February 2014 (CDC, 2014). GHSA was intended to provide financial and technical resources to countries to address gaps in their public health systems that prevent achievement of the IHR (2005) core competencies. Sixty-seven countries are members of GHSA today (GHSA, 2019), and the number continues to grow. Unlike IHR (2005), GHSA focuses only on public health threats caused by infectious diseases. The initial set of action packages focused on antimicrobial resistance, zoonotic disease, biosafety and biosecurity, immunization, national laboratory system, real-time disease surveillance, reporting, workforce development, emergency operations centers, linking of public health with law and multisectoral rapid response, and medical

countermeasures and personnel deployment (GHSA, 2018a). BTRP-funded activities overlap with and could contribute to GHSA action packages on biosafety and biosecurity, national laboratory systems, real-time disease surveillance, emergency operations centers, and linking of public health with law and multisectoral rapid response (See Figure 2-1).

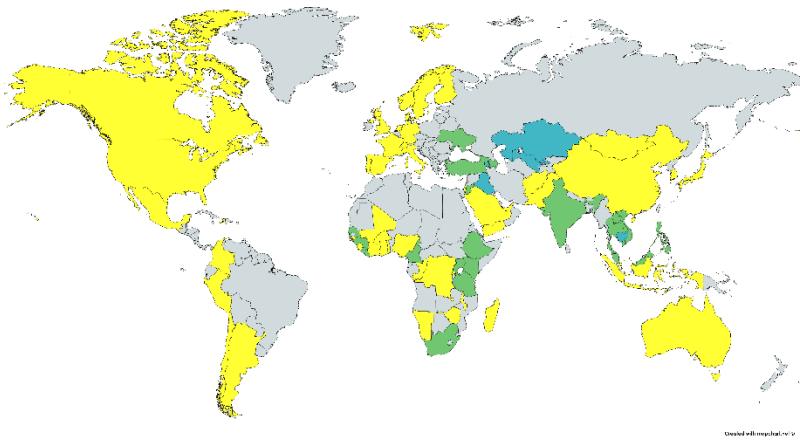


FIGURE 2-1 Map of GHSA countries, colored in yellow; countries which partner with BTRP, colored in blue; and, countries which participate both in GHSA and are cooperative partners with BTRP are colored in green.
SOURCES: Brooks and Newman, 2018; GHSA, 2019; U.S. DOD, 2020a.
Created using mapchart.net.

At the 2017 GHSA Ministerial Meeting in Uganda, member states agreed to extend the GHSA another 5 years. The GHSA 2024 Framework, which was released in 2018 (2018b), affirmed GHSA's mission, vision, core principles, and strategic initiatives; established a secretariat function to support communication among GHSA members; and created task forces on advocacy and communication, stakeholder engagement, accountability and results, and action package coordination to aid in achieving the GHSA strategic initiatives. In addition, GHSA established a new action package on sustainable financing to promote national-level investment in preparedness for new and emerging infectious disease outbreaks. BTRP's recent efforts in promoting multilateral cooperation to address biological threats and sustainability by enhancing partner country capabilities to detect, monitor, and prevent biological threats aligns with the original and 2024 objectives of GHSA. BTRP's continued inclusion of experts from human and animal health, security, and scientific sectors in

its activities could support GHSA objectives. Consistent with the vision articulated in Chapters 5 and 6 of this report, BTRP could also engage government funders and philanthropic organizations to promote long-term support for continuing capability-building in biosafety, biosecurity, pathogen surveillance, training and workforce development, and other relevant areas. Furthermore, BTRP could engage the GHSA leadership on metrics and evaluation, building on its commissioned report on Measuring Cooperative BioEngagement Program Performance (Young et al., 2014).

WHO also developed the Joint External Evaluations (JEE) tool (WHO, 2016b), which is a voluntary external assessment process that identifies gaps in capacity, determines a country's level of health security capacity; and measures progress toward a country's ability to prevent, detect, and respond to infectious diseases threats. Progress has been achieved with the support of GHSA, member countries, and the Alliance for Health Security Cooperation, which currently has 73 members and focuses on developing multisectoral capability-building towards achieving the IHR (2005) core capacities (AHSCa). The country assessment process involves four phases: (1) self-assessment; (2) external evaluation; (3) country planning; and (4) capacity building. As of July 2019, 100 JEEs have been conducted since the first JEE was conducted in February 2016 (AHSCb; WHO, 2019f), 92 of which are available on the WHO website (WHO, 2019a). Box 2-1 highlights selected examples of recommendations of priority actions identified through the JEEs (WHO, 2017a, b, c). Forty-eight countries have completed National Action Plans for Health Security (NAPHS) to address gaps identified through the JEEs, and 12 countries have initiated development of their NAPHS (WHO, 2019c).

Under GHSA, efforts have been undertaken to improve data sharing through the implementation of the JEEs. Although nearly all JEE Mission Reports are available online, questions remain about how the assessment information should be used and who should have access to it (WHO, 2019a). Some experts have argued for a coordination center with ties to WHO to compile and coordinate this information, and others call for a more coordinated and streamlined JEE process. The JEEs serve as a guide to inform country capability needs for biosafety and biosecurity, biosurveillance, and other IHR (2005)-related capacities. In addition, the JEEs provide opportunities for multisectoral coordination to address country needs. JEEs, NAPHS, and other analyses can complement BTRP's assessments of a partner country's capabilities, identifying gaps that are prioritized by partner countries, and developing evaluation metrics for BTRP activities in priority countries.

U.S. efforts under GHSA generally involve strengthening existing programming toward global health security that is aligned with GHSA goals. Although GHSA is a multisectoral effort, the National Security Council is the responsible body for overall strategy and coordination for the U.S. government's global health security program. Key implementing agencies include the Department of Defense (DOD), U.S. Agency for International Development (USAID), HHS, and Department of State (White House, 2019). Coordination across relevant U.S. departments and agencies will need to improve in order to implement a whole-of-government approach to global health security. In 2019, the U.S. government issued the Global Health Security Strategy (GHSS), which provides the United States' overarching approach to prevention, detection, and response to biological threats internationally and documents roles and responsibilities of each department. A critical component of GHSS is continuous communication and coordination among U.S. government agencies involved in implementing the strategy.

OIE has developed the Performance of Veterinary Services (PVS) Pathway, the OIE's flagship capacity-building platform for the sustainable improvement of national veterinary services. "Cyclical in nature, the PVS Pathway provides a robust mechanism for the continuous improvement of national veterinary services, through a staged approach using a set of proven tools and methods to evaluate, plan, cost, and support the strengthening of national veterinary services" (OIE, 2020a). The initial "PVS Evaluations comprise a 2- to 6-week mission, (which) delivers a thorough, qualitative assessment of the performance of a country's veterinary services and their compliance with OIE international standards. It is an external evaluation conducted by a group of OIE trained and certified experts, who collect and analyse baseline information and evidence collated during the mission, including an extensive field component. The mission uses the proven OIE PVS tool, (through which) 45 critical competencies are systematically evaluated via documentation reviews, interviews, and physical observations against five qualitative graded levels of advancement, each with detailed descriptions or indicators to transparently guide the process" (OIE, 2020b). So far 37 missions have been completed (as of August 2019); 30 reports are available on the OIE website.

BOX 2-1
Selected Priority Actions Relevant to Biosafety and Biosecurity Capacities from the Joint External Evaluations of Selected Countries

Indonesia

- Complete ongoing work to finalize a broader national strategic plan for biosafety and biosecurity in laboratories in Indonesia, bringing together laboratory functions in different ministries to address the International Health Regulations (2005) technical areas such as zoonotic disease, laboratory systems, workforce development, food safety, real-time surveillance, and antimicrobial resistance in a single overarching plan.
- Develop a continuously updated and monitored nationwide inventory of high-consequence agents in storage.
- Educate and deploy a nationwide function for maintenance and control of laboratory safety facilities and equipment.
- Develop a master training and certification scheme for biosafety and biorisk officers in both the human and the animal sectors, accredited and certified by relevant international bodies such as the World Health Organization, United Nations Food and Agriculture Organization, World Organisation for Animal Health, and/or the International Federation of Biosafety Associations.

Thailand

- Ensure the detection and follow-up of incidents by biosafety officers. Serious potential for actual incidents should be investigated and lessons learned.
- Develop and strengthen national training on biosafety and biosecurity using a unified public and animal health manual with equal outreach in the public health and animal health sectors.
- Enhance existing networks among ministries, such as the emerging infectious disease laboratory network, by including responsible biosafety officers from the public health and animal health sectors and from other related ministries.

Uganda

- Expedite enactment of the biosecurity legislation to ensure designation of a national competent authority for biosafety and biosecurity and to develop an implementation plan.
- Develop harmonized national guidelines for licensing and regulation of laboratories across sectors.
- Develop and execute a comprehensive pathogen consolidation plan across sectors.
- Integrate biosafety and biosecurity training into pre-service curricula.

INTERNATIONAL HEALTH SECURITY PARTNERS

In addition to governments, intergovernmental and multilateral organizations, nongovernmental organizations, academic institutions, and the private sector play major roles in preventing, detecting, and responding to emerging, reemerging, and intentionally introduced pathogens. These entities generally fall into four major but overlapping categories: (1) international health; (2) development; (3) security; and (4) science. Although detailed descriptions of all efforts and entities involved in each of these categories is beyond the scope of this report, the diversity of actors is relevant to understanding the system in which BTRP is working to address biological threats.

Several intergovernmental efforts and entities exist to address infectious diseases affecting humans, animals, and/or plants, including the IHR (2005) (WHO, 2019e), GHSA, and OIE. In addition to the country members of GHSA (GHSA, 2020), two nongovernmental entities (the Private Sector Roundtable and GHSA Consortium) serve as members of the GHSA Steering Group and task forces, and several additional academic, nonprofit, and private-industry organizations contribute to GHSA Action Package implementation. OIE, which was established in 1924 to address animal diseases globally, has 182 member countries and is affiliated with more than 70 intergovernmental and regional organizations (GHSA, 2020; OIE, 2020c; USAHA, 2019). FAO, which is a specialized UN agency aimed at combatting hunger, has 194 member countries, works in more than 130 countries, and provides emergency response to outbreaks of transboundary animal diseases (e.g., highly pathogenic avian influenza, foot-and-mouth disease, peste des petits

ruminants [sheep and goat plague], and Rift Valley fever, and plant pathogens (FAO, 2019c, 2019e; Jungcurt, 2017)). FAO also hosts the International Plant Protection Convention (FAO, 2020b).

International organizations, universities, nonprofit organizations, private industry, and philanthropic organizations play significant roles in preventing and responding to health threats and risks. The Coalition for Epidemic Preparedness Innovations is an example of an international public–private partnership established in 2017 by the Wellcome Trust and the governments of Norway and India to help fund and coordinate the development of new vaccines against WHO priority pathogens (CEPI, 2019). Other examples include Gavi, the Vaccine Alliance, which was created in 2000 to promote equal access to vaccines for children in poor countries through public–private partnerships (Gavi, 2019), and the International AIDS Vaccine Initiative, which is a nonprofit organization focused on addressing challenges of human immunodeficiency virus and tuberculosis (IAVI, 2019).

Nonprofit, academic, and government organizations build country capabilities to detect and report pathogen outbreaks, train scientists and clinicians on biosafety and biosecurity concepts, and respond to public health emergencies and transboundary disease threats. Scientists in university, private-sector, and government laboratories help to characterize infectious diseases and outbreak strains; develop and test vaccines, medicines, diagnostic tools, and new technologies for biosurveillance; and educate future generations of scientists. All of these entities can support the promotion and adoption of norms of behavior with respect to biosecurity of pathogens and biosamples, an initiative best conducted through personal networks of trust. Experts from academia and think tanks conduct a variety of activities (e.g., advocacy, global governance, and evaluation and metrics) to monitor and support progress toward achieving global health, health security, and security objectives. For example, NTI, a Washington, DC-based nonprofit organization "recognizes that threat reduction is a shared responsibility between governments and the private sector. (They) raise awareness, advocate for solutions, facilitate implementation of solutions, and foster new thinking about these challenges" (NTI, 2020b).

Because key information about many of these programs and activities are shared among practitioners at conferences, by establishing a presence at these key meetings BTRP could identify experts to engage, be better informed about emerging advances, and identify biosecurity-related issues to address. Support and encouragement for BTRP participation at such

meetings and conferences would benefit its efforts to better engage with international partner countries and with organizations that have a similar mission. The landscape is complex, overlapping, and sometimes competitive, and the optimal way to understand what is going on is to participate.

Support for the broad spectrum of global health security efforts is provided by an equally diverse group of funders, including private donors, philanthropic organizations, and government funding agencies. Funders of global health, national security, development, and scientific research support global health security activities. Private funders include the Open Philanthropy Project, Skoll Global Threats Fund, Bill & Melinda Gates Foundation; multinational organizations such as the Asian Development Bank and the World Bank Group; and philanthropic arms of private industry, such as the Pfizer Foundation. Government funders include a variety of organizations, such as the U.S. CTR programs (e.g., DOD BTRP and the Department of State Biosecurity Engagement Program), the Global Partnership Against the Spread of Weapons of Mass Destruction (GPWMD, 2017), the European Commission Horizon 2020 (European Commission, 2019), USAID, and the development agencies of other countries (e.g., U.K. Department for International Development (U.K. Government, 2019)), the U.S. Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control, and other similar organizations.[1]

FINDING 5.4: Navigating the diverse landscape of international experts, implementing organizations, coordinating organizations, and funders can be difficult given the sheer number of entities involved. To be most effective, any actor engaging in these efforts–including BTRP–must leverage existing capabilities, cooperate with other funders regardless of any difference in mission, and promote deconfliction of activities in countries where human and financial resources are limited. To obtain the most information and understand the necessary response, these actors also need to coordinate with one another and to communicate and share information for the immediate public health needs and for generating research data for the future.

[1] See Appendix C for a more detailed list of organizations and descriptions involved in global health security.

DATA SHARING RELEVANT TO GLOBAL HEALTH SECURITY

Developing better analytical and data-sharing capabilities within and between countries is essential for biological threat reduction efforts to succeed. For example, a more detailed understanding of human and animal migration pathways is needed to more effectively assess disease threats. However, the issue of sample and data sharing has presented significant challenges, especially since 2006, when H5N1 avian influenza was a significant public health concern (Fidler, 2008).[2] Numerous countries have passed laws regulating sample and data sharing within the biodiversity and access and benefit-sharing context (CBD, 2019). Some countries, including Indonesia, have now strengthened their policies to require material transfer agreements and approval for sharing of samples and data with foreign scientists, and the penalty for noncompliance now includes fines and prison time (Rochmyaningsih, 2019). Achieving the goals of biological threat reduction requires the capacity to safeguard samples that contain virulent strains of a pathogen. Without such assurances, transport of samples out of a country could be labeled biopiracy. To be able to transfer samples, BTRP could negotiate material transfer agreements with partner countries, perhaps using a common template agreement that is tailored to different countries to ensure consistency in sample and data sharing.

FINDING 4.2: Sample and data-sharing are critical to early detection of transboundary outbreaks, but access to this information may be limited because of strict sample and data-sharing policies in partner countries. Delays in data access could delay reporting to international health organizations, alerting neighboring countries to the potential threat, and initiating emergency response activities in a timely manner, including development of field ready diagnostic tests, and planning of clinical trials of countermeasures, including therapeutics and vaccines.

[2] There was an objection to isolates from samples being used for seasonal vaccine development because a company stood to profit from the use of the sample, but none of the profit would be allocated to the country that provided the sample. Moreover, the country of origin would have to buy the vaccine at unaffordable prices.

SECURITY AND DEFENSE OF AGRICULTURE AND FOOD SUPPLIES

As the world population continues to grow, agriculture also is changing to meet food production needs. In 2017, FAO identified five key trends: (1) increased human population growth with concomitant increases in agriculture production; (2) increased complexity of food production systems and consolidation of small producers resulting in larger, more complex industries; (3) increased susceptibility of agriculture to the changing climate and natural and human-made disasters; (4) greater impact of agriculture industries on the environment; and (5) increased competition between industries for natural resources to continue food production (FAO, 2017). The report states that changes in agriculture must be made to avoid some of the observed trends threatening longer-term food security. In 2018, food insecurity was said to impact an estimated 820 million people in the world and potentially disrupt political infrastructure in affected countries (Deaton and Lipka, 2015; FAO, 2019d), suggesting threats to agriculture could represent significant risk to national and regional security (FAO, 2019b). In addition, high food insecurity results in malnutrition, which impedes the immune response to infection and increases morbidity and mortality. It also drives people to move into environments that represent an enhanced threat of infection.

Expanding BTRP's current efforts in biosurveillance of animal and plant pathogens would promote early warning of and response to transboundary zoonotic diseases and potentially destabilizing effects on governments and populations (See Table 2-1 for a list of select diseases at the human-animal-environment interface and the potential health and financial burdens they may cause). Foreign animal diseases that do not directly affect humans, such as foot and mouth disease (FMD) or African swine fever (ASF), and diseases that only sporadically cause human disease such as highly pathogenic avian influenza (HPAI), can destroy large populations of food production animals, which, in turn, could initiate economic and subsistence disasters. For instance, USDA estimates that an outbreak of FMD in the United States could cost anywhere from $15 to $100 billion (USDA, 2017). The 2014-2015 incursions of H5N2 HPAI among U.S. poultry led to the culling of an estimated 50 million birds at a cost in excess of $2 billion (FAO, 2019a; USDA, 2017).

The recent explosive spread of ASF in Asia is an example of how these animal and food security threats can rapidly create hardship. From initial detection in China in August 2018 through October 2019, ASF has spread

rapidly to Cambodia, the Democratic People's Republic of Korea, Laos, Mongolia, Myanmar, the Republic of Korea, and Vietnam (FAO, 2019a). This outbreak has become a major swine industry disruptor that is rapidly changing the economics of pork in China and Vietnam, resulting in a 30 to 40 percent increase in the cost of pork (Economist, 2019), and a 63 percent increase in orders to import pork products into mainland China (Gu and Singh, 2019). Such long-term economic distress and food security problems can destabilize nations, even when direct transmission of infection to humans is unlikely without genetic modification of the agents that permit it to breach species barriers and spillover to humans.

Some primarily animal pathogens also can infect humans with varying degrees of efficiency. Since 2013, HPAI H7N9 strains in China have infected millions of domestic poultry birds and more than 1,500 humans with a reported case-fatality rate of 39 percent (Wang, G.-L. et al., 2019), although this may reflect only symptomatic cases, as it does not incorporate information on mild or asymptomatic infections. Some pathogen threats to humans are found naturally in domestic animals, but cause the animals little or no harm, and as a result are designated reservoir species. For example, the MERS-CoV, which circulated with little evidence of disease in camels, has infected more than 2,500 people in 27 countries with a reported mortality rate of 35 percent (WHO, 2019b). Controlling both types of pathogens (those affecting animals only and those affecting humans but not their animal hosts) requires collaboration between the human and animal health sectors, their institutions, and their professional staff in a One Health approach. Examples include the recent control of HPAI H7N9 infections in humans through vaccination of poultry (Wang, G.-L. et al., 2019), and the reductions in human infections with MERS-CoV through multiple public health interventions including steps to prevent human exposure through camels, camel waste, and camel milk (WHO, 2019g). Such interdisciplinary collaborations have value for controlling many zoonotic and environmental pathogens (e.g., those found in water or soil).

These outbreaks exemplify the rapid spread of agricultural pathogens within countries and to neighboring countries and trade partners, emphasizing the importance of having disease surveillance systems in place for pathogens currently circulating in the food systems of affected countries, but not yet epidemic or pandemic (FAO, 2019a; Huang et al., 2013; Huong Giang et al., 2016; Tong-Qing et al., 2010; Zhou et al., 2019).

FINDING 5.1: Outbreaks of animal and plant pathogens that adversely affect the agricultural system and food

industry can directly or indirectly impact human health and have the potential to lead to destabilization of societies and economies, and/or national and regional conflicts.

TRAVEL AND TRADE

Globalized trade and modern transportation are increasing the movement of infectious disease threats (Saker et al., 2004). Similarly, introduction of a novel disease to a geographic region might lead to continued autochthonous spread of the disease far beyond the initial cases, for example, West Nile virus introduction, or dengue virus in several countries, including the United States. A 2006 report identified three main threat consequences from modern transportation network expansion: (1) infectious disease pandemics; (2) vector invasion events; and (3) importation of vector-borne pathogens (Tatem et al., 2006). The increasing volume and speed of travel allows people to move from one point on the Earth to virtually any other place well within the incubation period of many infectious disease pathogens. Dissemination of infection across the globe can occur within 24 hours. These factors continue to determine the spread of pathogens, witnessed today by the incredibly rapid movement of influenza A(H1N1)pdm09 virus (Colizza et al., 2007), the changes in the geographical spread of *Aedes aegypti* and *Aedes albopictus* mosquitos (Els et al., 2018), and the rapid geographical expansion of arboviral pathogens transmitted by these mosquitos, such as dengue, Zika, and chikungunya viruses (Solimini et al., 2018). Although some of these pathogen expansion trends can be attributed to environmental factors favoring the pathogen or vector (e.g. climate, including temperature, humidity, and precipitation) and human factors other than travel (e.g. human population density, increasing incursions of larger numbers of humans into pristine forest and other ecosystems, and environmental destruction that increases vector breeding), it is the rapid and expanding global movement of people, animals, and international trade in agricultural products that is the primary contributor to the spread of infectious diseases that threaten national and regional security (Findlater and Bogoch, 2018). Several examples reflect the silent movement of pathogens via people, reservoir species such as bats and birds that fly long distances, and insect vectors that are trapped and transported on airplanes and find large numbers of susceptible hosts and local vectors capable of amplifying infection rates. Some of these examples include: (1) the recent appearance of Nipah virus in Kerala in

the southwest of India, which is thousands of miles from its endemic location in Bengal (Paul, 2018); (2) the spread of Ebola virus in urban centers of West Africa in 2014 and in the northeast of the Democratic Republic of the Congo in 2018; (3) the introduction and spread of West Nile virus into the United States in 1999 (Roehrig, 2013); (4) the first local transmission of chikungunya virus in the Americas, as identified in Caribbean countries and territories in 2013; and (5) the emergence and pandemic spread of Zika virus in Brazil in 2016 (Proenca-Modena et al., 2018).

FINDING 1.1: The emergence and dissemination of pathogens as reservoir and vector hosts spread into new geographic areas, as well as through movement of humans, international travel, and trade in potentially infected animals, plants, and animal and plant products can cause disease outbreaks in geographically distinct regions and countries with no prior knowledge of or experience with the agent, exposing susceptible humans, animals, or plants, providing opportunities for health risks, economic disruption, and destabilization, and increasing the risk of local outbreaks.

TABLE 2-1 Disease Impacts at the Human–Animal–Environment Interface

Disease	Situation	Financial Cost	Health Burden	Human–Animal–Environment Interface	Source
Highly pathogenic avian influenza	January 2004-January 2009, Asia; human and animal health service costs, compensation, production and revenue losses to the livestock sector; losses primarily to smallholder producers in East Asia affecting livelihoods, trade opportunities, food and nutrition security and safety	$20 billion	486 human cases with 282 deaths	Wild birds mixing with backyard poultry; agricultural intensification without sufficient biosecurity; food security challenges	FAO, 2004; WHO, 2015
Antimicrobial resistance	Estimated cumulative impacts by 2050	$100 trillion (up to $6.1 trillion/year in high-impact scenario)	10 million human deaths annually	Agriculture/aquaculture contribute to direct transmission of resistant strains and antimicrobial dispersion; reduced efficacy threatens both health and food production	Jonas et al., 2017; Review on Antimicrobial Resistance, 2014
Severe Acute Respiratory Disease (SARS)	November 2002-July 2003; trade and travel disrupted in China; spread to 29 countries	$41.5 billion	8,500 cases, 813 deaths	Bat–human contact facilitated disease emergence; live markets may have had an amplification role	World Bank, 2012

East Coast fever	Annually for Kenya, Malawi, Tanzania, and Zambia, from endemic disease; death or reduced growth and productivity	More than $200 million		Tick-borne agricultural disease (cattle, sheep, and goats); threat to livelihood, food and nutrition security	DFID and GalvMED, 2010; Minjauw and Mcleod, 2003
Schistosomiasis (zoonotic)	Based on estimated 14 percent total schistosomiasis (zoonotic and non-zoonotic) burden; heavily impacting parts of Southeast Asia, some Africa		10 million DALYs annually	Ecological changes from anthropogenic activity (damming and irrigation) create favorable habitat for vector; non-zoonotic forms can also reduce livestock productivity	Torgerson and Macpherson, 2011
Top 13 neglected zoonotic diseases of importance to low-income livestock keepers	Zoonotic gastrointestinal disease; leptospirosis; cysticercosis; zoonotic tuberculosis; rabies; leishmaniasis; brucellosis; echinococcosis; toxoplasmosis; Q fever; zoonotic trypanosomosis, hepatitis E; and anthrax		2.4 billion cases and 2.2 million deaths annually	Various environmental determinants and agricultural exposures	Grace et al., 2012

NOTE: DALY, disability-adjusted life year
SOURCE: All figures from Table 2-1 in Berthe et al., 2018, p. 30.

LABORATORY SYNTHESIS OF PATHOGENS

Advances in genetic engineering technologies, including DNA and RNA sequencing and synthesis, and precise editing of genes have lowered the barriers to obtaining pathogens without the need for samples from nature. Use of these, and other advances in molecular biology, to create a pathogen in the laboratory for the purpose of economic gain or to deliberately infect populations for malicious political or military advantage is conceivable and may occur at any time. Examples of advances that enable acquisition or manipulation of pathogens are described here.

Researchers in the United States described the first-ever chemical synthesis of a pathogen (poliovirus) by stitching together short pieces of DNA complementary to the poliovirus genome that were purchased from a commercial service provider, and demonstrated that the synthesized copy of the genome could be used to produce virus that replicated in tissue culture cells (Cello et al., 2002).

Since then, several viruses have been produced from sequence alone through a similar chemical synthesis approach. In 2017, a Canadian research group published the recreation of the extinct horsepox virus, which is a close relative of vaccinia virus (the historical vaccine strain for smallpox), from published sequence information (Noyce et al., 2018). This experiment involved close collaboration between the researchers and the DNA synthesis provider to create the 30 kilobase fragments of the horsepox virus, which presented its own challenges; the required use of DNA structures (specifically, hairpin sequences) taken from the vaccinia virus; and production of the live virus using a helper virus replicating system in tissue culture cells (Gryphon Scientic, 2019).

Although U.S. and Canadian regulators were diligent in analyzing the potential direct risks associated with this work and its publication, this research led many security experts to be concerned about the implications of adversaries replicating similar experiments in order to recreate smallpox itself (Greenfeildboyce, 2018; Koblentz, 2018; Kupferschmidt, 2018; Kushner, 2019). Although the technical know-how and resources needed, and legal restrictions on access to smallpox virus genetic sequences, suggest that these concerns may apply to a very small number of adversaries, the United States' current select-agent-list-based policies for biosecurity and biodefense work may limit the ability to counter harmful exploitation of the knowledge, skills, and methodologies involved in this and similar work. Despite the difficulty in translating the methods from

horsepox to smallpox (DiEuliis et al., 2017), the implications of this research on acquisition of pathogens highlights the need to monitor science and technology advances beyond a specified list of pathogens and the potential for malicious exploitation. For example, reverse genetics is an established approach to synthesizing virus from sequence alone, which was the method used to resurrect the 1918 influenza virus in 2005 from sequences obtained from cadavers frozen in permafrost (Tumpey et al., 2005), and to create the Ebola virus strain from the 2018-2019 outbreak in the Democratic Republic of the Congo for the purpose of strain characterization (McMullan et al., 2019).

In 2010 and 2016, the J. Craig Venter Institute reported it had created a synthetic bacterial cell and minimal viable bacterial cell, respectively (Hutchison, 2016; IOM, 2011; JCVI, 2008, 2010, 2016). Although the researchers were able to create synthetic bacterial cells at a cost of $40 million (Hotz, 2010), they experienced hurdles in generating live, replicating bacteria from those genomes, including the need for complementarity of genome sequence and cellular parts. In early 2019, U.S. researchers described the creation of live bacteria using chemical synthesis of a rewritten bacterial genome (Venetz et al., 2019), indicating the increasing sophistication of synthetic genomics methods.

In addition to synthesizing viruses and bacteria, the emergence of CRISPR-based genome editing tools has elicited concern about their potential use to create harmful pathogens. In 2016, genome editing was classified as a weapon of mass destruction in a report by the U.S. Office of the Director of National Intelligence (Regalado, 2016; U.S. DNI, 2016). This classification shifted gene editing to an emerging technology to monitor in the 2017 version of the report (U.S. DNI, 2017), and has been discussed at the Meeting of Experts of the Biological and Toxin Weapons Convention (Australian Government, 2018; Mackby, 2018; UN, 2018). Despite these concerns, genome editing tools have been used by researchers for beneficial purposes such as to examine the function of genomic and extra-genomic sequences (Ford et al., 2019; Rousset et al., 2018; Wang et al., 2018) and develop new approaches for treating infections (Bakhrebah et al., 2018; Hamers, 2018; Shabbir et al., 2019).

FINDING 4.3: Methods for engineering and synthesizing viruses and bacteria are being democratized, enabling easier access to pathogens created or modified from gene sequence data. Although the skills, knowledge, and human and financial resources needed to create or modify live pathogens from chemical synthesis, reverse genetics, or genome editing

are specialized and high, their use may be possible by scientists from nation states and well-resourced non-state actors intent on using microbial pathogens for malicious purposes.

FINDING 2.2: New scientific advances, including multi-use technologies, methods, and information highlight the need for more robust approaches for analyzing the anticipated and unanticipated consequences of scientific efforts, including misuse, reducing potential risks, and reaping the scientific benefits for prevention and detection of biological risks.

EMERGING BIOTECHNOLOGY

Several significant changes and advances in biotechnology have occurred during the past decade, which have significant implications for the biological threat landscape and for medical progress. Although these changes do not encompass all advances in biotechnology, they do illustrate the need to account for different individuals, organizations, countries, and fields that could enable or limit threat reduction investments or enhance vulnerabilities and risk in partner countries.

Design and development of biological systems and examination of biological data have expanded well beyond the biomedical and biological sciences to include trained specialists in engineering, computer information and data, and material sciences. In addition, expertise also resides in formally untrained practitioners from the do-it-yourself and amateur biology communities, some of whom may be technically competent but lack the essential ancillary training of the professional workforce, including the ethical norms and legal boundaries about what is permissible science and behavior, and the reinforcement provided by professional peers and formal institutions. These new practitioners simultaneously have enabled new industries, digitalization of biology, and design of new technologies to manipulate biological materials while also challenging current governance and oversight structures within and outside the United States. Fields such as synthetic biology, which is distinguished from genetic engineering by the use of engineering-based problem solving (i.e., the design–build–test–learn cycle), have been a primary means through which both technically and nontechnically trained individuals have engaged in the biological sciences. Information may be

disseminated via various social media platforms and chat groups, rather than through peer-reviewed literature or at high-level academic conferences. These changes have resulted in new international competitions involving high school and college-level students in bioengineering, new applications in industrial chemistry and biology, new platforms for vaccine and therapeutics development, and new design-based approaches for manipulating biological systems and enabling the creation of non-natural materials, synthetic pathogens, and novel organisms.

Advanced biotechnology integrates expertise from teams of scientists and engineers from multiple disciplines, optimizing the speed of development and commercial potential of new technologies, applications, and services in health and the life sciences. This environment has facilitated entrepreneurial efforts, spawning numerous companies that combine computational design, robotics, and bioengineering to create new organisms that produce desired products including chemicals and their precursor molecules, drugs and their precursors, and proteins including biologically active toxins. Further facilitating these efforts is the use of genome editing tools that enable precise genetic changes in an organism's DNA. Although genome editing tools are more advantageous for modifying plant, animal, and human cells than many bacteria, viruses, and yeast, for which established and robust engineering technologies exist, the growing awareness of the risks of genome editing tools to national and international security has elicited concern among security experts.

Similarly, biology has become significantly more dependent on computation and information science systems. The increasing reliance on software to collect and compile data, digital databases that allow for deposition and recall of scientific data, computational algorithms and cloud-computing environments to analyze data, design software to engineer biological systems, and laboratory control systems has enabled a whole new set of opportunities for scientific advancement and challenges for national security. Real and potential compromise of these software systems has introduced a new set of problems that often do not conform to pathogen-based threat reduction measures but could have significant effects on human and animal health systems, agriculture, industry, and economic stability. In addition, the Fourth Industrial Revolution (World Economic Forum, 2019) in biotechnology (i.e., the coupling of digital and physical systems in the biological sciences) has provided opportunities for countries that have strong talent in computer and data science to become competitors to the United States in these fields. One possible outcome of

this situation is the exploitation of data and these capabilities by adversaries against U.S. entities and interests. Although the United States and its allies likely will continue innovating and advancing biology and biotechnology, they will not be the only voice internationally in setting norms for responsible science, a phenomenon currently being observed through the completed and proposed plans for editing of live, viable human embryos. Differences among countries' norms for ethical life sciences (including professional and behavioral norms against the development, production, and stockpiling of biological weapons, or the use of biotechnology for destructive purposes) could counteract past and current BTRP efforts.

Enabling advances in these and other fields is the operating mission of existing and new funders. In 2017, *Science* reported that less than 50 percent of research conducted in the United States is funded by the U.S. government (Mervis, 2017; NSB, 2018). Nongovernmental funders include philanthropic organizations, private companies, venture capital, foreign governments, and even the public through crowdsourcing. This expansion of funders provides opportunities for researchers to secure support for innovative and high-risk/high-reward projects, while simultaneously diluting requirements for oversight of research. For example, the Canadian researchers who synthetized horsepox virus from published genetic sequence data, received funds from a private U.S. company (DiEuliis et al., 2017). In addition, investments in biotechnology are viewed as important to the social and economic well-being of increasing numbers of countries internationally, including some low-income and/or conflict-ridden countries. BRTP's objectives align well with broader efforts to ensure international norms against the use of scientific knowledge, skills, technologies, and equipment to harm people, animals, and plants.

FINDING 6.2: The biological sciences and biotechnology are advancing at a pace that far exceeds current security assessments. Although the future is always hard to predict, the potential for DOD to anticipate current and future capabilities and uses cannot be based on current scientific and technological activities alone, but rather must be amplified by accessing insights into where that science is going, what is the leading edge, and what are the hot topics and breakthrough achievements. This requires a sufficient and critical mass of well-trained scientists from diverse fields within the agency. The ability of these scientists to contribute

fully will be strengthened by participation in high-level scientific conferences, reading of relevant publications, and networking with academia and leading biotechnology companies. They could also benefit from engagement with a high-level external scientific advisory group composed of experts in diverse scientific disciplines, particularly individuals with relevant international experience.

DATA SECURITY

Several years ago, BTRP began building national and regional capacity to detect emerging pathogens through molecular diagnostics (i.e., next-generation sequencing and bioinformatics analysis), rather than traditional microbiological techniques (i.e., culturing of pathogens in the laboratory), and through regional networks for bat surveillance (Fair, 2017; U.S. DOD, 2015). The data generated through sequencing, shared among partners, analyzed using software, and stored in digital formats may be vulnerable to cyber-attack. Data and software provenance and integrity is extremely important for these biosurveillance efforts to help diagnostic and research scientists accurately identify and characterize pathogens circulating in wildlife and infecting animals and humans. Therefore, breaches of the information systems that generate, transmit, and store data and the software that is used to analyze data can compromise the results, which could alter detection of biological threats and determination of their origins (i.e., naturally occurring, accidental, or intentionally released) (Berger and Schneck, 2019; Murch and DiEuliis, 2019).

FINDING 2.3: Facilities and information systems using cybersecurity and data security approaches are vulnerable to exploitation by malicious actors who could access, monitor, steal, or manipulate data and analytic results remotely and without notice, or disrupt the flow of data to scientific partners. Cyber-related threats now include threats to facilities and information systems, harmful use of genomics and advanced data analytics, and the development of new biological systems.

POLICY FRAMEWORK FOR BTRP PLANNING AND INVESTMENT

Although BTRP is a component of the Defense Threat Reduction Agency, it receives its programmatic determinations through a process led by the Office of the Secretary of Defense for Policy (OSD(P)). This process involves identification of priority countries and overarching initiatives through consultation[3] with BTRP leadership in accordance with the National Security and National Defense Strategies. In addition to aligning BTRP efforts with the National Security Strategy and National Defense Strategy objectives, OSD(P) has three criteria it uses to determine with which countries BTRP should partner: (1) countries where biological threats exist; (2) countries that have poor infrastructure to address biological threats and risks; and (3) countries at risk of state and non-state use of biological agents as weapons. OSD(P) works closely with the Department of State and Congress to coordinate efforts and seek approval for country engagement on topics of national security interest. This determination process can be lengthy (at times taking years), in part because requests for new determinations may be deprioritized for other, more pressing requests, and due to the limited capacity of OSD(P) to review multiple requests simultaneously. However, once this process is complete and Congress has given its approval, the determination is made and sent to BTRP for implementation. At this stage, BTRP is responsible for developing its 5-year strategy for threat reduction within the determinations provided. Although the determination process can be long and BTRP plans 5 years in the future, it does have some authority to allocate funds for emerging issues if the need arises, as described further below.

Throughout its existence, BTRP has revised its approach several times in response to changing conditions to achieve its goals of (1) facilitating "elimination and safe and secure transport and storage of biological weapons, components, related materials, and delivery vehicles"; (2) preventing "proliferation of biological weapons, components, and related materials, technology, and expertise"; and (3) preventing "proliferation of weapons of mass destruction-related materials, equipment, and technology that could be used for the design, development, production, or use of biological weapons and their means of delivery" (Newman, 2018). Since

[3] Previously, consultation involved an advisory group called the Threat Reduction Advisory Committee, which ended on December 16, 2019 (Federal Register, 2019).

2009, when the National Academy of Sciences (NAS) published its report, *Global Security Engagement: A New Model for Cooperative Threat Reduction*, BTRP has expanded its investments into at least 27 countries in four continents and has supported projects in three broad categories: (1) building in-country capabilities for detection and surveillance of biological agents; (2) conducting research on pathogens of interest; and (3) enhancing safety and security of laboratories that handle biological agents. For several years, BTRP has been authorized to support programs to prevent and detect incidents involving especially dangerous pathogens, including pathogens on the Biological Select Agents and Toxins list, emerging pathogens, and naturally occurring pathogens that may cause public health emergencies of international concern. These categories also reflect priority actions for IHR (2005) and GHSA. BTRP defines country-specific engagements through the Program Objective Memorandum process in which it charts its 5-year plan for investments in countries and regions of interest, promoting sustainable, goal-oriented planning for its investments. This process does not prevent BTRP from being agile in an outbreak or other emergency situation if its unique capabilities are needed. Throughout this process, BTRP can work with combatant commands to provide support for regional initiatives if they fall within the scope of BTRP guidance and legal authorization. BTRP collaborates with governmental partners in-country to assess and/or identify needs and collect funding proposals that align with the Program Objective Memorandum for the respective country. Finally, BTRP can interact with embassies to promote its initiatives and programs.

Box 2-2 provides the legal framework for BTRP by statute, the National Defense Strategy, the National Security Strategy, the National Biodefense Strategy, the National Strategy for Countering WMD Terrorism, and the Global Health Security Strategy.

FINDING 1.2: BTRP is constrained by both political and geographic requirements that inhibit its ability to respond nimbly to emergent threats. As a result, BTRP is unable to keep pace with the speed at which science and technology are changing the biological risk landscape, reducing its ability to preclude or mitigate potential threats as they emerge.

BOX 2-2
Legal Framework for BTRP

Congressional Authorizations. The Department of Defense (DOD) Biological Threat Reduction Program (BTRP) is authorized by 50 U.S. Code 3711, which provides DOD authorities to engage with foreign countries to "prevent the proliferation of biological weapons, weapons components, and weapons-related materials, technology, and expertise, which may include activities that facilitate detection and reporting of highly pathogenic diseases or other diseases that are associated with or that could be used as an early warning mechanism for disease outbreaks that could affect the Armed Forces of the United States or allies of the United States, regardless of whether such diseases are caused by biological weapons" (USC 50§3711). This authority is limited to "equipment, goods, and services," but does not include provision of direct funds "for a project or activity carried out under the program." This statute states that all cooperative threat reduction contracts "are focused and expanded to support specific relationship-building opportunities, which could lead to the development of the Program in new geographic areas and achieve other benefits of the Program" (USC 50§3711). DOD has flexibility in obligating funds from prior fiscal years for projects and activities that may "assist the United States in the resolution of critical emerging proliferation threat" or "permit the United States to take advantage of opportunities to achieve long-standing proliferation goals" (USC 50§3712). These projects can be funded for up to 5 years. In addition, up to 15 percent of funds in a given fiscal year can be obligated to urgent threat reduction needs, if threats to proliferation of "biological weapons or weapons-related materials, technologies, or expertise must be addressed urgently" (USC 50§3713). DOD also may obligate funds for addressing urgent threats if the President determines that such a threat must be addressed immediately (USC 50§3713). To implement a project, DOD can enter into agreements with anyone, including foreign governments, international organizations, multinational entities, and any other entities (USC 50§3715).

National Defense Strategy. The 2018 National Defense Strategy highlights biotechnology as one of several technological advances that "ensure we will be able to fight and win the wars of the future," but also will be accessible to

"state competitors and non-state actors," including the Democratic People's Republic of Korea, which was specifically identified as having biological weapons capabilities. Beyond these statements, the strategy does not include specific information about biological threat reduction. However, it does include several statements that are relevant to the Defense Threat Reduction Agency/BTRP's work. The strategy promotes development of "new partnerships around shared interest to reinforce regional coalitions and security cooperation" and use of consistent messaging to "encourage alliance and coalition commitment, greater defense cooperation, and military investment." The strategy calls for strengthening "existing bilateral and multilateral partnerships" and building "new relationships" with local partners "to address significant terrorist threats that threaten U.S. interests and contribute to challenges in Europe and the Middle East." More broadly, the strategy supports counter-weapons of mass destruction (WMD) efforts and enhancing relationships with countries, including in the Western Hemisphere, that "contribute military capabilities to shared regional and global security challenges." Finally, the strategy calls for "combined actions with [the] U.S. interagency to employ all dimensions of national power," including assisting with "efforts of DOS, Treasury, DOJ, DOE, DHS, DOC, USAID, IC, LE,* and others to identify and build partnerships to address areas of economic, technological, and informational vulnerabilities."

National Security Strategy. Strengthening U.S. capabilities to counter bioterrorism (or, biological WMD) and new and emerging infectious disease threats has been a national security priority for Presidents Clinton, Bush, Obama, and Trump. The 2018 National Security Strategy calls for working with "other countries to detect and mitigate outbreaks early to prevent disease" caused by naturally occurring, accidental, and deliberate biological threats. The strategy supports enhancing in-country efforts to strengthen healthcare systems and global health security to counter zoonotic threats, and working with partners to improve safety and security measures in laboratories that handle dangerous pathogens. In addition, it states that the United States must prevent nuclear, chemical, radiological, and biological attacks and "better integrate intelligence, law enforcement, and emergency management operations to ensure frontline defenders the right information and capabilities to respond to WMD threats from state and non-state actors." Keeping

nuclear, chemical, radiological, and biological agents secure and eliminating the "spread of WMD and related materials, their delivery systems, technologies, and knowledge" also are included in the strategy. Detection and disruption of nuclear, chemical, radiological, and biological agents are priorities identified in the strategy and are relevant to BTRP's efforts to building country capabilities for detecting biological threats before they affect U.S. interests.

National Strategy for Countering WMD Terrorism. The National Strategy for Countering WMD Terrorism (2018) includes 8 objectives: (1) denying terrorists access to dangerous materials, agents, and equipment; (2) detecting and defeating terrorist WMD plots; (3) degrading terrorist WMD technical capabilities; (4) deterring support for WMD terrorism; (5) globalizing counter-WMD efforts; (6) strengthening U.S. defenses against WMD terrorism; (7) enhancing state, local, tribal, and territorial preparedness against WMD terrorism; and (8) avoiding technological surprise. Biological threats feature prominently in this strategy, highlighted specifically in the first objective.

National Biodefense Strategy. Consistent with the 2016 legislation that called for the development of a new, comprehensive national strategy for biodefense (USC 6§104) and the 2018 National Security Strategy, the 2018 National Biodefense Strategy expands the definition of biological threats to include naturally occurring, accidental, and deliberate outbreaks. The National Biodefense Strategy highlights biological risk management as enabling activities that seek to prepare for, prevent, and respond to any biological threat. The goals of the strategy include: (1) enabling risk awareness to enhance biodefense decision-making; (2) preventing bioincidents across the biodefense enterprise; (3) enhancing preparedness efforts to mitigate the effects of bioincidents; (4) enabling rapid response to bioincidents; and (5) facilitating recovery after bioincidents. The strategy calls for promoting domestic and international biosecurity and information-sharing to enhance early warning and pathogen monitoring. In addition, the strategy promotes global health security activities, including the "development and implementation of national legal frameworks," "assessments of country capacity to prevent, detect, and respond to bioincidents," and strengthening "country capacity to prevent, detect, and respond to bioincidents." The strategy

continues by calling for efforts to "deter, detect, degrade, disrupt, deny, or otherwise prevent nation-state and non-state actors" acquisition or use of biological weapons, to strengthen biosafety and biosecurity practices and oversight, and to enhance international preparedness capabilities. All other provisions in the strategy are exclusively domestic in focus.

Global Health Security Strategy. The Global Health Security Strategy (GHSS), released in 2019, promotes early detection and mitigation of outbreaks, supporting the objectives of the 2018 National Security Strategy, and highlights the cost-effectiveness of investment in prevention and preparedness over response. GHSS seeks to "complement and build" on U.S. global health assistance programs to further enhance global health security objectives of strengthening laboratory and epidemiological capacity in low-income countries to address "epidemic-prone infectious disease threats" regardless of origin (i.e., natural, accidental, or deliberate). GHSS goals are to: (1) strengthen partner country capabilities for global health security, which includes working toward compliance with IHR (2005), Biological and Toxin Weapons Convention, and other international health and security frameworks; (2) increase international support for global health security through bilateral, regional, and multilateral diplomatic, health, and security efforts and engagement with nongovernmental entities working to prevent, detect, or respond to biological threats; and (3) strengthen U.S. capabilities for preparedness and resiliency toward biological threats by addressing gaps identified in the U.S. Joint External Evaluation and National Action Plans for Health Security. GHSS highlights geographic priorities, relevant activities (e.g., research, outbreak response, humanitarian response, biosafety, and biosecurity), and the roles and responsibilities of U.S. agencies and departments. According to GHSS, DOD plays a role in: (1) coordinating DOD activities that align with the Global Health Security Agenda and related objectives, implementing "military-to-military or military-to-civilian capability-building efforts," and conducting medical countermeasure research; (2) coordinating and communicating with defense ministries on global health security; and (3) providing emergency assistance and support to the U.S. Agency for International Development and U.S. Department of Health and Human Services in infectious disease emergencies.

* DOS = Department of State, Treasury = Department of the Treasury, DOJ = Department of Justice, DOE = Department of Energy, DHS = Department of Homeland Security, DOC = Department of Commerce, USAID = U.S. Agency for International Development, IC = United States Intelligence Community, LE = Law Enforcement

METRICS AND EVALUATION FOR BIOLOGICAL THREAT REDUCTION PROGRAMS

Metrics and evaluation are an important part of any program, not only to guide continuing improvement, but also as a way to enable funders to assess progress toward achieving their goals and advocate for their budgets. At the request of BTRP, the RAND Corporation published a conceptual framework in 2014 for measuring the performance of bioengagement initiatives (Young et al., 2014). This framework focused on building capacity, capability, and sustainability in partner countries using a combination of quantitative and qualitative metrics. Two years earlier, NAS completed its study on metrics for DOD Cooperative Threat Reduction. This report highlighted key concepts, such as the need to clearly state the program's objectives and role in addressing biological threats and risks, jointly develop objectives with partner countries to enable buy-in and sustainability, prioritize and refine the metrics over time, and allow for independent evaluation. Furthermore, the NAS committee stressed the importance of tailoring metrics to the scale, scope, and objectives of funded projects and of evaluating achievement toward overall project goals rather than a compilation of measurable activities. In addition to these efforts, the Department of State Biological Engagement Program supported at least two initiatives to develop metrics for its bioengagement program, and other groups have also proposed frameworks for evaluating success of implemented programs (Gryphon Scientic, 2019).

Drawing on these efforts, measuring the success of a project, country portfolio, or a single initiative across several countries involves a two-step process. Together, these steps help to identify the goals or activities that are achieved, factors that promote or enhance successful implementation, and hurdles that need to be overcome before goals are achieved. Although quantitative measures can be identified for specific activities (e.g., the number of individuals trained), achievement of the overall goal of the

effort (e.g., to enhance regional leadership of a partner country in biosafety and biosecurity) likely can only be assessed using qualitative measures. Furthermore, successful achievement of measurable evaluation criteria does not necessarily indicate that the intended goals of the effort have been achieved, a concept that is supported by the 2012 NAS report. Similarly, despite the fact that certain measurable outcomes of a project or activity may indicate failure, achievement of the overall goals may still be achieved. "It is possible to successfully accomplish what is easily measurable and fail in the engagement." The converse is also true (NAS, 2012, p. 3). As facilitating factors and hurdles are identified throughout project implementation and the evaluation process, they can be incorporated into lessons learned (and, possibly inform the development of best engagement practices) for consideration in future engagements. Another relevant consideration for evaluating country portfolios is the existence of frameworks, such as the JEEs, that countries already may be using to identify gaps, prioritize their own investments and activities, and coordinate with external partners and funders. Developing activity- and goal-based evaluation approaches that can be used to support, complement, and coordinate with the JEE or another process increases the potential for partner country buy-in and sustainability of capabilities.

FINDING 4.4: Measuring threat reduction from engagement programs is difficult. Common quantitative metrics are ineffective. The program needs to continue to develop and try out new approaches, such as the use of a quasi-qualitative rubric for measuring achievement of individual activities and overall goals of projects, country portfolios, and program initiatives. Such non-traditional measurements provide opportunities to course-correct when hurdles are encountered, support conditions and factors that facilitate achievement of goals, and promote partner country buy-in and sustainability of capabilities. This approach to metrics can help to demonstrate accountability, and provide greater awareness of program results and context of engagement, to DOD senior leaders, Congress, and other relevant stakeholders.

3

Addressing Biothreats through Successful Engagement

KEY MESSAGES

- Working effectively in host countries depends on the ability to communicate with local leadership, and to coordinate with multiple actors–both domestic and international. This, in turn, depends on diplomatic skills and the ability to develop, deepen, and sustain personal relationships of trust with counterparts in the host country.
- Biological Threat Reduction Program (BTRP) initiatives rely on partner country interest, perception of need, and governance structures, which can be achieved best when the diplomatic skills needed to work closely and respectfully with country partners are well developed.
- Biosecurity is not only directly affected by critical scientific disciplines, but also by interdisciplinary perspectives, and indirectly by social, economic, and cultural concerns that may be unique to the BTRP partner country.

BENEFITS OF SCIENTIFIC ENGAGEMENT TO BIOTHREAT REDUCTION

Engagement of scientists has been a cornerstone of biological threat reduction programs since their formal inception in the 1990s. The U.S. Department of Defense (DOD) promoted peaceful use of scientific knowledge and skills in the former Soviet Union with scientific partnerships. During the past decade, these engagements have provided opportunities to broach the concepts of biosafety and biosecurity with scientists in countries that never supported offensive bioweapons research and development, and to enhance biosurveillance capabilities in partner

countries using safer technologies, such as next-generation sequencing. More generally, scientist engagement ensures that activities are appropriate for the local research and public health, policy, threat and risk, and socio-cultural contexts. Furthermore, partnerships among physicians, veterinarians, public health practitioners, and scientists help to build local One Health (interlinked human, animal, plant, and environmental health) capabilities, enabling countries to prevent, detect, and respond to health security threats. Engagement also provides opportunities for scientists to become part of international research and health networks, which enables sharing of norms, awareness-raising of emerging threats and threat mitigation strategies, access to training programs and funding opportunities, and expert consultation. Long-term partnerships promote the realization of the benefits to scientists and the international community.

What Principles Guide Successful Biosecurity and Health Security Programs?

Biosecurity investments focus on natural, accidental, and intentional biological threats. More broadly, DOD investments in global health security help to prevent the spread of human and animal infectious diseases and reduce the risk of biothreats to deployed U.S. military forces, American citizens living or traveling abroad, and as a consequence to local populations as well. "At the core of global health security is a strong health system with the resources and personnel necessary to identify infectious disease threats and respond quickly before regional or global transmission" (White House, 2019, p. 7). Successful biosecurity and health security assistance programs are guided by particular principles of engagement, listed here from strategic to practical.

- All biological threats—natural, accidental, and intentional—are most effectively treated as a single challenge with many dimensions.
- To maximize biosecurity and global health security, all countries need to address naturally occurring, accidentally caused, or intentionally introduced threats and risks although the specifics of those threats and risks and associated activities will differ in different countries.
- The overall biosecurity mission encompasses anticipation, deterrence, prevention, detection, response, mitigation, and recovery. Action or intervention is possible at every stage.

- Biosecurity investments focusing on prevention and preparedness are far more cost-effective than those focusing on response.
- Successful and sustainable engagements need to be tailored to the needs of a particular country and formulated with an understanding of the overall context, which encompasses political, military, social, economic, and cultural dynamics.
- Those tailored engagements may include, if appropriate, the collaborative, multisectoral, and transdisciplinary approach known as One Health, which recognizes the interconnections among people, animals, plants, and the environment.
- Host governments need to take ownership of and support programs for such programs to be effective and sustainable.
- Biosecurity investments need to be flexible and timely while trying to anticipate future threats–both the *what* and the *where*, even if the *when* cannot be estimated.

Successful programs match people, and the most effective engagements involve collaborative partnerships and strong relationships among trusted, credible, and knowledgeable interlocutors built over time; through trust in such relationships, contentious issues can more readily be resolved and trust between nations can be enhanced. Establishing such trusted relationships is challenging, however. Each country has its own professional culture, bureaucratic tendencies, systems of incentives and disincentives, traditions and practices, policies and procedures associated with even minor tasks, not to mention schedules of holidays, celebrations, observances, and vacations. Navigating these complexities is not easy and requires a deftness of professional engagement that is as difficult to cultivate as it is essential to success.

- The most effective programmatic investments build on existing infrastructure and complement other related or overlapping programs.
- Strengthening biosafety and biosecurity systems requires interdisciplinary, whole-of-government collaboration, to include foreign, defense, finance, health, agriculture, environment, law enforcement, education, and other departments/ministries.
- Strengthening of such systems requires facilities to identify, secure, safely monitor, and store dangerous pathogens, including clinical and environmental samples that may contain viable dangerous pathogens.
- Promoting a culture of biosafety, biosecurity, and responsible conduct in the life sciences and identifying and responding effectively to biosafety and biosecurity emergencies is also essential.

- Programs need clear lines of authority, accountability and responsibility; transparent data and information systems; and a robust monitoring and evaluation framework.
- The impact of biosecurity and biosafety engagement will be maximized by fostering linkages, synergies, and partnership among experts in regional and global networks; we are better off working together than separately.

FINDING 1.4: Natural, accidental, and internationally caused outbreaks can have similar consequences for health, the economy, and national security. Despite the initial cause of the outbreak, they also have similar requirements related to common prevention, detection, response, and recovery initiatives. There are advantages to addressing these events as different manifestations of the same family of challenges. An integrated view of biological threats prevents bureaucratic boundaries from interfering with partnerships and progress. Natural, accidental, and intentional outbreaks may have ambiguous origins but the capabilities needed to address them overlap. Ultimately, needs of force protection and national health and safety may be similar in most cases, especially those with the broadest potential national security impact.

The Importance of Coordination and Communication to Engage Successfully

No U.S. government program currently has or should be expected to have the authority or the capability to act on every aspect of biosecurity; but today, organizational divisions and boundaries in the United States and globally can interfere with realizing improvements in efficiency and cost-effectiveness. To address that problem, BTRP needs to be part of a regular interagency coordination mechanism focused on mission problems and opportunities rather than on agencies and jurisdictions. Similarly, there should be regular intergovernmental discussions to connect and coordinate U.S. government and international community efforts to anticipate problems and develop interventions throughout the biological threat lifecycle.

BTRP would benefit from engaging more deeply with experts across the U.S. government and with a variety of scientists from numerous institutions that hold meetings at various public scientific forums on the

broad spectrum of natural, accidental, and intentional biological threats (e.g., the International Conference on Emerging Infectious Diseases, American Society for Microbiology, Infectious Diseases Society of America, Association of Healthcare Emergency Preparedness Professionals, and American Biological Safety Association).

BTRP endorses interdisciplinary coordination in approaching complex problems, such as preparing for naturally occurring emerging infectious disease threats through One Health approaches. However, BTRP is insufficiently engaged with agricultural institutions and One Health programs. With interest in working with international partners for better global health, and in particular, infectious diseases, increased communication with these organizations to better coordinate funds and avoid unnecessary duplication of efforts in regions would be beneficial. This would increase the effectiveness of the funding on all three sides—the U.S. government, the U.S. or other nongovernmental organizations, and the country partner.

Deeper understanding and engagement with agricultural institutions and agricultural businesses is important for improved biosecurity, as many new and emerging pathogenic threats are projected to be zoonotic (Mark et al., 2016). Several other organizations have related efforts with which BTRP should more thoroughly engage: U.S. Department of Agriculture, including the Agricultural Research Service, the Animal and Plant Health Inspection Service, the Food Safety and Inspection Service, and the new National Bio and Agro-Defense Facility under construction in Manhattan, Kansas; U.S. Agency for International Development efforts to strengthen global capacity for detection and discovery of zoonotic viruses with pandemic potential, and the Infectious Disease Detection and Surveillance project improving the quality of real-time surveillance of antimicrobial resistance and zoonotic diseases; the World Organisation for Animal Health (OIE); the Food and Agriculture Organization of the United Nations (FAO); and veterinary and agricultural colleges.

ONE HEALTH

The One Health approach is increasingly endorsed by many professional, governmental, and international organizations as the best approach for addressing complex problems such as emerging infectious diseases, food security, and antimicrobial resistance (See Box 3-1 for the example of the Bat One Health Research Network). As the U.S. Centers

for Disease Control and Prevention (CDC) notes, "One Health is not a new concept, but it has become more important in recent years. This is because many factors have changed interactions between people, animals, and our environment. These changes have led to the emergence and reemergence of many diseases" (CDC, 2018).

BOX 3-1
The Bat One Health Research Network (BOHRN)

"Scientists hypothesize that some of the world's most deadly emerging zoonotic diseases are found in bats, including Nipah, Hendra, and Marburg viruses. However, because bats contribute significantly to the health and diversity of many environments around the world, a conservation-minded approach to their study is necessary" (BOHRN, 2019).

In this regard, the Defense Threat Reduction Agency/Biological Threat Reduction Program sponsored a meeting in June 2017 that coincided with the Second International Symposium on Infectious Diseases of Bats in Fort Collins, Colorado. During this meeting, the attendees established a steering committee for the Bat One Health Research Network (BOHRN), began preliminary actions to build a self-sustainable disease surveillance network, and identified initial objectives needed to develop a comprehensive research strategy to characterize and address global bat-associated disease threats.

BOHRN is a global network that convenes multi-disciplinary and One Health–focused scientists, policy makers, research scientists, and medical/veterinary practitioners with interests in bat-related research involving pathogens of security concern. The network builds on community standards and best practices for research." BOHRN identifies and shares "information on research-funding opportunities offered by multiple institutions. Most importantly, this network fosters international relationships among collaborators, agencies, and organizations, which can produce long-term, sustainable partnerships that withstand changes in government and organization budgets, priorities, postures, and policies.

One Health promotes an integrated approach to infectious disease, linking efforts toward promoting human, animal, plant, and environmental health. Involvement of FAO in the Global Health Security Agenda

(GHSA) suggests that opportunities to more effectively include plant pathogens in the discussions, through the agriculture and food system, may be developing as a critical and currently unmet need of global health security initiatives (See Box 3-2). The danger of emerging plant pathogens and the potentially devastating effects of a pandemic affecting critical food crops is much enhanced by the widespread practice, especially in large-scale agriculture, of monocropping (McDonald and Stukenbrock, 2016).

BOX 3-2
Bioengagement on Agricultural Pathogens

Since the mid-1990s, the Biological Threat Reduction Program (BTRP) has supported research collaborations between the U.S. Department of Agriculture (USDA) researchers and scientists in partner countries. As concerns about agricultural pathogens increased since 2001, these engagements focused more on detection and characterization of pathogens that could have devastating effects on international agriculture and food systems. For example, one USDA researcher, Dr. Claudio Afonso, has been supported by BTRP, among other funders, to collaborate with scientists in partner countries on research that informs biosurveillance of Newcastle disease virus (Butt, 2018). These scientists learn how to use molecular detection technologies to identify and characterize viral strains safely and securely, and provide opportunities to engage with the international scientific and animal health communities and serve as leaders in their home institutions and countries. BTRP supports similar research efforts with scientists in partner countries.

One deficit in many One Health training and implementation programs is the common tendency to neglect the food–animal production industry (Gray and Mazet, 2019). Within these industries, many new pathogenic threats are emerging or being amplified, threatening both livestock and, directly and indirectly, humans as well. This situation is caused, in part, by the increasing scale of modern industries, providing large, dynamic populations of animals that can be decimated completely if exposed to a pathogen that cannot be controlled by current veterinary and biosecurity practices. Outbreaks in these larger animal populations may also affect animals on smaller farms. The now-endemic pathogen could become susceptible to continued pressures to evolve and possibly become more virulent to humans and/or animals (Gray and Merchant,

2018). Examples include antimicrobial-resistant pathogens in poultry and swine, which have been linked to human morbidity (Marshall and Levy, 2011), and the many types of influenza A virus, which now freely circulate in swine (Borkenhagen et al., 2019) and could have pandemic potential in humans.

A decade ago there were anticipations of global spread of African Swine Fever (ASF) and measures to prepare to prevent or respond to a pandemic outbreak were not systematically implemented prior to the current rapidly spreading multi-country outbreak of ASF in Asia (Costard et al., 2009). Box 3-3 highlights an example of a BTRP engagement that builds on these One Health concepts.

BOX 3-3
International Federation of Biosafety Associations

The International Federation of Biosafety Associations (IFBA) was established in 2001 as a not-for-profit organization whose members are regional and national biosafety associations. IFBA's mission is to advance biosafety and biosecurity in research, industry, and human and animal health sectors by providing opportunities for professional certification in these areas, promoting best practices for biorisk management (e.g., a consolidated risk management framework to address accidental and deliberate biological risks in laboratories), raising awareness about biological risks, promoting partnerships to address biological risks, and assisting with biosafety and biosecurity policies. Because IFBA provides professional certifications, it does not conduct any training itself. However, it supports its members in identifying training resources, best practices, and training needs. IFBA works with stakeholders from all relevant disciplines–including architects of laboratories, facility engineers, scientists, biorisk management professionals and biosafety officers, and policymakers–and with regional and intergovernmental organizations, such as the World Health Organization, World Organisation for Animal Health, Biological and Toxin Weapons Convention, Alliance for Health Security Cooperation, Association of Southeast Asian Nations, and Interpol.

FINDING 5.2: The inextricable links among human, animal, plant, and environmental health highlight the risk of natural or human-made pathogens in the food system, along trade and travel routes, and through changes in the environment. Each of these factors can either severely affect production of major plant food crops and meat products, or promote the appearance and spread of new potentially zoonotic infectious disease threats to humans in addition to their impacts on the affected animal populations. These risks could result in significant health, social, political, and economic consequences leading directly to political and civil unrest–especially in countries with pre-existing marginal or unstable governmental systems and weak infrastructure.

FINDING 5.3: Inadequate provision of fundamental needs, such as food and clean water, enables transmission of environmental pathogens into the human population and increases opportunities for conflict, which present a different type of security risk.

TRUSTED RELATIONSHIPS ARE CRITICAL TO SUCCESS

As stated earlier in this report, the success of an international engagement program typically is not achieved solely because of the program, the training, the research, the introduction of a new technology, or even the money (Carmeli et al., 2012). While formal institutional relationships are, of course, critical, highly successful and sustainable engagements are often the result of two or more individuals who may come from widely diverse backgrounds in their respective home countries but who see a common need, generally agree regarding how to address that need, and are able to work together in an environment of openness and trust. It is not unusual for the most effective relationships to be formed between individuals of similar stature in their respective communities (Brown and Franz, 2016).

This is not the first time that the importance of human relationships in Cooperative Threat Reduction (CTR) programs has been underscored. One of the recommendations in the 2009 National Academy of Sciences report called for the recognition, “that personal relationships and professional networks that are developed through U.S. government CTR

programs contribute directly to our national security and that new metrics should be developed to reflect this" (NAS, 2009, p. 13).

It is easier to measure activities than to measure the impact of relationships. Seeking success and program efficiency, the DOD CTR Program has spent hundreds of thousands of (engagement) dollars asking domestic academics and nongovernmental organizations (NGOs) to design systems of metrics with which to evaluate the effectiveness of engagements. There is little evidence that these costly and often very complex schemes have been useful or even used. In 2016, some senior staff members from BTRP and their collaborators authored a paper titled, *Scientific Collaborations: How Do We Measure the Return on Relationships?* (Fair et al., 2016). This paper, particularly coming from within BTRP, is an important recognition of the principle and the consistent identification of relationships of trust as a critical factor underlying successful collaborations.

This study committee underscores the notion that human relationships of trust not only contribute to the effectiveness of engagement programs but are critical to success, sustainability, and the positive security effects that must be generated. When these relationships are established between serious and professionally compatible individuals, confidence, trust, openness, and truly effective communication often results. The BTRP publication describes the value of visualizing and quantifying scientific social networks that develop from a specific event–such as a training workshop–to estimate the impact of collaborations on a field or mission, such as reducing the threat of infectious diseases. This depends on support of investigators to "communicate and coordinate their research, training, and educational activities across disciplinary, organizational, geographic, and international boundaries," and the use of alternative metrics to generate real-time evidence of research influence (Fair et al., 2016, p. 6). This may be through social media as a means of assessing how the work is being discussed and shared, and by whom, including researchers as well as the public. The committee also recognizes that this return on relationships (sometimes referred to as "ROR") concept (Fair et al., 2016, p. 2) is a hard lesson for U.S. engagement programs and implementers to absorb and operationalize, and that it will require considerable discussion and development of tools tied to assessing the impact of CTR programs for the concept to be fully adopted.

FINDING 3.1: Successful programs match people from the two partner countries who have the necessary technical and

diplomatic skills and the willingness to develop relationships of trust through working together toward common goals. These interpersonal relationships form the resilient core of the larger institutional relationships.

There are a number of prior examples of U.S. government-led and -supported global programs that have succeeded and improved response to infectious disease threats, and provide insights for BTRP to consider.

LEARNING FROM DISPARATE EXPERIENCE

An Example of Success Fighting against a Deadly Infectious Disease Pandemic Threatening Stability and Security: The U.S. President's Emergency Plan for AIDS Relief (PEPFAR)

HIV/AIDS, a threat of zoonotic origin, has been an ongoing pandemic for nearly four decades. While there has been enormous progress to control and treat HIV, the virus still defies global efforts to halt transmission. In the early to mid-1990s, before highly active antiretroviral therapy became affordable for large numbers of people, the pandemic grew dramatically. Many believed it not only threatened the stability of the hardest-hit countries, but also represented a security threat for countries like the United States.

For the first time in history, the United Nations Security Council discussed a health issue as a threat to international peace and security. Vice President Al Gore presided over the meeting on January 10, 2000 (UN, 2000b) as United Nations (UN) Secretary-General Kofi Annan explained the security implications of the pandemic:

> The impact of AIDS in [southern and eastern Africa] is no less destructive than that of warfare itself. Indeed, by some measures it is far worse. Last year, AIDS killed about ten times more people in Africa than did armed conflict.
>
> By overwhelming the continent's health services, by creating millions of orphans and by decimating health workers and teachers, AIDS is causing social and economic crises which in turn threaten political stability. It also threatens good governance, through high death rates among the elites, both public and private.

> In already unstable societies, this cocktail of disasters is a sure recipe for more conflict. And conflict, in turn, provides fertile ground for further infections. The breakdown of health and education services, the obstruction of humanitarian assistance, the displacement of whole populations and a high infection rate among soldiers—as in other groups which move back and forth across the continent—all these ensure that the epidemic spreads ever further and faster. (UN, 2000a)

During his State of the Union address in January 2003, President George W. Bush announced what has come to be known as the President's Emergency Plan for AIDS Relief (PEPFAR), which received strong bipartisan support from Congress.

PEPFAR is the largest commitment by any nation in the world to address a single disease and is generally viewed as one of the most significant and successful global health initiatives ever undertaken. It is a prime example of the U.S. government generating trust and respect from citizens and governments. Initially authorized at a level of $15 billion over 5 years, the PEPFAR appropriation for FY 2018 totaled more than $6.5 billion, with 79 percent for bilateral HIV programs and 21 percent allocated to the Global Fund to Fight AIDS, Tuberculosis and Malaria (KFF, 2019b).

The program has saved millions of lives over the years. In FY 2018, through PEPFAR support, nearly 14.8 million people received antiretroviral therapy and nearly 6.4 million were supported through orphans and vulnerable children programs (PEPFAR, 2019b). As of September 2018, PEPFAR has "supported testing services for nearly 95 million people; prevented more than 2.4 million babies from being born with HIV, who would have otherwise been infected; provided care for more than 6.8 million orphans and vulnerable children; supported training for more than 270,000 new healthcare workers; and, supported antiretroviral treatment for more than 14.6 million people" (PEPFAR 2018).

In recognition of the security implications of the HIV/AIDS pandemic, particularly when the partner country military is itself significantly infected by the virus, DOD has been an important provider of PEPFAR assistance.

DOD implements portions of the PEPFAR programs by supporting HIV/AIDS prevention, treatment, and care; providing strategic information; supporting human capacity development; and facilitating

"program and policy development in host militaries and civilian communities of 73 countries around the world. These activities are accomplished through direct military-to-military assistance, support to NGOs and universities, and collaboration with other U.S. government agencies in-country. Members of the defense forces in 13 PEPFAR focus countries have been the recipients of DOD military-specific HIV/AIDS prevention programs designed to address their unique risk factors, in addition to treatment and care programs for their personnel. In these 13 countries alone, military programs have the potential to make an impact on more than 1.2 million people, including active-duty troops, their dependents, employees, and surrounding civilian communities. DOD supports a broad spectrum of military-specific HIV-prevention programs, infrastructure development and support (including laboratory, clinic and hospital facility renovation, equipment, and training), and treatment and care activities" (PEPFAR, 2019c).

PEPFAR's focus on prevention, care, and treatment of HIV/AIDS requires a very high level of collaboration within the U.S. government, with civil society and the private sector, with a multitude of bilateral and multilateral institutions, and with many other stakeholders. Cooperation with the host government and its military forces is fundamental to the success of the program.

An essential element of PEPFAR's success, and one worth emulating, has been its use of a coordinating mechanism known as Country Operational Plans. PEPFAR emphasizes that it "is committed to continually strengthening its partnership with host-country governments to ensure alignment between PEPFAR contributions and national priorities and investments. Collaborative planning between PEPFAR and host-country governments is critical to ensuring that prioritized interventions are scaled, geographic priorities are shared, and that all available resources for HIV/AIDS in the country are utilized optimally" (PEPFAR, 2019a, p. 109).

In a presentation at a 2018 National Academies of Sciences, Engineering, and Medicine workshop in Amsterdam focused on assisting infectious disease laboratories in low-resource countries, Jonathan Towner of CDC said that it is often easier to add on to an existing laboratory than to build a new laboratory. In that respect, the many HIV diagnostic laboratories established by PEPFAR across Africa have become a great resource for combating other infectious diseases when additional capacities were needed. Towner provided examples: CDC converted the HIV diagnostic laboratory in Luanda, Angola, and built on the HIV

laboratory in Gulu, Uganda, for diagnostic work on viral hemorrhagic fevers. This study committee notes that these established laboratories are more than buildings and equipment. They are useful because they are institutions, with trained people, practices, organization, relationships, and established supply chains. Utilization of these investments is a model of how to leverage engagements (NASEM, 2019).

An Example of the Spread of a Deadly, Previously Unknown Pathogen that Was Stopped through Effective Governmental Action: The SARS Outbreak (2003)

One particularly dramatic example of an emerging infectious disease outbreak is the 2003 Severe Acute Respiratory Syndrome (SARS) outbreak, a contemporary example of the sudden appearance of a previously unknown pathogen that spread around the world as infected individuals rapidly traveled to distant countries via air routes. It eventually infected at least 8,096 persons with proven or probable SARS, resulting in 774 deaths (CDC, 2016).

The sequence of events is now well known. The initial indication of a new outbreak reached public attention via a report in ProMED-mail (Program for Monitoring Emerging Diseases) on February 10, 2003, followed by a report on February 11 that the Chinese Ministry of Health was aware of 300 cases of an atypical pneumonia syndrome in Guangdong province in southern China (ISID, 2003a, b). One month later, cases were also identified in Hong Kong and Vietnam, and the World Health Organization (WHO) and CDC issued health alert notifications (WHO, 2003). Laboratory analysis at CDC, the Bernard Nocht Institute for Tropical Medicine in Hamburg, Germany, and Queen Mary Hospital, University of Hong Kong, indicated the cause to be a previously unknown coronavirus, soon to be named SARS (Drosten et al., 2003; Ksiazek et al., 2003; Peiris et al., 2003). Over the next 4 months, as the outbreak affected Canada and the United States, CDC assigned more than 800 staff to the response, both domestically and internationally. CDC issued infection control guidance for patients with suspected SARS, interim laboratory biosafety guidelines for handling and processing specimens from these patients, and guidelines for management of exposures to SARS in healthcare and other institutional settings. CDC also provided travel alerts and advisories for U.S. citizens regarding travel to high-risk destinations. CDC contributed the equivalent of 46,714 days of work to the SARS response, met nearly 12,000 flights, and distributed more than 2.7 million

health alert notices to passengers arriving directly and indirectly from affected areas. When ill passengers were reported on a flight arriving in the United States, they were met by members of the CDC quarantine staff to evaluate the affected passenger for possible SARS, provide referrals to a healthcare provider, collect locating information from other passengers, and coordinate with federal, state, and local public health authorities (IOM, 2004).

By the end of the outbreak there were 438 probable and suspect cases of SARS in Canada, primarily in Toronto, including 44 deaths and 25,000 Toronto residents placed in quarantine (Health Canada, 2003). By contrast in the United States there were just eight proven, 19 probable, and 137 suspected SARS infections reported, with no fatalities (CDC, 2003). Had the United States not taken sufficient action to prevent the spread of SARS into the country, the SARS outbreak undoubtedly would have resulted in many U.S. fatalities and huge expenditures. By operating as it was designed and should do, including quick action, a prepared public health system, and a vigorous response prevented a larger outbreak with serious outcomes.

SARS heightened awareness among the international public health and political communities that every country faced biothreats, ranging from newly emerging diseases to bioterrorism, that might not be foreseeable, and it spurred completion of the revised International Health Regulations (IHR) (2005). The outbreak also demonstrated the importance of disease surveillance of transborder diseases through networks and underscored the nexus between animal health and human health, with concerns ranging from small wet markets to large-scale agricultural operations. Rapidly moving pathogens of pandemic concern are at the human–animal intersection. And it is noteworthy that the second wave of SARS, in Toronto in May 2003, is believed to have come from relaxed use of infection-control precautions–thereby emphasizing the critical role of strict biosecurity and biosafety procedures. The U.S. government's response to SARS carries lessons for the many government agencies working to reduce biological threats, including the Defense Threat Reduction Agency and BTRP, to improve disease surveillance and biosecurity aspects of the response to prevent, mitigate, and control outbreaks in partner countries. Through effective engagement, BTRP can contribute to establishing the means by which emerging diseases can be detected early and response can be initiated safely, securely, and rapidly.

An analysis done at the U.S. Air Force Counterproliferation Center explains the direct relevance to military commanders to outbreaks such as SARS:

> Several key points for military commanders should be highlighted from the international lessons learned regarding quarantine and SARS. First and foremost is the understanding that the most severe biologic event a commander may encounter is a previously unknown disease with human-to-human transmission, primarily involving the respiratory route. A new disease like SARS, or a genetically altered agent that may be used by a bioterrorist, requires additional planning for this worst-case scenario. Quarantine needs to be part of the strategy, as was shown with SARS. Second, delay in implementing quarantine can have devastating effects that result in loss of situational control as occurred in China. Decisive actions must be taken and coordinated up the chain of command prior to a commander having sufficient information to make a decision. Third, healthcare workers are at highest risk of becoming exposed or infected prior to identification of the outbreak, which may result in the need for quarantine of entire medical facilities. Fourth, cooperation between support agencies is critical to educate the community, encourage medical identification and treatment, increase patient compliance, enforce requirements when needed, and obtain overall buy-in from the public. Fifth, broad legal and policy challenges exist in responding to an infectious disease outbreak, and guidance is needed to orchestrate a prompt and effective response. This should be addressed prior to a crisis. Sixth, the quarantine implementation plan chosen by leadership should provide the best opportunity to contain the disease without enforcing excessive or unrealistic restrictions on a community as occurred in China and Taiwan. Finally, each disease is unique, requiring an understanding of its epidemiology to ultimately develop a definitive treatment strategy; however the initial response prior to identification of the infectious agent should be non-specific and cover a worst-case scenario. (Miller, 2005)

An Example of a Previously Known Pathogen Unexpectedly Appearing in a New Location and the Response to a Sudden Transboundary Biological Threat: Ebola in West Africa (2014-2016) and in the Democratic Republic of the Congo (2018-Present)

The Ebola virus outbreak in West Africa in 2014-2016 was an eye-opener and a wake-up call to the continuing critical deficiencies in the national, regional, and global mechanisms for detecting, reporting, and responding to an epidemic as envisioned under IHR (2005), and the potential global threat from infectious disease outbreaks. The best reconstruction of the West Africa outbreak tracks to the death of one young infant in the Forestière region of Guinea at the end of December 2013. The outbreak grew dramatically and spread over the following months, and the strain was identified in mid-March 2014 as Ebola Zaire. By the end of March 2014, the coordinator of the Médecins Sans Frontières project in Conakry, Guinea, cautioned, "We are facing an epidemic of a magnitude never before seen in terms of the distribution of cases in the country" (Samb, 2014).

Guinea, Liberia, and Sierra Leone were ill-equipped for such a disaster because chronic poverty and civil war had undermined local health systems, and there was therefore an insufficient number of doctors and nurses. On top of this, years of civil war and violence had left the populations wary of authority and government, and without trust in the urgently needed outside assistance, rumor and conspiracy theories abounded.

BTRP made significant contributions in the early stages of the outbreak. Dr. Carl Newman, chief scientist for BTRP, informed the committee that, beginning in March 2014, BTRP–through "strategic positioning and good old-fashioned serendipity"–supported laboratories running Ebola diagnostics in Sierra Leone and Liberia. BTRP had a pre-existing project working at the Kenema Government Hospital in Kenema, Sierra Leone, focused on understanding the seasonal variability of Lassa fever to help improve surveillance. BTRP's existing contract enabled it to rapidly pivot from the research project on Lassa fever to providing diagnostics for Ebola. The U.S. Ambassador to Liberia then asked BTRP to establish such diagnostic capacity in Liberia (Newman, 2018).

BTRP (then known as the Cooperative Biological Engagement Program [CBEP]) later described the work in its list of annual accomplishments:

> CBEP supported the U.S. and international efforts to stem the ongoing Ebola Virus Disease (EVD) outbreak in West Africa and prepare at-risk countries for potential EVD cases. This outbreak underscored the unique and unpredictable nature of the biological threats that CBEP seeks to reduce by enhancing BS&S [biosafety and biosecurity] practices as well as BSV [biosurveillance] systems. Through provision of equipment, training, and transportable laboratory diagnostic capability, CBEP contributed substantively to the EVD outbreak global response…. [This] showcased CBEP's nimbleness to support activities in the fight to control the EVD outbreak that devastated Guinea, Sierra Leone, and Liberia. In doing so, CBEP positioned itself as a cornerstone and major contributor to activities in the region carried out by the U.S. interagency and members of the international community handling this emerging threat. (U.S. DOD, 2015)

Within WHO, there was some pressure early-on from certain members of its Regional Office for Africa to downplay the problem for political, economic, and trade reasons. It was not until August 8, 2014, that WHO Director-General Margaret Chan declared the outbreak a Public Health Emergency of International Concern (PHEIC). By then, it was the largest Ebola outbreak ever recorded up to that time (WHO, 2014).

The UN, many governments, foundations, NGOs, and the private sector responded. Existing institutional aid relationships fostered provision of assistance from the United Kingdom to Sierra Leone, France to Guinea, and the United States to Liberia. President Barrack Obama directed that this be a national security priority, and on September 16, 2014, he announced that, at the request of the Liberian government, a military command center would be established in Liberia to support civilian efforts across the region (White House, 2014).

The UN Security Council held an emergency meeting and on September 18, 2014, determined that the "unprecedented extent" of the Ebola outbreak in West Africa constituted a threat to international peace and security. The Security Council emphasized that "the outbreak is undermining the stability of the most affected countries concerned and, unless contained, may lead to further instances of civil unrest, social tensions and a deterioration of the political and security climate" (UN, 2014).

The U.S. military responded rapidly, as described in a subsequent DOD study:

> While the military dealt with force health protection in the past (e.g., 1918 Spanish flu pandemic), Operation UNITED ASSISTANCE was the first U.S. military operation to support a disease-driven foreign humanitarian assistance mission. The international community's lack of preparedness to respond to the scale and severity of the Ebola outbreak and delayed decision making allowed the disease to spread, complicating the subsequent Department of Defense and international response. The unique aspects of the mission, the evolving Department of Defense roles, the lack of understanding of the operational environment, and force projection shortfalls presented challenges in establishing an expeditionary base in an austere environment. (U.S. DOD, 2016)

By the time the PHEIC related to Ebola in West Africa was eventually lifted on March 29, 2016, a total of 28,616 confirmed, probable, and suspected cases were reported in Guinea, Liberia, and Sierra Leone, with 11,310 deaths (a case fatality rate of almost 40 percent) (WHO, 2016c).

Following the West Africa Ebola epidemic, several groups, including the National Academies Commission on a Global Health Risk Framework for the Future, undertook lessons-learned exercises and proposed actions to improve global health preparedness and response for future infectious disease threats. One of the lessons learned from the 2014-2016 outbreak was the confirmation that Ebola can suddenly emerge in a part of Africa in which it was not previously recognized to be a threat. The lack of prior experience with Ebola in West Africa had the effect of skewing diagnostic considerations to other well-described pathogens known to be present in the area, such as cholera and Lassa fever, contributing to the delay in making the correct diagnosis. The belief that the Ebola virus was not circulating in the region was, in fact, a myth, as there already was serosurveillance evidence, albeit limited, that chimpanzees and humans had previously been infected. It is not clear that human virulent Ebola Zaire was present in West Africa long before the outbreak in 2014-2015. These positives could be cross-reactive with other Filoviruses or non-

virulent Ebola viruses not yet characterized. If the data are not entirely convincing, there is some evidence that where there is smoke, there is fire.[1]

Early identification and counteraction are critically important to a successful response to emerging biological threats. In reality this means that some assets and capabilities need to already be in place for response because: (1) outbreaks can arise in unpredictable locations; (2) disease transmission can be fast; and (3) effective response often requires familiar and trusted relationships.

This work is security work, not just public health work, and this is what DOD does. Although what outbreak will happen at a given time is unpredictable, vulnerabilities to significant outbreaks are observable (See Box 3-4). BTRP was well positioned in West Africa before the 2014 Ebola virus pandemic, which was fortuitous but not accidental. To be effective in the future, biothreat reduction programs will have to anticipate needs and position themselves where those needs are likely to arise.

BOX 3-4
Outbreak Characteristics

While historical assessments of the outbreak characteristics of an emerging virus pathogen are an important basis for predicting the course of an outbreak, they do not preclude the potential for dramatically different outbreak dynamics in the next outbreak.

To their credit, the WHO Member States and Secretariat recognized that WHO leadership and performance during the West Africa Ebola outbreak were not at an optimal level. WHO instituted major institutional reforms, including creation of a Health Emergencies Program and establishment of the Contingency Fund for Emergencies (WHO, 2017d, 2020a). And the World Bank established the Pandemic Emergency Financing Facility to provide surge financing (PEF, 2019).

These new mechanisms came into play in August 2018 in eastern provinces of the Democratic Republic of the Congo (DRC), an area of

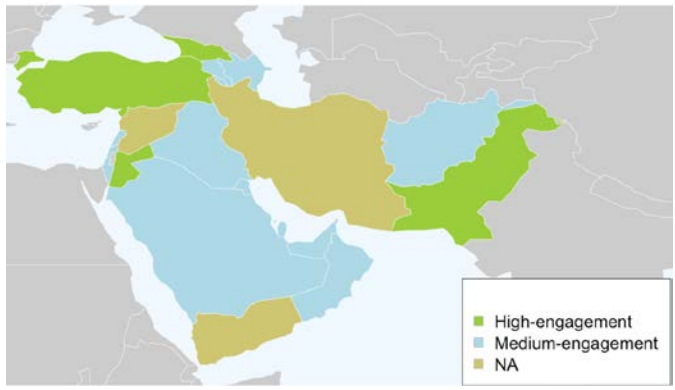
[1] In the 1990s, there was an outbreak of Tai Forest Ebola Virus in an Ivory Coast chimpanzee population, and subsequent human infection in a veterinarian. Therefore, if this variant is present, it is certainly possible others – including the bat species of Ebola – are also there (Boisen et al., 2015; Formella and Gatherer, 2016; Keita et al., 2018; O'hearn et al., 2016; Schoepp et al., 2014; Formenty, Boesch, et al., 1999; Formenty, Hatz, et al., 1999).

active armed conflict, extreme poverty, poor healthcare accessibility, and major distrust for authority figures and the government by the population. Given the known presence of the virus elsewhere in DRC and previous outbreaks of Ebola in other nearby countries, such as Uganda, the fact that it had not been identified previously in this part of DRC was not a reassurance that it would not at some time be introduced. The challenges of controlling this continuing outbreak and limiting its spread in a conflict zone are enormous, with more than one million displaced persons, security concerns for health workers attempting to identify cases, immunize, and track and monitor close contacts in areas where cross-border movement of people is common. As of January 2020, more than one year since it first was detected, there were more than 3,400 confirmed and probable cases with a death toll above 2,100, which makes it by far the second-worst epidemic of the virus on record (WHO, 2020b).

Ebola outbreaks have ranged all the way from East Africa to West Africa, and the committee does not underestimate the difficulties in trying to predict where an Ebola outbreak could occur or, given limitations on resources, what could be done in advance to preposition bioengagement programs and surveillance capabilities (particularly in areas of conflict). Nevertheless, one needs to ask if all of this could have been better anticipated. It is difficult not to ask the "what if" questions: What if there had been investments to establish an effective disease surveillance system before the outbreak occurred? What if community engagement and support for improved healthcare systems had been initiated? BTRP was part of the response to Ebola in West Africa in 2014 and needs to be part of forward-looking discussions in the future so that it, too, will be better prepared for the next infectious disease event with national security implications. One means of participating in forward-looking discussions is through professional, scientific networks (See Box 3-5).

BOX 3-5
The Western Asia Bat Research Network (WAB-NET)

The Western Asia Bat Research Network (WAB-NET) is a collaborative, sustainable network of wildlife researchers and public health experts in the region. The network includes representatives from more than 12 countries (Afghanistan, Armenia, Azerbaijan, Georgia, Iraq, Jordan, Kuwait, Lebanon, Oman, Pakistan, Qatar, Saudi Arabia, Turkey, and United Arab Emirates) in Western Asia.



WAB-NET aims to promote bat disease surveillance through capacity building and collaboration, and, to enhance knowledge of the diversity and distribution of native bat species and their associated viral communities.

During the network's meetings, the members are able to discuss research opportunities that are unique to the region, and outline potential hypotheses that could be tested through an active network of bat researchers studying bat-associated viral associations.

In this regard, the Middle Eastern researchers have opportunities for collaboration through WAB-NET that lead to the improvement of local and regional capacity for zoonotic disease investigations and early detection.

In a region that is politically unstable, WAB-NET could facilitate cross-border research cooperation and continually work to guard against threats posed by zoonotic disease outbreaks. Thus, the network could serve as an instrument for stability and security of the region through early detection of zoonotic disease threats.

An Example of a Successful DOD Joint Program on Filoviruses and Severe Sepsis: The Joint Mobile Emerging Disease Intervention Clinical Capability, Uganda (Ongoing)

The Makerere University Walter Reed Project (MUWRP) in Uganda was established in 2002, and is one of five international research sites established by DOD through a program centered at the Walter Reed Army Institute of Research. The intention was to establish the capacity to detect outbreaks originating in an unstable region of DRC that cross the border

to Uganda. This project includes an isolation ward, diagnostic laboratory, and clinical research capacity. MUWRP serves as the coordinating entity for the Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) program, as follows:

> The Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) program is a collaboration between U.S. and Ugandan researchers. JMEDICC provides a platform for clinical trials in filoviruses during an outbreak setting. The JMEDICC program is establishing a pilot demonstration of the capabilities at Fort Portal Regional Referral Hospital, in Kabarole District. This platform includes establishing an Isolation [Unit], strengthening the hospital laboratories to provide services beyond traditional hospitals in Africa, training staff in advanced supportive care and scientific rigor, conducting clinical research on sepsis and establishing mobile capabilities to conduct clinical research during an outbreak anywhere in the country. This platform will allow for rapid response to test the new therapeutics or medical countermeasures during the next Filovirus outbreak. MUWRP is the coordinating entity in Uganda and works closely with the Infectious Diseases Institute. (MUWRP, 2019)

As a mechanism to provide training through actual research collaborations, JMEDICC initiated the Austere Environment Consortium for Enhanced Sepsis Outcomes (ACESO) study, through the Henry M. Jackson Foundation and the U.S. Naval Medical Research Center. It is aimed at identifying the causes of sepsis in this region of Uganda and improving "survival for patients with sepsis in resource-limited settings through early recognition, diagnosis, and evidence-based clinical management" (MHRP, 2020). Because ACESO was there, local staff were being trained to safely identify and care for patients with Ebola or other emerging infections, track and monitor contacts, and implement studies of natural history and new interventions. It was also available to address the potential arrival of Ebola-infected individuals from the outbreak in DRC. The investment in the JMEDICC program is an example of anticipation. Because it was there at a potentially vulnerable border crossing, Ugandans were prepared and able to react quickly and effectively when a family

incubating Ebola crossed the border from DRC in August 2019, and they effectively prevented further transmission within Uganda.

Examples of Proactive International Engagement: Active Participation in Key International Meetings Focused on Biological Threats

BTRP, the European Union, Canada, and the United Kingdom provided support for and participated in the Second Global Conference on Biological Threat Reduction organized by OIE in 2017. More than 300 participants from 70 countries attended the conference, including delegates from OIE member countries, donors, scientists, and stakeholders from the animal, human, public health, and law enforcement communities.

The conference focused on four topics: (1) developments in nonproliferation instruments and global health security efforts; (2) international discourse on technology applications; (3) systems for promoting collaboration to facilitate preparedness efforts; and (4) biological threat reduction in the future (OIE, 2017). The conference featured side events on "Espionage, epizootics, and economics: safeguarding global animal health"; "Enhancing preparedness through simulated exercises and capability building"; and "Building interagency collaboration at the national and regional levels for biological threat reduction through simulation (table-top) exercises" (OIE, 2017, p. 2). During the conference, OIE identified several overarching themes, including the need to promote collaboration, peaceful use of science and technology advances, international security and health security instruments, and sustainability and self-reliance, all of which are relevant to BTRP's mission. In its final report, OIE listed several recommendations for addressing these themes and promoting One Health approaches to threat reduction (2017).

By contrast, BTRP senior leadership would have benefited from participation in the November 2018 GHSA Ministerial Meeting in Bali, Indonesia. More than 600 delegates from 49 countries attended, including a large delegation from the U.S. government led by the Deputy Secretary of Health and Human Services and including the Deputy Assistant Secretary of Defense for countering weapons of mass destruction. At the Ministerial Meeting and in several side meetings, GHSA Action Package 3 on Biosafety and Biosecurity was discussed at length. An event on GHSA-relevant Contributions of the Defense and Security Sectors in Support of Civilian Authorities featured speakers from the U.S. Pacific

Command and the African Partner Outbreak Response Alliance as well as the Indonesian surgeon general. A U.S. Deputy Assistant Secretary of Defense stated publically, "We encourage defense sectors to use GHSA's frameworks to prevent, detect, and respond to threats." The Bali Ministerial Meeting, and especially the side meetings, resulted in rich and productive discussions involving ministers and senior officials from around the world. They served to advance awareness and collaboration on global health security broadly and on biosafety and biosecurity specifically, while maintaining the important catalytic role of GHSA through the newly approved GHSA 2024 framework. Such engagement and participation of BTRP at these meetings is essential for the program to remain current and scientifically informed, as well as to establish networking connections with key leaders from around the world.

4

Key Roles for the Department of Defense in Biological Threat Reduction

KEY MESSAGES

- The Department of Defense (DOD) provides a wide range of direct and indirect support to ensure the nation's security globally, including biosecurity and biosafety.
- The Biological Threat Reduction Program (BTRP) operates outside of the United States to make positive change possible and, if appropriately synchronized with the rest of DOD and U.S. government agencies as well as other local partners, can be of significant value in reducing the likelihood of surprises in the form of vulnerabilities and threats, including infectious disease or other political, economic, or social events affecting the security environment, all in a cost-effective manner.
- The critical elements of BTRP success are difficult to replicate on a large scale. Appropriate diplomacy and an understanding of human relations significantly improves the likelihood of successful initiatives. BTRP has the potential to combine diplomatic skills with its location in DOD to maximize the impact and cost effectiveness of its efforts.

"The Department of Defense provides the military forces needed to deter war and ensure our nation's security" (U.S. DOD, 2019c). Under this broad mission, DOD supports U.S. government programs in global health playing multifaceted and evolving roles, which are increasing in scope. Some see DOD's global health efforts as manifestations of soft power and diplomacy. Others see elements of DOD's involvement as advancing medical infectious disease research; developing new diagnostics for infectious disease control and prevention; and tracking, preparing for, and responding to infectious outbreaks around the world (KFF, 2019a). DOD's

work also helps strengthen other countries' efforts to address infectious diseases (KFF, 2013, 2019a; Michaud et al., 2012a, 2012b). Still others see DOD's global health efforts as "force health protection and readiness, medical stability operations, and threat reduction" (Michaud et al., 2012, p. 9). Detailed analyses of DOD's substantial global health efforts, with a chief focus on infectious disease threats, are recorded in recent reports by the Kaiser Family Foundation (KFF, 2013; Michaud et al., 2012a, 2012b).

The role of BTRP in supporting DOD's global health missions has traditionally fallen, and will likely continue to fall, under the deterrence part of the DOD's mission statement. While there may be instances in a post-conflict setting in which BTRP could be asked to engage in securing weapons of mass destruction or helping redirect weapons scientists, the vast majority of its efforts will likely occur in countries struggling to work safely and securely with infectious agents during a local outbreak with global pandemic potential. This may increasingly occur in post-conflict settings, such as in Liberia and Sierra Leone during the Ebola outbreak (2014-2015), or in areas with groups or militias in armed conflict with the local and national government, as in the northeast of the Democratic Republic of Congo at the present time.

Outside Contiguous United States Army and Navy Service Laboratories have been operational for much longer than has the Cooperative Threat Reduction Program (CTR). The mission of the laboratories overlaps with that of BTRP, but has traditionally been built primarily on science and health bases with a secondary focus on biosecurity. The disease surveillance and research conducted in those laboratories has consistently proceeded from the perspective of human or animal health rather than that of infectious agents or laboratory security, unlike the perspective from which BTRP has operated. Yet, these laboratories have, for more than seven decades, contributed significantly to U.S. national security. They have done this through disease surveillance, applied research in regions where important diseases are endemic, and particularly through building strong working relationships of trust with local scientists. These relationships also contribute to the local scientists' awareness of potential disease threats and risks to their own nation and elsewhere in the world. While individuals deployed to these laboratories frequently turnover every 2 to 3 years, it is the longevity of the initiative that has contributed so much to these personal connections. Less easily measured, but critical nonetheless, good public and human, animal, and plant health in the engaged country also contributes to social, economic, and political stability in the region. These laboratories have

made a clear contribution to U.S. national security from an almost purely health platform.

BTRP engages in health-oriented efforts as well (e.g., diagnostic platforms and disease surveillance systems), but with a greater focus on pathogen and laboratory security, work that reduces the likelihood that often unique endemic pathogens can somehow be obtained and exploited, particularly in the present era, by sub-state actors or groups. Whereas the service laboratories—as well as the Centers for Disease Control and Prevention (CDC), U.S. Agency for International Development, and assistance programs such as the President's Emergency Plan for AIDS Relief, and the President's Malaria Initiative—focus primarily on health, BTRP engagements provide a primarily security-oriented perspective.

Since its evolution into CTR 2.0 much of the BTRP mission has been focused on engaging people to promote professional/technical capabilities to address current and future biothreats, naturally occurring, accidentally caused, or intentionally introduced. Specifically, such engagement can connect infectious disease laboratories around the globe, usually government supported and run, to facilitate sharing of principles, values, ethics, proper procedures, and awareness of threats and risks that can change the way those responsible think about their jobs and responsibilities to their own nation and to the global community. BTRP is in many ways a unique program, focused on a specific spectrum of challenges, working as part of the broader DOD to seek to deter conflict while always preparing for it. BTRP operates outside of the United States to make positive change possible and, if appropriately synchronized with the rest of DOD and U.S. government agencies as well as other local partners, can be of significant value in reducing the likelihood of surprises in the form of infectious disease vulnerabilities and threats or other political, economic, or social events affecting the security environment, all in a cost-effective manner.

Numerous opportunities exist for DOD to deter hostilities and contribute to national security and global health, and some are precisely aligned with the work of BTRP, including the following:

- Effectively engage military medical expertise in other countries
- Draw on U.S. military medical capabilities and special expertise in microbiological threats within the U.S.-based and at overseas DOD medical research laboratories
- Promote consolidation of infectious disease archives/sample libraries
- Focus on security for agent and clinical sample repositories, facilities, and workers

- Provide logistics and support for response when DOD's capabilities are unique (regardless of the size of BTRP's contribution relative to the overall challenge)
- Fill gaps between U.S. government programs in response to emerging threats
- Provide funds to implementing agencies
- Access funds designated as security-related versus funds allocated for foreign assistance
- Respond rapidly to arising global health security needs
- Engage with partner countries through sustained scientific programs

Given these opportunities, it seems very likely that BTRP will continue to play important roles in identifying and rapidly responding to emerging biological threats, especially when they threaten the stability of local and regional partners, and have potential to impact the United States.

BTRP must anticipate the complex array of diverse, modern biological threats and have the latitude to partner with other U.S. agencies to seize opportunities worldwide to mitigate these threats and risks. This means, in part, identifying locations vulnerable to emergent biological threats, vectors for transmission, and technologies that introduce new capabilities that can be used for positive or negative purposes. Perhaps most important, anticipating threats, means engaging with the local people who can help prevent, counter, and respond. Those professionals, whether government, military, or academic, are important partners, and cooperation needs to be nurtured and sustained over time.

To address such emergent threats and risks, the Office of the Under Secretary of Defense for Policy and BTRP must monitor and, when possible, anticipate future vulnerabilities. BTRP is in a position to assess security as well as training needs and develop and implement a plan to prepare and bolster local capabilities to detect and respond to biothreats whether they be natural, accidental, or intentional. In order for BTRP to respond more quickly and effectively, it will need broader authority and flexibility to tailor engagements to the current, anticipated, and novel new biothreats.

Because such threats do not respect bureaucratic or geographic boundaries, programs, such as BTRP, that counter those threats need flexibility. BTRP needs the ability to work beyond the U.S. government's Select Agents and Toxins List (CDC, 2017) because serious natural, accidental, and intentional biological threats may arise from pathogens not designated as selected agents. Given the broad geographic and topical

scope of potential biothreats, BTRP, in collaboration with others, should have the flexibility to determine where to work and what efforts to undertake, rather than being unduly limited by restrictions that do not consider emerging novel pathogen threats that often appear in unexpected places. This does not mean that BTRP can or should take on every part of DOD's larger global health security mission, or engage in every place from which a biothreat might emerge. Rather, strong interagency discussions should determine which agency, within the U.S. government and internationally, is best able to address newly identified needs and has the optimal ability to work with a given country. However, BTRP needs to be flexible enough to fill the inevitable gaps when and where its unique capabilities are needed.

U.S. INTERESTS ABROAD

In addition to protecting the homeland, DOD plays a critical role in protecting U.S. interests abroad. U.S. military forces are deployed in more than 165 countries around the world, with more than 170,000 of its active-duty personnel serving outside the United States and its territories (U.S. DOD, 2019b).

U.S. men and women in uniform are not only at risk of combat and new and diverse terrorist threats, but are also at risk of exposure to common as well as exotic and endemic infectious diseases. In addition, some of these diseases could be highly contagious and/or resistant to current treatment, given the increasing threat of antimicrobial resistance around the world. Moving personnel in and out of regions of disease endemicity puts the homeland at risk from highly contagious viruses, which might affect human or animal populations, either of which could have devastating effects on the economy. Recent, vaccine-preventable infectious diseases have reappeared in the United States, largely due to reduced immunization rates in some U.S. communities, as occurred in 2019 with measles when there were 1,282 individual confirmed cases of measles in 31 states, which was the largest number reported in the United States since 1991, primarily in communities where large numbers of people are unvaccinated (CDC, 2019; Statistica, 2019). The introduction of drug-resistant pathogens represent a similar concern (White House, 2019).

A recent review of the medical literature for the years 1955 to 2018 has documented how thousands of U.S. or other nations' military service

members have acquired infectious diseases during their deployments and transmitted, or at least had the potential to transmit, these pathogens to their peers, other contacts in deployed settings, and sometimes close contacts upon returning home (Zemke et al., 2019). Examples of military personnel-associated pathogen transmission include a large cholera outbreak, to movement of pandemic influenza to new regions, and importations of malaria, antibiotic-resistant enteric pathogens, pediatric diseases, and sexually transmitted diseases. Although perhaps not always a primary concern, moving military personnel in and out of regions of novel pathogen endemicity always puts them, their military colleagues, and family and friends, and ultimately the homeland, at potential risk, especially in the case of highly contagious pathogens. Even if secondary transmission is uncommon, exposure can result in many infections and considerable morbidity and possible mortality. It is beyond prudent that BTRP remain deeply engaged in understanding and anticipating such novel pathogen transmission risk where troops are or are likely to be deployed.

Military personnel and other travelers also have the potential to unknowingly serve as transmitters of pathogens that infect domestic animals or food agriculture, which could pose a threat to the economy and to food security. As was discussed in Chapter 2, there is great potential today for an international traveler to unknowingly import a pathogen such as African Swine Fever (ASF) virus into the United States or another susceptible country, which could result in a disaster for pork industries.

BTRP currently contributes to U.S. and international biosecurity by assisting countries through training for laboratory staff in improving laboratory diagnostics, disease surveillance, and early-warning capabilities, and by helping countries secure collections of pathogens or tissues. BTRP is engaged in such activities in many parts of the world, thus helping to protect deployed U.S. military personnel, U.S. diplomatic corps, and less directly, the locally resident American population most of whom travel back to the United States on a regular basis and represent potential microbial transport hosts. It was evident in the West Africa Ebola outbreak that the repatriation of a small number of known infected American residents represented a grave and possibly disruptive concern to many communities, even though highly effective precautions against secondary transmission were in place. In fact, the two transmission events to nurses in Texas (Hennessy-Fiske et al., 2014)—which involved a Liberian national index case not known to be infected with Ebola when he arrived in the United States, who then became ill, was hospitalized, and

died of Ebola infection—should have been prevented by better infection control and communication among hospital staff.

Because BTRP's work requires close relationships with senior foreign government representatives, as well as technical and professional staff, there are opportunities to build long-term relationships of trust. Where relationships of trust exist, honest communication of both good and bad news is more likely. This is evident, for example, where the U.S. Army and Navy service laboratories have been running for decades in collaboration with military counterparts in various countries around the world. Trusted relationships are also important to the success of mid-term projects supported by BTRP, although the benefit is likely to be less direct when the projects are conducted by individuals without a depth of experience and/or without continuity in staffing.

FINDING 7.1: Within DOD, BTRP plays a critical role in advancing national biosecurity interests internationally.

Awareness of Potential Emergent Infectious Disease and Biothreats

When communication, particularly resulting from relationships of respect and trust among professionals is ongoing, BTRP personnel are more likely to obtain an understanding of potential risks and threats before they become severe. In certain situations, the host country may not want to share detailed epidemiological information with DOD or other foreign entities, including the World Health Organization (WHO), even though the International Health Regulations (IHR) (2005) require that countries detect, assess, and report public health events to WHO. The threat to local trade, tourism, and reputation may readily suppress sharing of critical information, and overwhelm the duty to report. Therefore, much of the work of BTRP has been undertaking to forge relationships between the host country's public health professionals, military officers, and WHO professionals, in support of IHR (2005). If BTRP can encourage sharing of data, whether with the United States or with WHO or with the World Organisation for Animal Health, BTRP will enhance the likelihood that the international community can engage to help countries respond and more rapidly control an outbreak. Compared with CDC's international programs, BTRP is unique in that it has: (1) a natural common language with foreign military forces; and (2) a fundamental interest in biological security as well as the broader health mission. While global health is important, and may be a shared concern with counterparts in other countries, military partners share a common concern for biosecurity.

Although the Department of State Biosecurity Engagement Program conducts similar biosecurity and biosafety training, it has neither the compatibility with foreign militaries nor the diagnostics and health surveillance expertise that characterizes the engagement of BTRP with its foreign partners.

FINDING 1.3: At its best, BTRP activities improve facilities, procedures, and practices and establish strong, trusted relationships with laboratories and laboratory personnel in complex political and technical settings around the world, and by doing so provide unique functions for improved local and U.S. national security. BTRP needs greater flexibility in its geographic and programmatic operations such that it can truly function at its best.

Coordination and Synchronization to Maximize Bioengagement Efforts

Working closely with American embassies, BTRP plays an important role in the broad spectrum of the U.S. government's global health security diplomacy. The U.S. government and the international community cannot effectively reduce the threat of, and respond to, outbreaks without the cooperation of the host country. Effective engagement skills are essential for BTRP professionals who interact with counterparts from foreign governments on biosecurity concerns, and such skills need to be a critical part of the hiring/assignment process.

There is an increasing number of infectious disease outbreaks occurring worldwide (e.g. hemorrhagic fevers, flaviviruses, novel coronaviruses, influenza A viruses, and ASF), which highlights the significant role BTRP can play in the U.S. government's global health preparedness and response efforts. However, the committee has observed that senior DOD officials as well as those from other U.S. government agencies are frequently not fully aware of BTRP's international capabilities. With senior DOD leadership support, BTRP's capabilities and resources could be more widely known. CDC often promotes its accomplishments more effectively than BTRP. While publication in scientific literature is not a primary goal for BTRP, BTRP professionals should continue to document accomplishments and publicize more widely, in furtherance of the mission to enhance biosecurity. Such occasions may include a regular newsletter, a more robust website, and greater conference attendance.

SUPPORT TO AND COORDINATION WITH DOD AD BEYOND

The next crisis might be a natural epidemic or pandemic to which DOD is called to provide support, or the next crisis might emanate from the biological weapons program in a failed state, analogous to the agreement to destroy Syrian chemical weapons as recently as late 2013. While the Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict may continue to be the first to respond, when the President calls on DOD to respond, as was observed in the Ebola 2014 outbreak in West Africa, BTRP knows, communicates with, supports, and even deploys DOD medical and non-medical biodefense Research Development Test and Evaluation assets necessary for a DOD response in times of biological crisis.

BTRP's budget is relatively small and the global challenges it seeks to address are enormous. The important work with which BTRP is charged requires not only requisite technical knowledge, but also the preexisting interpersonal relationships that create trust. The critical elements of BTRP success are difficult to replicate on a large scale; just hiring contractors and providing a project budget is insufficient. Appropriate diplomacy and an understanding of human relations significantly improves the likelihood of successful initiatives. In Chapter 3 of this report, the committee discusses the need for and relevance of staff training in diplomacy, and the human relations skills necessary in situations as fraught and politically delicate as those encountered by BTRP professionals. BTRP, existing within DOD, has the potential to combine diplomatic skills and its location in DOD to maximize the impact and cost effectiveness of its efforts.

BTRP professionals who engage in negotiations to implement partnerships would benefit from opportunities to enhance their skills in the tradecraft of health diplomacy. For example, BTRP could take advantage of the 3-day course on Global Health Diplomacy offered by the State Department's Foreign Service Institute. The course is described as follows:

> This course introduces U.S. government policies and programs aimed at helping resource-constrained countries prevent and manage threats from infectious and noninfectious diseases. Students discuss how the United States incorporates domestic health programs into our bilateral and multilateral diplomatic efforts. Participants will learn about the "tradecraft" side of health diplomacy–

> working with other U.S. government agencies at post and understanding the role of non U.S. government organizations in the host country. (Foreign Service Institute, 2020)

FINDING 7.2: Because BTRP is just one of several U.S. government programs conducting health security engagement, both the strategic vision and success of biosecurity programs rely on actions by the U.S. government as a whole, host governments, and international partners.

FINDING 7.3: Using the integrated view of biological threats and threat reduction, the U.S. government will be more effective and efficient if it identifies and prioritizes the threats and applies resources to those threats through the departments, organizations, offices, and channels that are best poised to address the associated needs. These channels are the various medical, military, diplomatic, humanitarian, scientific, and security programs of the U.S. government and its partners at home and internationally, which are able to intervene in different ways and in different contexts to eliminate, reduce, or mitigate threats at the most opportune and effective stage of threat development. Strong interagency coordination must drive these prioritization and resource allocation efforts if the needs are to be addressed and unnecessary duplication of efforts and costs are to be avoided.

5

Strategic Vision and the Way Forward

In the next 5 years, the U.S. Department of Defense (DOD) Biological Threat Reduction Program (BTRP) should encourage, engage, support, and help drive the U.S. government's development of a durable interagency mechanism that draws on medical, military, diplomatic, scientific/technical, and other expertise to address the full set of biological threats and risks to the deployed U.S. military forces, U.S. interests overseas, and the homeland, seeking to intervene and eliminate, reduce, or mitigate risks at the most opportune and impactful stage of biothreat development. An effective mechanism will have greater geographic flexibility; and will demonstrate better awareness and prevention of threat development, and more timely response; and will partner effectively within DOD, with other U.S. government agencies, and with other nations, international organizations, nongovernmental organizations (NGOs), the private sector, and academia. Likewise, an effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies.

CURRENT APPROACHES OF THE BIOLOGICAL THREAT REDUCTION PROGRAM

In the past, Cooperative Threat Reduction (CTR) programs redirected bioweaponeers to peaceful pursuits. As the threats changed, BTRP has helped partners consolidate and secure vulnerable pathogen collections. BTRP has assisted international partners in upgrading high-containment infectious disease laboratories, trained trainers in laboratory safety and security, and helped establish local, national, and regional disease surveillance networks.

The previous chapters have traced the origins and evolution of BTRP at DOD from the original authorizing legislation in 1991 (commonly called the CTR authorizing legislation), to 2018, the 20th anniversary of

the Defense Threat Reduction Agency (DTRA), which is the DOD agency in which BTRP is administratively located. Over those two decades, life sciences advances, biotechnology, and pathogen epidemiology have changed significantly, and call for a new assessment of the biological threats to human, animal, and plant health and the implications for CTR. Several studies describing and assessing CTR programs have been published since their inception, including prior evaluations by the National Academies of Sciences, Engineering, and Medicine. The present report reviews the major developments over the past decade, considers the particular strengths and global connections of BTRP today, develops a new strategic vision for the next 5 to 10 years of BTRP activities, and makes recommendations to enable that vision to be implemented. One constant in this report is the recognition that many of the goals and activities supported by BTRP during the past decade remain relevant today, although there are new dimensions and new concerns that must be addressed. BTRP's current official mandate is to:

- Consolidate and secure dangerous pathogen collections into central reference laboratories or repositories;
- Improve the safety and security of biological facilities;
- Enhance partner states' capabilities to detect, diagnose, and report bio-terror attacks and potential pandemics;
- Engage scientists with biological weapon-related expertise, wherever they may currently exist, in research that supports force protection, medical countermeasures, diagnostics, and modeling;
- Foster cooperation and collaborative research with partner institutes and scientists to strengthen the joint capacity to rapidly and accurately detect and diagnose high-consequence infectious disease outbreaks and related biothreats, and be prepared to collectively take appropriate action;
- Cooperate with partners to ensure the safety and security of dual-use research of concern; and
- Engage partners across agencies and organizations within and beyond the United States to limit potential threats and risks associated with cyber security.

Goals, Tools, and Approaches for Today and Tomorrow

International engagement is one of the most cost-effective tools available to prevent adverse events rather than to respond to them after they occur. By providing value to host countries' efforts to diminish their

risk of serious outbreaks, enhance disease surveillance, and increase the speed of response to avert or mitigate their varied consequences, bioengagement also reduces the risk to the deployed U.S. military forces, U.S. citizens living or traveling abroad, and the population in the United States. In this context, the BTRP mission aligns strongly with the National Defense Strategy of 2018.

Based on study of the origins and evolution of BTRP, and changes in the scientific, social, political, and physical environment in which emerging infectious diseases have affected local populations and raise the prospect of regional and global spread, this chapter presents the committee's perspectives on the critical issues that underlay the development of a new strategic vision for the agency. The intent is to sharpen the program's focus, facilitate its adaptation to new realities, and better ensure the success of its mission. A set of recommendations designed to enhance the capacity of BTRP to deliver necessary and appropriate support to realize the vision is presented in Chapter 6.

The Changing Context of Biothreats and Biorisks

Biological threats, including natural, accidental, and intentional threats to the United States and its interests overseas, including U.S. allied countries' military forces and citizens, and the social, political, and physical environments in which they arise, are growing more challenging and at a faster rate than in previous decades. Drone use, targeted assassinations, and breaking of the taboo against the use of chemical weapons are realities. While the taboo against the use of biological weapons has not been breached on a large scale, nature continues to provide less-than-subtle hints of the potential impact of biothreats, and there is documented interest by terrorists in biological weapons. There are examples of probing with chemicals and pharmaceuticals, which prompts the question "What is 'war' today?" How can we be prepared for, attribute, and respond to the myriad of potential threats? How can we achieve early warning or even be cognizant of developing threats?

The biodefense and public health communities are now grappling with scenarios in which preparedness and response to disease outbreaks caused by natural or intentional threats, accidental releases, or those arising from scientific advances, are part of a single spectrum of challenges. These challenges affect the United States and global populations at a time when physical distance from the origin of outbreaks no longer provides protection. At the outset of CTR programs, a major goal and metric for

evaluation of impact was to redirect scientists who had participated in state-supported offensive bioweapons programs to peaceful pursuits using their skill sets in new and highly valued ways. While the threat of intentional use of biological weapons by state or non-state entities has not diminished, even if programs the size and scale of the former Soviet biological weapons programs no longer exist, the threat from the widely reported large, multi-country natural events, currently dominates the implementation of the most recent National Strategy for Biosecurity. Furthermore, the origins of outbreaks may be ambiguous because existing tools are often too coarse to definitively attribute them to pathogen evolution in nature or deliberate manipulation in a laboratory.

The boundaries between risk and threat continue to blur and converge at a quickening pace. As the National Biodefense Strategy of 2018 states that the lines between naturally occurring and evolving infectious disease agents, accidents in the course of legitimate research deemed to be justifiable based on careful risk-to-benefit assessment, intentional misuse of biology, and surprises arising from the biotech revolution are becoming less distinct. This suggests the need for strategies to prevent both risks and threats, and to be prepared to act rapidly and effectively when the need arises. The consequences of not planning strategically and acting rapidly and effectively can be great, as in West Africa in 2014–2016, and currently in the Democratic Republic of the Congo (DRC). Naturally occurring disease can seriously destabilize countries and regions, occurring as a "perfect storm" in settings in which civil society is fragmented, authority is fragile, and resources to address emerging outbreaks are limited. Intentional introduction of disease agents can have a similarly destabilizing effect, and may be even more challenging if they have been deliberately modified to be more destructive and/or to resist existing medical countermeasures. At present, the source of modifications at the genetic level may not be readily attributable to evolution in nature or mutation created and introduced in a laboratory, but regardless of source, anticipating problematic settings, improving biosecurity capacity, and building personal relationships between local and U.S. personnel can significantly contribute to reducing the threat of outbreaks.

The Global Consequences of Disease Outbreak

Against the backdrop of ongoing transportation of people and trade in animals and plants, greater access to information, mistrust of authority, dissemination of misinformation and rumor, increasing geopolitical

volatility, corruption, famine, drought, warfare, terrorism, and global migrations of humans escaping violence and persecution or just seeking a better life, there are greater risks of disease outbreaks now than ever before (Coleman, K. et al., 2016). For example, an outbreak of foot-and-mouth disease in the United States would have catastrophic consequences for the multi-billion dollar livestock industry. Hayes (2012) (in USDA, 2013) estimated economic impact of $12.8 billion dollars, annually for 10 years ($128 billion in total). Such threats extend to the U.S. military deployed in areas where these phenomena are present, and are due to the potential of rapid global dissemination of infectious disease, including to the United States.

Greater global connectivity increases the ease of transmission and broadens the reach of infection, which in turn demands faster, more effective response. Given the speed of travel around the globe, an individual in one country with a highly communicable disease can arrive in any other country in approximately 24 hours or less. Outbreak timelines are being compressed and as a result so is the time available to plan and implement an effective response to an outbreak. Improving systems and capacity for biosecurity, especially in unstable or active conflict zones where BTRP would have strategic advantages to engage, can be of critical importance.

Easier access to knowledge relevant to dual-use technologies and tools for previously unimagined biological research and technology capabilities can also set the stage for accidental as well as intentional threats. As noted in Chapter 2, methods for engineering and synthesizing microbial pathogens have already enabled competent molecular biologists to construct viable infectious pathogens simply from genetic sequence information. Digitalization of biology and design of new technologies to manipulate biological materials also challenge current biological governance and oversight structures within and outside the United States. The potential for devastating local impact and secondary global ripple effects of outbreaks is increasing as these advances accelerate.

The Mission Is Growing More Complex for DOD

DOD, including DTRA and BTRP, is aware of these realities. Similarly, it is also aware of technical and political changes in the conduct of conflicts, such as the use of drones for surveillance and combat and advances in biotechnology that permit the acquisition and manipulation of disease agents. While the existing norms, treaties, and other commitments

against the use of biological weapons has not been breached on a large scale in recent decades, there are clear indications that these moderating forces are strained.

How can the United States and the international community be prepared, receive early warnings, or even be cognizant of developing biothreats? What parts of the U.S. government, and which department or entity within the multiple components of government, are capable, prepared, and willing to address these biothreats? As is described in the next section, the committee believes it will take many U.S. government programs working together and with other governments, international organizations, and nongovernmental partners to address these challenges. DOD and BTRP have an essential role to play in that effort.

Support for BTRP Within DOD Will Pay Significant Dividends in Preparedness and Response

DOD has long held essential, interwoven parts of the bioengagement mission, including protection of deployed U.S. military forces and U.S. interests overseas in the event of disruption of critical functions, such as transportation and trade. History informs us that international bioengagement by DOD contributes to military readiness, planning, and force protection important for U.S. national security. For example, the U.S. Army and Navy overseas laboratories provide essential information on endemic infectious diseases and emerging outbreaks and have helped to identify and validate medical countermeasures or prevention strategies. At the same time, they promote and sustain critical professional relationships of trust where they operate, which are necessary for the transparent exchange of information and insight.

BTRP currently plays a distinctive role in DOD's engagement to reduce biological threats, and can play an even greater role in the future. BTRP establishes critical lines of communication with foreign governments and responsible individuals; supports operational and situational awareness where it can operate; and invests in building capacity that promotes biosecurity, and ultimately provides additional support for security to deployed U.S. military forces, Americans traveling abroad, and the United States itself. BTRP efforts support the host nation as well. The important role BTRP plays is highly effective, particularly relative to its very small portion of the DOD budget.

A Diverse Set of Actors Is Needed to Address the Complex Biothreat Landscape

DOD is not the only or even the central mission holder in an integrated effort to address biological threats. Different parts of the U.S. government, and international and nongovernmental organizations have unique strengths to contribute to the prevention of and/or response to natural, accidental, and intentional biological threats in various contexts. The Centers for Disease Control and Prevention (CDC) and other parts of the Department of Health and Human Services, the Department of State, the U.S. Agency for International Development (USAID), the Department of Agriculture, United Nations agencies, NGOs, the private sector, academic partners, and subject-matter experts more broadly are also critical to enhancing efficiencies and leveraging scarce human and physical resources to reduce the increasing and more complex biothreat landscape.

Multiple organizations with missions related to international biosecurity should work together more effectively to address common challenges to maximize the overall impact of collective efforts. U.S. biosecurity programs seek to work with countries that have special vulnerabilities to security and public health threats, the desire to build capability and capacity to detect, identify, and analyze emerging infectious diseases, and a willingness to cooperate with U.S. and international entities prior to and when incidents occur. There are often multiple organizations with experience working in numerous countries and with their neighbors, on a wide range of biosecurity-related problems.

Consider a hypothetical but plausible situation that could arise in Southeast Asia.

- BTRP has an existing partnership with country A to build laboratory capacity, establish more secure sample libraries, provide training for laboratory and other personnel, sponsor research as part of a larger regional network focused on zoonotic disease, and establish professional and personal relationships and channels of communication.
- USAID is active in the same country and its neighbors (countries B and C), spending more than $100 million per year to improve basic health through delivery of vaccines, promotion of good hygiene, and HIV/AIDS relief, including laboratory testing.
- The National Institutes of Health sponsors joint research on emerging infectious disease with the Ministry of Health in country B, and with a university medical center in country A.

- CDC provides experts who spend months at a time working in country B, helping to improve laboratory practices and upgrade a legacy laboratory to deal with more difficult pathogens.
- Country C has an Institute Pasteur laboratory that participates in the same regional network of researchers on zoonotic diseases with conferences and joint research organized by the EcoHealth Alliance.
- The State Department's Biological Engagement Program sponsors a nonprofit organization to conduct biosecurity training and upgrades at laboratories in country C.
- Most of these organizations provide information to the World Health Organization (WHO) and participate in regional WHO conferences. As part of its commitment under the Global Health Security Agenda to implement the WHO International Health Regulations (2005), country B is conducting a Joint External Evaluation, while country A is considering doing the same.

In this hypothetical situation there is little or no obvious and unnecessary redundancy, which is good. Likewise, all of these efforts are valuable in and of themselves. Rather than being conceived as a series of separate efforts, though, they could be linked with a coordinated and cooperative strategy to strengthen global health security. Furthermore, the hypothetical situation noted here reflects routine circumstances. Should an outbreak occur in one of these countries, public health and security needs may rapidly change and would increase urgency, and all of the preexisting and additional resources would be needed for an effective response. Pre-established laboratories, pre-deployed protective equipment and pre-existing expertise in handling dangerous pathogens, pre-established supply chains, and pre-existing networks of people and their collaborative relationships would be invaluable in rapidly and effectively responding to an emerging infection or epidemic.

Each of these organizations involved in the hypothetical scenario brings unique capabilities, from the expertise in CDC personnel, to the flexible funding of BTRP and logistical capabilities of DOD, the diplomatic relations conducted by State, the strengthened healthcare infrastructure developed and the Disaster Assistance Response Team deployed by USAID, and the decades of collaboration in the Institut Pasteur resulting in enhanced indigenous capability and operation in the country and the region.

As the above hypothetical scenario indicates, DOD's programs are unique in that they provide a national security focus, while other U.S. government departments and agencies involved in international health

engagement programs are primarily focused on civilian health and biosafety challenges. Moreover, in contrast to the excellent programs of CDC and USAID, the mission of DOD's programs is first and foremost to support the deployed U.S. military forces and the United States and its interests overseas (Philpott, 2019). By carrying out this function, BTRP engagement programs also directly contribute to U.S. national security by providing early warning and situational awareness. BTRP also indirectly contributes to national security by establishing regular communication around mutually relevant security topics with international scientists and clinicians who have relevant knowledge and tools. Open dialogue among equals builds understanding and promotes individual relationships of trust. Understanding and trust between technically competent individuals, particularly over the long term, contributes further to trust and understanding among leaders in ministries and governments. Where trust exists, transparency increases. BTRP is perfectly placed within DOD to engage with global partners to create the necessary common ground to address biosecurity and biosafety priorities, consistent with the current National Defense Strategy.

While there is no perfect solution to today's extremely complex global challenges in biosecurity, the committee fully appreciates that BTRP's engagement program is a critical component of DOD's mission to protect the nation and its military forces. Because of its knowledge on the ground and its position within DOD, BTRP not only knows, communicates with, and supports, but may also even deploy advanced technologies developed through DOD medical and non-medical biodefense research, development, testing, and evaluation programs (CRS, 2019) necessary for DOD to anticipate, prevent, or respond to an urgent need in times of biological crisis. The next critical health crisis might be one for which BTRP already has existing relationships and partnerships through resources already invested. DOD may be called upon to provide emergency support for a naturally occurring pandemic, or to safely contain and eliminate a biological weapons program in an unstable situation. While the resources of the Office of the Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict (ASD SO/LIC) (Tadjdeh, 2019) will likely continue to be the first place to which the President turns when ordering a DOD response, as in Sierra Leone during the 2014 Ebola outbreak in West Africa, success is predicated on being able to draw on existing relationships and resources already invested in a host country, developed prior to an outbreak, when civilian assets may be overwhelmed.

But resources are limited, and BTRP as well as other partners must address the perennial mandate to produce the best outcome as efficiently as possible. Not only is it right to use funds efficiently and effectively, it is also the way to strengthen BTRP. By building sound working relationships with other U.S. government, NGO, and global networks of experts, BTRP can leverage its resources more effectively and be better attuned to threats, risks, and even successes around the world. BTRP's common interests in prevention and early engagement with potential partners abroad, albeit viewed through a biosecurity lens, may include epidemiology, genetic engineering, point-of-care or other field-enabled diagnostic methodologies, disease surveillance and secure storage of biological samples, and response, including countermeasure development. Working together on these common interests may be of direct benefit to the host country (whether those partners are from the military or other relevant parts of government) as well as to the United States. Aligning interests, resources, and outcomes can achieve greater effectiveness for all partners and avoid unnecessary duplication of efforts.

The Need to Anticipate, Detect, and Respond Rapidly to Threats

To effectively and efficiently address natural, accidental, and intentional incidents, the U.S. government must be able to anticipate, detect, and, if called upon, respond rapidly to these threats, regardless of their origin as disease outbreaks, including those that arise as a consequence of unanticipated outcomes of life sciences or biotechnology advances. This begins with identifying risk factors, needs, and opportunities. Disease surveillance extends beyond detection of disease outbreaks to noting and responding to the conditions that feed and lead to infectious disease risks and threats. For example, a lack of domestic clinical and research laboratory infrastructure or poor domestic public health capabilities, insecure storage of agents and potentially infectious biological samples, limited training in biosafety procedures in the laboratory or clinical settings, and inadequate numbers of subject-matter experts to prevent and respond to infectious diseases may allow an outbreak to occur where it may have otherwise been preventable. Effective surveillance and improved infrastructure must also be paired with sustained efforts to identify opportunities to act prior to an outbreak.

For example, by building surveillance capacity to identify known and new pathogen threats in nature, it may be possible to prevent outbreaks, or at least to be prepared to efficiently identify and quickly deploy

diagnostics and medical and/or public health countermeasures. The current novel coronavirus outbreak is a case study for rapid response capacity, and a polymerase chain reaction (PCR) test (Corman et al., 2020) was rapidly developed and implemented. Although there are no known proven and safe medical countermeasures, work on a vaccine candidate and screening of therapeutics has begun, even as the usual personal and environmental containment procedures, case identification and contact tracing, screening of travelers, good clinical management practices, and universal precautions are implemented. These efforts can also help to build the partner-country capacity to respond more quickly and more effectively to a bioterror attack resulting in an outbreak. Such efforts could include training, improved infrastructure, partnership with international experts, and access to diagnostics, therapy, and vaccines. Providing help and building country capacity to protect or at least mitigate the impact of an outbreak affecting a local population has a direct effect on protection for deployed U.S. military forces. This is a major benefit of the efforts to assist international partners in upgrading high-containment infectious disease laboratories, to train local trainers in laboratory security and safety, and to help establish local, national, and regional disease surveillance networks. Whether before, during, or after an outbreak, for which BTRP or other DOD programs have been engaged, they have aided partners in consolidating and securing valuable pathogen collections so they may be effectively used to develop countermeasures and reduce the risk that they can be misused. The latter is particularly important because the size of the global workforce with expertise in enormously powerful new biotech capabilities has increased greatly, raising new concerns regarding individual or small-group attempts to create new deadly or drug-resistant strains of pathogens. Advances in science have increased threats in a variety of ways, including the ability to manipulate virulence, and/or create drug and vaccine resistance in a relatively unsophisticated laboratory environment in almost any country. Timely information on such pursuits, gained from a network of trusted international partners, is now more valuable than ever.

Cooperative programs are likely to function most effectively when personal engagement has occurred and the people involved from the relevant agencies and organizations know and trust one another before a biological crisis occurs. Positive examples of such advanced engagement that allowed for rapid response otherwise unavailable include BTRP's support to the Lassa Fever Ward in Kenema, Sierra Leone (Wilkinson, 2015), including laboratory capacity and training efforts. The pre-existing

program meant that reliable diagnostic platforms were available before the onset of the West African Ebola outbreak beginning in 2014, requiring primarily new primers to adapt PCR technology for the Ebola virus. Similar BTRP engagements before the 2017 outbreak of Marburg disease in Uganda installed laboratory diagnostic equipment at the Uganda Virus Research Institute, the Central Public Health Laboratories, and 15 district laboratories under the Ugandan Ministry of Health, and improved genomic sequencing capabilities and data analyses. These efforts can be credited with reducing the impact of the outbreak and facilitated subsequent DOD engagement.

As previously discussed, the Ebola outbreak in West Africa in 2014–2016 and the ongoing and expanding outbreak in the northeastern regions of the DRC illustrate two new scenarios of "bio-insecurity" and the need for anticipatory thinking. First, in Guinea, Sierra Leone, and Liberia, the legacy of the previous years of civil instability, violence, oppressive government, widespread distrust of authority, and dire poverty contributed to the power of conspiracy theories fueling rumors and mistrust of government and, by extension, international responders. This insecurity and lack of trust contributed to the massive nature of the outbreak, including almost 12,000 Ebola deaths officially registered and the breakdown of the healthcare system and the suspension of routine health services. The ongoing 2018 outbreak in the northeastern provinces of DRC involves an area of continuing unrest, with multiple anti-government armed militias, and major distrust of the government by the local population. As a result, individuals or organizations identified as working with the government, including international health and humanitarian groups, are distrusted by association. These cases illustrate the fact that local insecurity has taken on a new dimension as with the presence of organized armed insurgent groups which are now specifically targeting healthcare and outbreak control initiatives to identify and treat patients, track contacts, and halt the chains of transmission. This local insecurity enables the outbreak to be sustained, grow, and spread, threatening neighbors and, eventually, U.S. interests.

A strategy incorporating the factors of anticipated social and/or environmental instability in determining where and when BTRP should seek to engage with a host country would be a departure from the past, but would address a DOD imperative to protect military servicepersons from health threats in places to which they may be deployed.

Success at anticipating and responding to perceived threats or opportunities is varied and sometimes imprecise. Cases in which it is

feasible to anticipate and identify a specific need, and in which one can, in advance of an incident, identify the specific biosecurity consequences of not engaging are rare. However, there are also cases when analysts know that a high-consequence pathogen is likely to emerge in a country or a region, even if they do not know exactly what it will be and when it will occur. The important counter-threat action in such cases is to establish a flexible capability to detect and respond quickly when something does arise.

BTRP's resources are relatively small and have been shrinking in recent years (See Appendix B for CBEP/BTRP funding levels from 2007–2020). For geopolitical and epidemiological reasons, BTRP should not engage a state or partner just because it can, but rather engagement should be informed, strategic, and likely to yield benefits. The committee outlines a strategic vision in which strategic, country-level engagements can be pursued. The limited resources that BTRP has at this time make careful selection of engagements even more critical. Likewise, ending aspects of partnership must only be done after careful analysis of options as connections and activities that are well established would have to be rebuilt.

The transportation and communication revolutions have provided the capability of anticipating where the next hot spots most likely may be, and to a greater degree of accuracy than ever before. For BTRP to take a strategic view will require careful articulation of why engagement is required, where it is required, what the specific need is in the context of the local circumstances, and what resources are required—including human resources. The committee asserts that the strategic vision outlined in this report, focusing on improved mechanisms for implementation, can provide an essential framework within which to improve the effectiveness of BTRP.

Geographic and Programmatic Flexibility for BTRP

To the extent that BTRP, together with a range of domestic and international partners, can use its collective abilities to more rapidly and precisely anticipate the location and potential sources of biological threats and opportunities, it will increase its ability to articulate where and why it should engage in a variety of geographical areas and topics. The potential for a greater reduction of risk through earlier and sustained engagement based on trust and shared interests is enabled by the ability to act as soon as human and financial resources will feasibly allow.

Programmatic flexibility is essential for effective and efficient implementation of bioengagement efforts. The time between the anticipation of an incident and its occurrence has shortened due to increased speed of travel and advances in the biological sciences. As a result, there is often insufficient time to seek required determinations to allow BTRP to engage in a geographic region before a situation becomes critical and a response much more expensive—and sometimes less effective—than it would have been years or even months earlier.

There are a number of countries and regions in which such biological engagement programs could make a significant positive difference in local stability and, as a consequence, positively affect U.S. national security, but for which a geographical determination to engage has not yet been made by Congress. A prominent example can be found in Latin America and the Caribbean, where the prevailing view of the determination authority has for years been that, since there is no perceived significant biological or bioterrorist threat, bioengagement through BTRP is not a priority. Yet there are Latin American countries at risk of outbreaks of major emerging infectious diseases, exemplified by the recent increase in incidence of yellow fever, dengue, and Zika viruses. Some Latin American countries also experience political and economic instability. Such factors could have significant adverse implications for rapid and effective action to prevent or mitigate an emerging outbreak that threatens health security for the United States. The Black Sea region is another critical contested area where BTRP could represent the U.S. government and create opportunities to cooperate and enhance biosecurity. BTRP should be enabled to creatively and strategically use all existing authorities and carefully seek to understand needs and opportunities worldwide; this is essential to address current and long-term threats posed by natural, accidental, and intentional biological incidents.

Modern biosciences are increasingly interdisciplinary, dual-use, and rapidly evolving in unknown and unpredictable ways, whereas in the earlier days of CTR bioengagement programs the focus was on a small number of states using industrial-scale methods to make traditional bioweapons that involved a relatively limited sector of biosciences and relevant research. Given this evolving landscape of risks, threats, and opportunities, BTRP should continue to focus on anticipating where bioengagement may be both possible and beneficial to reducing risk. As a result, to remain effective and relevant, BTRP's engagements must be sufficiently flexible in content and substance. In addition to having flexibility to selectively engage around the world where biorisks and

biothreats are present or can be anticipated to emerge, BTRP would be better-positioned to address the full range of challenges if it also had the scientific expertise within the organization as well as access to external scientific experts to identify new threats that may emerge from unanticipated consequences of cross-disciplinary sciences, some of which could be used for harm.

Because engagements are with humans, not technologies or pathogens, BTRP officials should be proactively communicating with their counterparts in engaged countries and have the flexibility to undertake broadly relevant activities in true partnership with their host-country colleagues. This will invariably result in greater relevance of the program to the needs and priorities of the engaged country and its personnel, and increase the likelihood of success, and thus sustainability, with domestic personnel and resources.

BTRP evaluates progress in its engagements on a regular basis. If this is part of a larger DOD and interagency evaluation of efforts in a country or region, then these evaluations afford opportunities to refine the approach to engagement. This could mean modifying BTRP staffing needs, the composition of partners, revising their roles, creating new networks, and sharing lessons learned and best practices. It may also prompt the interagency or the programs to thoughtfully terminate unproductive partnerships. Overall, a U.S. government-wide strategy and better coordination and communication across U.S. government agencies would be beneficial.

Since it is very difficult to scale the success of BTRP's engagements, just hiring contractors and providing a project budget will not necessarily lead to proportional gains in success. To allow for the greatest return on the investments made with increased flexibility, BTRP would benefit from an increased number of technical experts in the program. With more technical experts, decisions on how to best support countries to strengthen their capabilities to detect, diagnose, and report on diseases can be more effective. It takes experience to discern what is really required to help a country partner, particularly when there are a variety of requests and solutions offered from multiple directions. Often, suggested solutions come from well-meaning people on all sides, but the solutions need to be scientifically sound to help move missions forward. In other times, prioritization of projects may benefit from scientific knowledge such that sequencing of implementing solutions can be most effective.

Personal Relationships and Networks as the Foundation for Successful Engagement

Connections to people and their institutions are the common thread through all of BTRP's efforts, whether for biosurveillance, establishing norms, building laboratory capacity, strengthening biosecurity and biosafety rules and practices, or enabling anticipation of threats and rapid, effective response. Threats and risks are much more dynamic than they were during and just after the Cold War. The words of Nobel Laureate Joshua Lederberg, speaking of preventing biological warfare, continue to ring true: "There is no technical solution. It needs an ethical, human, and moral solution. But would an ethical solution appeal to a sociopath?" (Preston, 1998, p. 65) Partners and partner countries are allies in countering threats from state and non-state actors, and while CTR programs have focused on technical solutions for the past 30 years, with some success, it is also clear that human relationships of trust developed through long-term engagements contribute both directly and indirectly to national security, and can even be deterrents to aberrant behavior.

Agreements between trusted peers and colleagues, in addition to strengthening national security through open lines of communication and operational awareness as described above, often enable efforts to improve disease surveillance, enhance the security of repositories of biological agents and clinical specimens, and train research and response teams to work safely in the laboratory and reduce the risk of exposure, across the spectrum from patient care to burial of those who succumb. When an outbreak occurs in a country where BTRP is engaged, whether natural, accidental, or deliberate in origin, such relationships can cut through the chaos of the moment and streamline the rapid implementation of a healthcare and containment response. Together with the ability to secure samples of infectious diseases, this can increase the likelihood that clinical research and trials of medical countermeasures or vaccines can be implemented, including assessment of innovative approaches developed through DOD research and development.

The 2009 National Academy of Sciences report *Global Security Engagement: A New Model for Cooperative Threat Reduction* encouraged the development of global networks of individuals and organizations with a common interest in biosecurity threat and risk reduction. Whether the source of the biothreat is natural, accidental, or intentional, an interest in collective brainstorming and action focused on complex, shared health-security concerns of importance were encouraged. Such networks can

become a powerful tool for communication, thoughtful partnerships in leadership roles, security, and stability. Multilateral networks at the intergovernmental level allow people to work together, and leverage investments in funding, which, in turn, foster more opportunities for information exchange, development of personal relationships, and appropriate action. One such multilateral forum is the Global Health Security Agenda (GHSA). BTRP has supported some of the biosecurity/biosafety components of GHSA and thereby has extended the impact of its resources, expanded its influence, and promoted an improvement in functional capacity of the involved nations where BTRP is engaged in a strategic manner. In the future, greater engagement with GHSA, as well as similar linkages with other initiatives, such as the Mekong Basin Disease Surveillance consortium (Connecting Organizations for Regional Disease Surveillance, 2019), the Bat Project, and the Alliance for Health Security Cooperation, could continue to extend the influence of BTRP and promote greater efforts toward biosecurity.

Protection of U.S. military forces or other U.S. civilians in a country at risk of an outbreak is enhanced when collaborations and trained healthcare workers are in place before cases are reported, and when local citizens are aware they can benefit from the partnership. A contemporary example of this type of collaboration is that among the Infectious Diseases Institute at Makerere University in Kampala, Uganda, the U.S. Naval Medical Research Center, Walter Reed Army Institute of Research, and the Henry M. Jackson Foundation operating in Fort Portal, Uganda, near the border with DRC, where there is a devastating and continuing outbreak of Ebola since August 2018.

Effective engagement is an iterative process in which clear and honest communication is essential. Long-term success is fostered when key individuals find their counterparts to be not only knowledgeable but also approachable and interested in establishing a personal connection. This not only has implications for leadership, but also for programs' future successors. As the committee has reviewed BTRP's experience, we have come to believe that the essential linkages between BTRP and partners abroad require greater involvement of BTRP staff. Bringing more human resources into BTRP itself can allow for selection of professionals based on critical skills necessary to build relationships. Individuals involved at all levels require a set of interpersonal skills that include the ability to listen attentively and understand the needs and thoughts of BTRP leadership, the project managers and implementers, and the partners. BTRP leadership should remain aware of and promote the need to

carefully select, train if necessary, and encourage employees or contractors who demonstrate the diplomatic skills necessary to engage effectively and successfully carry out the program as envisioned.

BTRP professionals should be encouraged to remain in contact with international partners, even informally. The relationships of trust built will not only promote good will, but also allow U.S. partners to understand and more likely to be aware of any significant changes in the situation, good or bad, through communication with its partners. Although there is an emphasis on the development of capabilities among partners in host countries, and on the sustainability of efforts subsequent to the official end of some BTRP programs and projects, trusted relationships built over time through engagement should be maintained and encouraged. Such relationships can be promoted through a host of possible opportunities such as attendance at conferences, participation in regional and global professional networks, and even regular phone and video-conferencing options. Critically, engagement on personal and professional levels should not stop and start along project timelines.

Greater Visibility of the Experience and Expertise within BTRP

As described throughout the report, BTRP has a considerably broad portfolio of bioengagement projects and activities to advance biosecurity across the world as a means of protecting deployed U.S. military forces, U.S. interests overseas, and the homeland. BTRP has gained a great deal of experience and expertise working in a wide range of countries and regions on a host of critical issues. The depth and scope of this experience, however, is not well known within DOD, across the U.S. government including Congress, and among international partners. Likewise, the range of skills and assets that BTRP can contribute to addressing extant and evolving biorisks and biothreats is also not as well-known as it should be. To maximally contribute to U.S. and international efforts to reduce risks from natural, accidental, or intentional outbreaks and other bioincidents, BTRP must be allowed the resources and the platforms to be able to articulate its successes, including through participation in and organization of appropriate international scientific meetings and other modes of global communication. Further, BTRP must be allowed to offer its expertise and resources to other partners within and beyond DOD that may be addressing current or anticipated challenges.

As with any effective partnership, it is desirable to build a strong foundation prior to a time of crisis or stress that may test the durability of

the partnership. BTRP's relationships within DOD are no exception. BTRP must establish deeper and more effective connections across DOD and regularly engage and inform colleagues of issues of relevance to DOD, so that they can more rapidly come together to form partnerships to take action when necessary. It is imperative to ensure leadership support to advance partnerships as soon as possible. Failure to do so would result in BTRP remaining siloed, and many opportunities to enhance synergies will be missed, potentially leading to lives lost. Particularly, regular open and frank communication must be ongoing between BTRP and combatant commands, ASD SO/LIC, Office of the Assistant Secretary of Defense for Health Affairs, Office of the Under Secretary of Defense for Policy, and other relevant DOD partners. If BTRP can deepen such strategic interactions, including by sharing its successes and available expertise more broadly, it will further strengthen the base of understanding about BTRP and its mission and programs.

Given the complexity of the 21st century risk and threat landscape, DOD, other U.S. government partners, NGOs, academia, and international partners should have the opportunity to draw on the considerable assets that BTRP can offer in support of common security goals, and in which the United States has invested for two decades. Such significant expertise should be included as proactive and responsive efforts to address biothreats.

The number of governmental agencies and organizations from a large number of countries, international organizations, NGOs, and groups from the private sector and academia have created a rich and complex landscape of potential partners around the world, each contributing to the larger effort to reduce the threats and challenges from disease outbreaks and advancing biotechnology. Some of those organizations focus more extensively on scientific research, others on human and animal health. Still others focus on the promises and possible perils of biotechnologies. Taken together, the wide range of people and organizations involved in one or more aspects of countering biological threats requires more diligent awareness of others' programs and initiatives, their areas of geographic and substantive engagement, and their similarities and differences in goals and objectives among groups and organizations. As a result, to increase the positive outcomes of its work, BTRP must be present and active at meetings and conferences where other potential partners, especially those from host countries, are in attendance. Through such outreach and networking, BTRP can grow its awareness and understanding of others' work, and increase its opportunities for establishing and maintaining

trusted relationships. Further, by participating actively in such events, the unique set of capabilities, expertise, and assets that BTRP has to contribute can become more widely known around the world.

During the early days of the Nunn-Lugar CTR Program in the former Soviet Union, a small senior advisory group was used very effectively by DTRA, not only to assist with scientific reviews of projects under consideration for U.S. funding, but also, importantly, to advocate for the CTR Program. In these times of reduced funding and a dearth of advocates in Congress for CTR programs, a group of senior experts with relevant experience, could add a robust foundation to BTRP's efforts. One potentially important contribution of such a group could be helping to link BTRP professionals, BTRP-supported experts, and other partners together through regional and global networks. Annual meetings are one means by which these experts can meet and share experiences working on a daily basis in the laboratories. Participation in science conferences, introduction of experts across regions and/or areas of scientific expertise, and exchanges of scientific publications and visits may also enhance BTRP's impact.

THE STRATEGIC VISION FOR BTRP

With the rapid pace of change in the biosciences, new biorisks and threats can seemingly develop overnight. Indeed, anticipation and prediction of risks that may emerge from natural occurrences, accidental incidents, or intentional actions may be considered to be an impossible exercise. Yet, building on two decades of experience and expertise by implementing the pillars of the proposed strategic vision articulated in this report, DOD's BTRP is well poised to seize opportunities prior to events and provide early warning of local and regional biological threats, thereby improving the biosecurity of deployed U.S. military forces and U.S. interests abroad, and strengthening security of the U.S. homeland itself.

6

Key Findings and Recommendations

The distinctions between natural, accidental, and intentionally initiated outbreaks have blurred, and all can result in exposure of U.S. military, civilian, and animal populations to deadly diseases, creating catastrophic health, economic, and political impacts that potentially can destabilize nations and affect security in geographic areas of responsibility. By engaging and working collaboratively with partners and counterparts in selected countries at risk of biothreats, the U.S. Department of Defense (DOD) Biological Threat Reduction Program (BTRP) is well poised to improve the local capacity (including in remote or rural communities) in the host country to address biorisks and threats that could affect U.S. national security. Furthermore, by establishing and maintaining relationships with individuals, institutions, and networks, BTRP contributes to the security of the United States through both communication and action. However, the advances in biotechnology and its potential misuse discussed in this report, and vastly enhanced modes of communication and information transfer that reduces the timelines for interventions to reduce risks, warrants a review and refreshment of the vision for BTRP and its ability to meet its mission. This final chapter presents the committee's findings (numbered in relation to the recommendation they support) derived from a review of the past 20 years of engagements by BTRP. The findings lead to seven recommendations intended to position BTRP to adapt to new realities, to sharpen its focus, and to have the greatest positive impact on reducing threats and risks to deployed U.S. military forces, U.S. interests overseas, and the homeland over the next 5 years and beyond. The recommendations fall into three broad categories: (1) Authorities and Responsibilities; (2) BTRP In-Country Engagement; and (3) Connecting BTRP with Others on Biological Threat Reduction.

AUTHORITIES AND RESPONSIBILITIES

A Congressional Determination Authorizing BTRP Engagement Globally

Going forward, BTRP must be further empowered to anticipate where it should prioritize building connections and support partner-country efforts to prevent malicious use of biology, and to address emerging threats from infectious diseases, whatever their source. To pursue this, BTRP needs to be supported by having sufficient flexibility and to be able to act quickly, under the authority from DOD, to implement its scope of responsibilities and actions.

FINDING 1.1: The emergence and dissemination of pathogens as reservoir and vector hosts spread into new geographic areas, as well as through movement of humans, international travel, and trade in potentially infected animals, plants, and animal and plant products can cause disease outbreaks in geographically distinct regions and countries with no prior knowledge of or experience with the agent, exposing susceptible humans, animals, or plants, providing opportunities for health risks, economic disruption, and destabilization, and increasing the risk of local outbreaks.

FINDING 1.2: BTRP is constrained by both political and geographic requirements that inhibit its ability to respond nimbly to emergent threats. As a result, BTRP is unable to keep pace with the speed at which science and technology are changing the biological risk landscape, reducing its ability to preclude or mitigate potential threats as they emerge.

FINDING 1.3: At its best, BTRP activities improve facilities, procedures, and practices and establish strong, trusted relationships with laboratories and laboratory personnel in complex political and technical settings around the world, and by doing so provide unique functions for improved local and U.S. national security. BTRP needs greater flexibility in its geographic and programmatic operations such that it can truly function at its best.

FINDING 1.4: Natural, accidental, and intentionally caused outbreaks can have similar consequences for health, the economy, and national security. Despite the initial cause of the outbreak, they also have similar requirements related to common prevention, detection, response, and recovery initiatives. There are advantages to addressing these events as different manifestations of the same family of challenges. An integrated view of biological threats prevents bureaucratic boundaries from interfering with partnerships and progress. Natural, accidental, and intentional outbreaks may have ambiguous origins but the capabilities needed to address them overlap. Ultimately, needs of force protection and national health and safety may be similar in most cases, especially those with the broadest potential national security impact.

RECOMMENDATION 1: The Office of the Secretary of Defense for Policy should seek a global determination from Congress, which would give BTRP authority and flexibility to work when and where national biosecurity needs–and diplomatic opportunities–are identified or reasonably anticipated.

Mission and Engagement Flexibility

Knowledge and understanding of local partner capabilities in several key areas are essential to guiding biological threat reduction investments, including: (1) the ability to conduct ongoing disease surveillance, which entails identifying and reporting potential outbreaks at the earliest opportunity; (2) the ability to understand security concerns; (3) the ability to engage governments and civil society; (4) the ability to detect and address intentional threats to biosecurity; and (5) the ability to secure repositories of microbial agents and patient samples.

FINDING 2.1: The development of threat-specific prevention and detection approaches can be improved through anticipation of current and future threats presented by natural, accidental, and intentional incidents involving high-consequence pathogens and toxins and by misuse of

advances in scientific research, development, and application.

FINDING 2.2: New scientific advances, including multi-use technologies, methods, and information highlight the need for more robust approaches for analyzing the anticipated and unanticipated consequences of scientific efforts, including misuse, reducing potential risks, and reaping the scientific benefits for prevention and detection of biological risks.

FINDING 2.3: Facilities and information systems using cybersecurity and data security approaches are vulnerable to exploitation by malicious actors who could access, monitor, steal, or manipulate data and analytic results remotely and without notice, or disrupt the flow of data to scientific partners. Cyber-related threats now include threats to facilities and information systems, harmful use of genomics and advanced data analytics, and the development of new biological systems.

RECOMMENDATION 2: DTRA should give BTRP as much programmatic flexibility as possible to understand and broadly address the current and anticipated biosecurity and biosafety needs of each country where it engages. The needs may be underlying biosecurity challenges, so the actions may be one step removed from traditional activities, such as building in-country and regional networks, organizing focused scientific meetings, and developing emerging leaders.

BTRP IN-COUNTRY ENGAGEMENT

Personal Relationships Are Key to Successful Engagements

Engagements in collaborative biological threat reduction programs are first and foremost about humans. Science, health issues, technologies, procedures, and research on pathogens are tools, for good or sometimes for harm. It is critically important to recognize that to develop and maintain successful personal engagements, BTRP must listen more than it

directs, and deliver whatever commitments are made. Central to the mission goals–even if not fully attainable–is to develop trusted relationships between BTRP and its partners in the host country. As noted in Chapter 5, open dialogue among equals builds understanding and trust between technical experts, which over the long term contributes further to trust and understanding among leaders in ministries and governments. Where trust exists, transparency increases, rendering those areas less hospitable for sub-state groups or individuals with ill intent. Professionals working on cooperative programs need technical, interpersonal, and diplomatic competencies.

FINDING 3.1: Successful programs match people from the two partner countries who have the necessary technical and diplomatic skills, and the willingness to develop relationships of trust through working together toward common goals. These interpersonal relationships form the resilient core of the larger institutional relationships.

RECOMMENDATION 3: BTRP should select technical engagement professionals to represent the U.S. government in these important engagements with consideration of their communication, interpersonal, and diplomatic skills and, as necessary, provide training in diplomacy and on the political contexts in which they work to supplement their necessary science backgrounds.

Assessment and Planning Prior to Engagement

BTRP resources are relatively small in comparison with other DOD programs and have been shrinking in recent years. In this context BTRP should not engage an international partner just because it can. The transportation, communication, and computational revolutions have provided an enhanced capacity to identify hot spots for emerging new risks and threats with a greater degree of accuracy than ever before. As explained below, BTRP should take an even more strategic view and carefully articulate why it must engage, where it must engage, and with what resources, including the necessary human resources, it must engage.

FINDING 4.1: The International Health Regulations (2005) require all countries to achieve minimum core competency to detect, assess, report, and respond to public health, plant,

and animal health risks and emergencies of national and international concern. Not all countries have met these requirements, in significant part because of inadequate resources to implement assessment and capacity strengthening support at the country level.

FINDING 4.2: Sample and data sharing are critical to early detection of transboundary outbreaks, but access to this information may be limited because of strict sample and data-sharing policies in partner countries. Delays in data access could delay reporting to international health organizations, alerting neighboring countries to the potential threat, and initiating emergency response activities in a timely manner, including development of field ready diagnostic tests, and planning of clinical trials of countermeasures, including therapeutics and vaccines.

FINDING 4.3: Methods for engineering and synthesizing viruses and bacteria are being democratized, enabling easier access to pathogens created or modified from gene sequence data. Although the skills, knowledge, and human and financial resources needed to create or modify live pathogens from chemical synthesis, reverse genetics, or genome editing are specialized and high, their use may be possible by scientists from nation states and well-resourced non-state actors intent on using microbial pathogens for malicious purposes.

FINDING 4.4: Measuring threat reduction from engagement programs is difficult. Common quantitative metrics are ineffective. The program needs to continue to develop and try out new approaches, such as the use of a quasi-qualitative rubric for measuring achievement of individual activities and overall goals of projects, country portfolios, and program initiatives. Such non-traditional measurements provide opportunities to course-correct when hurdles are encountered, support conditions and factors that facilitate achievement of goals, and promote partner country buy-in and sustainability of capabilities. This approach to metrics can help to demonstrate accountability, and provide greater awareness of program results and context of

engagement, to DOD senior leaders, Congress, and other relevant stakeholders.

RECOMMENDATION 4: The Office of the Secretary of Defense for Policy together with BTRP should monitor and identify likely future potential infectious disease vulnerabilities in the changing threat landscape. As a part of this forward assessment process, BTRP should identify opportunities to bolster local partner countries' capabilities to detect aberrations from the norm early in an event or outbreak in order to better anticipate events through improved disease surveillance and better analytical capacity.

CONNECTING BTRP WITH OTHERS ON BIOLOGICAL THREAT REDUCTION

Build and Leverage Networks

It is as clear that BTRP cannot address every biological threat as it is axiomatic that funds should be used in a manner that can efficiently produce the best outcomes. Not only is this the right thing to do, it is also the way to strengthen BTRP programs by building sound working relationships with other agencies of the U.S. government, international partners, nongovernmental organizations, academic institutions, and private companies that appropriately take the lead in many circumstances. By leveraging these relationships more effectively, BTRP can be better attuned to the threats, risks, and opportunities in the field. Because these threats and risks are so diverse and address a wide range of partners, BTRP should coordinate with partners who focus not only on human health, but also on animal and plant health, the safety and security of food systems; trade and travel routes; and the social, political, and economic factors that affect these elements of biosafety and biosecurity.

FINDING 5.1: Outbreaks of animal and plant pathogens that adversely affect the agricultural system and food industry can directly or indirectly impact human health, and have the potential to lead to destabilization of societies and economies, and/or national and regional conflicts.

FINDING 5.2: The inextricable links among human, animal, plant, and environmental health highlight the risk of natural or human-made pathogens in the food system, along trade and travel routes, and through changes in the environment. Each of these factors can either severely affect production of major plant food crops and meat products, or promote the appearance and spread of new potentially zoonotic infectious disease threats to humans in addition to their impacts on the affected animal populations. These risks could result in significant health, social, political, and economic consequences leading directly to political and civil unrest–especially in countries with pre-existing marginal or unstable governmental systems and weak infrastructure.

FINDING 5.3: Inadequate provision for fundamental needs, such as food and clean water, enables transmission of environmental pathogens into the human population and increases opportunities for conflict, which present a different type of security risk.

FINDING 5.4: Navigating the diverse landscape of international experts, implementing organizations, coordinating organizations, and funders can be difficult given the sheer number of entities involved. To be most effective, any actor engaging in these efforts–including BTRP–must leverage existing capabilities, cooperate with other funders regardless of any difference in mission, and promote deconfliction of activities in countries where human and financial resources are limited. To obtain the most information and understand the necessary response, these actors also need to coordinate with one another and to communicate and share information for the immediate public health needs and for generating research data for the future.

RECOMMENDATION 5: BTRP should focus more attention and emphasis on linking experts inside and outside of BTRP, including leaders in partner countries, into regional and global networks to further BTRP's mission goals and enhance its awareness of technical and epidemiological developments. These

include extant threats to political, social, and economic stability and long-term partner government sustainability in the context of outbreaks of emerging infectious diseases in humans, food animals, or crops in order to improve biosecurity broadly in vulnerable and at-risk partner countries.

Bolster Internal Expertise and Seek Advice

BTRP is inherently an action-oriented organization within DOD designed to reduce the risk of biological threats, and therefore BTRP staff require pragmatic political skills in addition to contemporary understanding of the nature of these biological threats, whatever their origin. In conjunction with the need for additional scientific expertise affiliated with the Cooperative Threat Reduction (CTR) Program, and participation in relevant scientific and biosecurity meetings, BTRP would benefit from access to an external broad-based group of experts, including those who can consider traditional and emerging biological threats that may arise from new research strategies and tools. These advisory groups have long served the military, beginning during World War II and continuing from 1953 as the Armed Forces Epidemiological Board. During the early days of the Nunn-Lugar CTR Program in the former Soviet Union, a small, senior advisory group was used very effectively by the Defense Threat Reduction Agency (DTRA), not only to enhance understanding of the scientific issues underlying threat reduction and to assist with project reviews but, importantly, to advocate for the CTR Program. In these times of cutbacks and a dearth of advocates in Congress, a group of senior experts with relevant experience to advise BTRP could add a robust scientific foundation for BTRP's efforts and help to make the case for its programs for the foreseeable future.

FINDING 6.1: Preparing for and responding to existing and potential biosecurity threats requires an agile ability to consider traditional biological threats and the contributions of new research strategies and tools to understand the pathogenesis and epidemic potential of emerging pathogens.

FINDING 6.2: The biological sciences and biotechnology are advancing at a pace that far exceeds current security assessments. Although the future is always hard to predict, the potential for DOD to anticipate current and future

capabilities and uses cannot be based on current scientific and technological activities alone, but rather must be amplified by accessing insights into where that science is going, what is the leading edge, and what are the hot topics and breakthrough achievements. This requires a sufficient and critical mass of well-trained scientists from diverse fields within the agency. The ability of these scientists to contribute fully will be strengthened by participation in high-level scientific conferences, reading of relevant publications, and networking with academia and leading biotechnology companies. They could also benefit from engagement with a high-level external scientific advisory group composed of experts in diverse scientific disciplines, particularly individuals with relevant international experience.

RECOMMENDATION 6: BTRP should acquire greater scientific expertise on its staff and proactively engage with the broader scientific community to better understand technical and scientific developments in emerging infectious diseases. This engagement can be accomplished by some combination of participating in important scientific meetings, contracting with scientific organizations, establishing a scientific advisory group, and/or working with individual experts. The goal is to access expertise and experience working internationally on topics of biosafety and biosecurity, epidemiology, disease surveillance, security, biotechnology, industry, and related topics. These efforts will strengthen BTRP's ability to meet its responsibilities and obligations, and enhance its effectiveness.

Network within DOD and U.S. Government Agencies

The surprise outbreak of Ebola in West Africa and its rapid spread regionally and sporadic cases arriving in a number of other countries in Europe and North America has clearly sent the message that we must engage, communicate, and plan more effectively within DOD and DTRA, as well as with other departments, agencies, and initiatives of the U.S. government. BTRP must be seen and recognized as playing an important and unique role, not only to anticipate future biothreats and support

capacity strengthening, but also to rapidly mobilize and coordinate support for the immediate response to an infectious disease outbreak or an incident caused by intentional misuse. As a result of its role, BTRP should be included in critical discussions and coordination meetings.

FINDING 7.1: Within DOD, BTRP plays a critical role in advancing national biosecurity interests internationally.

FINDING 7.2: Because BTRP is just one of several U.S. government programs conducting health security engagement, both the strategic vision and success of biosecurity programs rely on actions by the U.S. government as a whole, host governments, and international partners.

FINDING 7.3: Using the integrated view of biological threats and threat reduction, the U.S. government will be most effective and efficient if it identifies and prioritizes the threats and applies resources to those threats through the departments, organizations, offices, and channels that are best poised to address the associated needs. These channels are the various medical, military, diplomatic, humanitarian, scientific, and security programs of the U.S. government and its partners at home and internationally, which are able to intervene in different ways and in different contexts to eliminate, reduce, or mitigate threats at the most opportune and effective stage of threat development in different contexts. Strong interagency coordination must drive these prioritization and resource allocation efforts if the needs are to be addressed and unnecessary duplication of efforts and costs are to be avoided.

RECOMMENDATION 7a: BTRP should establish closer working relationships with the combatant commands, Army Futures Command, Assistant Secretary of Defense for Special Operations/Low-Intensity Conflict, and the Office of the Assistant Secretary of Defense for Health Affairs for coordination and prioritization of limited resources, and the service laboratories as well as relevant interagency partners such as the Centers for Disease Control and Prevention and the National Institutes of Health, sharing its unique capabilities and insights

about biothreats. Through effective synchronization, these entities can assist one another to more effectively protect the force and the nation.

RECOMMENDATION 7b: Over the next 5 years, BTRP, working with its many DOD partners, should encourage, engage, support, co-lead, and help drive the U.S. government's development of a durable interagency mechanism that draws on medical, military, diplomatic, scientific, and other expertise to address natural, accidental, and intentional biological threats and risks to the deployed force and to the nation. An effective interagency mechanism will avoid unnecessary duplication, identify and close gaps, and explore possible synergies. Likewise, it will allow for greater geographic flexibility, more effective communication links, and will demonstrate better awareness and prevention of threat development, and more timely response. To enhance overall coordination, BTRP should partner effectively within DOD, with other U.S. government agencies, with other nations, as well as with NGOs, the private sector, and academia.

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A

Committee Biographies

David R. Franz (Co-chair from April 2019)

David R. Franz is an independent consultant. He served in the U.S. Army Medical Research and Materiel Command for 23 of 27 years on active duty and retired as a colonel. He served as commander of the U.S. Army Medical Research Institute of Infectious Diseases and as deputy commander of the Medical Research and Materiel Command. Prior to joining the Command, he served as group veterinarian for the 10th Special Forces Group (Airborne). Dr. Franz was the chief inspector on three United Nations (UN) Special Commission biological warfare inspection missions to Iraq, and served as technical advisor on long-term monitoring. He also served as a member of the first two U.S.–U.K. teams that visited Russia in support of the Trilateral Joint Statement on Biological Weapons and as a member of the Trilateral Experts' Committee for biological weapons negotiations. He is a member of the National Academy of Sciences' Committee on International Security and Arms Control. He previously served on the National Academies of Sciences, Engineering, and Medicine (NASEM) Board on Life Sciences, and the Health and Human Services National Science Advisory Board for Biosecurity. Dr. Franz also co-chaired the NASEM Committee on Strengthening and Expanding the Department of Defense's Cooperative Threat Reduction Program. Dr. Franz holds a D.V.M. from Kansas State University and a Ph.D. in physiology from Baylor College of Medicine.

Gerald T. Keusch (NAM) (Co-chair from April 2019)

Gerald Keusch is professor of medicine and global health at Boston University, where he serves as an associate director of the National Emerging Infectious Diseases Laboratory. He is board certified in internal medicine and infectious diseases. His research has ranged from the molecular pathogenesis of tropical infectious diseases to field research in nutrition, immunology, host susceptibility, and the treatment of tropical

infectious diseases and HIV/AIDS. He has held faculty positions at Tufts University, where he was director of training programs in infectious disease. He served as director of the National Institutes of Health (NIH) Fogarty International Center. Dr. Keusch is the recipient of three major awards from the Infectious Diseases Society of America (the Oswald Avery and Alexander Fleming awards for research and training excellence, and the Finland Lectureship). He attended Columbia College and earned his M.D. from Harvard Medical School. He is also a member of the National Academy of Medicine (NAM), and co-chaired the 2017 National Academies' report, *Integrating Clinical Research into Emergency Response: The Ebola Experience.*

Ronald M. Atlas (Chair, until April 2019)

Ronald M. Atlas was co-chair of the Public and Scientific Affairs Board Biodefense Committee of the American Society for Microbiology (ASM) and was professor of biology at the University of Louisville. He has served as president of ASM; as a member of the NIH Recombinant Advisory Committee; as chair of the National Aeronautics and Space Administration's Planetary Protection Committee; as chair of the Wellcome Trust Pathogens, Immunology and Population Health Strategy Committee; as a member of the Department of Homeland Security Science and Technology Advisory Committee; and as chair of the Board of Directors of the One Health Commission. He is author of nearly 300 manuscripts and 20 books, and has served on numerous National Academies committees. He is a fellow in the American Academy of Microbiology. Dr. Atlas is a pioneer of bioremediation and an expert on the clean-up of oil spills, and is also an expert in the detection of biothreat agents and the prevention of bioterrorism. He received his B.S. degree from the State University at Stony Brook, his M.S. and Ph.D. degrees from Rutgers, the State University of New Jersey, and his D.Sc. (honoris causa) from the University of Guelph.

Nesreen AL-Hmoud

Nesreen AL-Hmoud is the director of the Center for Excellence in Biosafety, Biosecurity, and Biotechnology at the Royal (Jordanian) Scientific Society. Dr. AL-Hmoud conducts research that focuses on the preservation of human health and biodiversity, specifically in the fields of biosafety, water and food safety, and the evaluation of risks from genetically modified organisms. She is particularly interested in

international scientific cooperation and works toward the development of scientific capacity that can benefit the broader scientific community, government agencies, local communities, and nongovernmental organizations in Jordan and the Middle East and North Africa (MENA) region. She focuses on research that involves a holistic approach to microbiology, molecular biology, virology, toxicology, and ecology. She is a frequent participant at international biosafety meetings, and has attended international governmental meetings at the Biological and Toxin Weapons Convention and the United Nations 1540 Committee. Dr. AL-Hmoud received her B.S. in biology from the University of Jordan, and her M.Phil. and Ph.D. in microbiology from the University of Abertay Dundee in Scotland.

David M. Barash

David Barash is the executive director of the Global Health Portfolio and chief medical officer for the GE Foundation. Dr. Barash is also co-chair of the Private Sector Roundtable, a collaboration of several multinational companies to support the work of the Global Health Security Agenda. He is a practicing emergency medicine physician with more than 30 years of experience. Prior to joining the GE Foundation, Dr. Barash was chief medical officer of Life Care Solutions. He was also founder and president of Concord Healthcare Strategies, where he provided strategic and operational expertise to medical technology investors and development-stage medical technology companies. He received his B.A. and M.D. degrees from Cornell University, and is a fellow of the American College of Emergency Physicians.

Kavita M. Berger

Kavita Berger is a scientist at Gryphon Scientific where she is building new programs on international bioengagement and science policy. She began her career in science and security policy in 2005 at the American Association for the Advancement of Science (AAAS), where she developed activities that engaged science policy and security experts on topics ranging from health security to biological weapons, enabling scientists to bring their knowledge and experience to current security policy dialogues and the security policy community to better understand the broader implications of science and technology. Dr. Berger has conducted forward-looking studies, such as the 2014 evaluation of the security implications of big data in the life sciences. She also has engaged

scientists across the MENA region and South Asia since 2009 to work together to prevent biosecurity threats. Her work in the MENA region promoted partnership and trust among U.S. and regional scientists to jointly reduce biological risks. Prior to joining AAAS, Dr. Berger conducted her post-doctoral research at the Emory Vaccine Center on pre-clinical research and development of HIV and smallpox vaccines. She received her B.S. in molecular genetics at The Ohio State University and her Ph.D. in genetics and molecular biology at Emory University.

Rear Admiral Kenneth W. Bernard

Rear Admiral Kenneth Bernard, U.S. Public Health Service (Ret.), is an independent consultant on security and health issues. He served as special assistant to President George W. Bush for biodefense on the Homeland Security Council from 2002 to 2005. Admiral Bernard chaired the White House Biodefense Policy Coordinating Committee, and drafted decision directives for President Bush on both "Biodefense for the 21st Century" and agricultural bioterrorism, and he was the White House point person on implementation of the Project Bioshield Act. After September 11, 2001, he created the position of special adviser for national security, intelligence, and defense to the Secretary of Health and Human Services (HHS). Prior to this service, Admiral Bernard worked as a professional staff member in the U.S. Senate, served on President Clinton's National Security Council staff, as the international health attaché at the U.S. Mission to the UN in Geneva, Switzerland, as the associate director for medical and scientific affairs in the Office of International Health at HHS, as international health policy adviser to the director of the U.S. Peace Corps, and as a medical epidemiologist at the Centers for Disease Control and Prevention. Admiral Bernard earned his M.D. from the University of California, Davis, and a diploma in tropical medicine and hygiene from the London School of Hygiene and Tropical Medicine. He is board certified in internal medicine.

Gregory C. Gray

Gregory C. Gray is a professor at Duke University in the Division of Infectious Diseases of the School of Medicine, the Global Health Institute, and the Nicholas School of the Environment. He also serves part-time as a professor in the Emerging Infectious Diseases Programme at Duke-NUS Medical School, Singapore, and as a professor of global health at Duke Kunshan University in China. Dr. Gray has conducted diverse epidemiological studies of infectious diseases for 25 years on five

continents. He has published more than 330 peer-reviewed scientific manuscripts and book chapters. Much of his work has involved identifying risk factors for occupational diseases, particularly for infectious diseases in a wide variety of occupational groups. He has served on numerous national expert advisory committees including those associated with the U.S. Armed Forces Epidemiological Board, the Infectious Disease Society of America, and the National Academy of Medicine. Dr. Gray earned his M.P.H. from the Johns Hopkins Bloomberg School of Public Health, and his M.D. from the University of Alabama at Birmingham.

Ambassador John E. Lange

Ambassador John E. Lange (Ret.) is senior fellow for Global Health Diplomacy at the UN Foundation. He has held leadership positions in the Global Polio Eradication Initiative and the Measles & Rubella Initiative. Previously, he spent 4 years at the Bill & Melinda Gates Foundation engaging in high-level global health advocacy with African governments. Ambassador Lange had a distinguished 28-year career in the Foreign Service at the U.S. Department of State, including service as Special Representative on Avian and Pandemic Influenza, Deputy Inspector General, Deputy U.S. Global AIDS Coordinator, Ambassador to Botswana, and Charge d'Affaires at the U.S. Embassy in Dar es Salaam during the August 7, 1998, terrorist bombing, for which he received the State Department's Distinguished Honor Award. Earlier, he had tours of duty in Geneva, Lomé, Paris, and Mexico City. Ambassador Lange co-chaired a NAM committee that issued a consensus report on investing in global health systems and authored a case study on pandemic influenza negotiations. He earned a B.A. from the University of Wisconsin–Madison, an M.S. from the National War College, and a J.D. from the University of Wisconsin Law School.

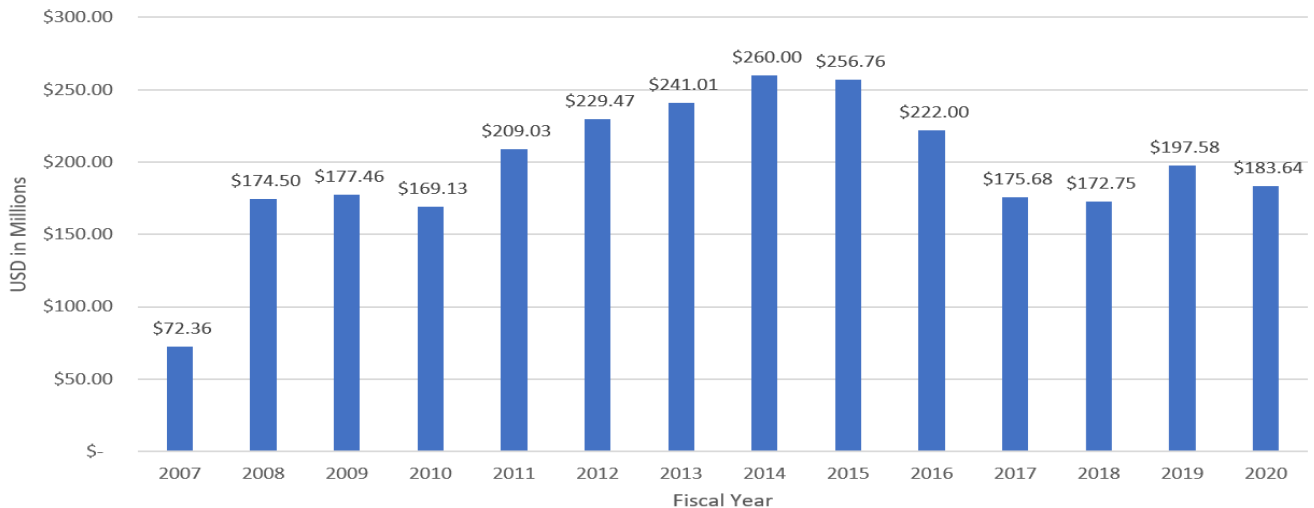
Mobolaji Oladoyin Odubanjo

M. Oladoyin Odubanjo is the executive secretary of the Nigerian Academy of Science and the chairman of the steering committee of the International Network for Government Science Advice. Dr. Odubanjo is a fellow of the Royal Society of Public Health and the chairman of the Association of Public Health Physicians of Nigeria (Lagos Chapter). He was a medical officer in the employment of a state government in Nigeria which saw him work in five hospitals across the state. He has served on the Board of the Global Organisation for Maternal and Child Health USA. He is also an

advisor to the Centre for Palliative Care Nigeria, an organization at the forefront of establishing palliative medicine in Nigeria. Dr. Odubanjo earned his MBBS and his diploma in child health from the University of Ibadan, and his M.Sc. in public health from University College London's Institute of Child Health.

B

Congressionally-Appropriated Funding for the Biological Threat Reduction Program (2007-2020)



SOURCES: Newman, 2018; Nikitin and Woolf, 2014, p. 42; U.S. DOD, 2017, 2019a, 2020a.
NOTE: The 2020 value is an estimate, not the actual allocated amount.

C

U.S. and International Agencies and Organizations Engaged in Global Health Security

U.S. GOVERNMENT AGENCIES

U.S. Agency for International Development (USAID)

USAID is an international development agency and a catalytic actor driving development results. USAID works to help lift lives, build communities, and advance democracy. USAID's work advances U.S. national security and economic prosperity; demonstrates American generosity; and promotes a path to recipient self-reliance and resilience. (USAID, 2020)

U.S. Armed Forces Research Institute of Medical Sciences (AFRIMS)

For 50 years, AFRIMS has been working in tropical infectious disease research and development. It has acquired new disease research missions and has refocused many times to meet new challenges. It now has programs in enteric diseases (infectious causes of diarrhea), malaria vaccine and drug research, viral diseases (especially dengue fever and hepatitis), an Entomology department dedicated to the study of disease vectors, and a retrovirology department that has been organized to execute vaccine studies for the HIV/AIDS virus. A recently initiated program to monitor new, emerging disease threats as a part of a Global Emerging Diseases Surveillance system is now underway. (AFRIMS, 2020)

U.S. Army Combat Capabilities Development Command (CCDC) Chemical Biological Center

The CCDC Chemical Biological Center is the primary Department of Defense (DOD) technical organization for non-medical chemical and biological defense. It fosters research, development, testing, and application of technologies for protecting warfighters, first responders,

and the nation from chemical and biological warfare agents. CCDC Chemical Biological Center is currently developing better ways to remotely detect these chemical and biological materials—before the warfighter or first responder ever enters the threat zone. CCDC Chemical Biological Center is also developing a new generation of technologies to counter everything from homemade explosives to biological aerosols to traditional and non-traditional chemical hazards. (CCDC, 2020)

U.S. Army Medical Research and Development Command (USAMRDC)

The U.S. Army Medical Research and Development Command is the Army's medical materiel developer, with responsibility for medical research, development, and acquisition. The USAMRDC's expertise in these critical areas helps establish and maintain the capabilities the Army needs to remain ready and lethal on the battlefield. (MRDC, 2020)

U.S. Centers for Disease Control and Prevention (CDC)

CDC works to protect America from health, safety, and security threats, both foreign and in the United States. Whether diseases start at home or abroad, are chronic or acute, curable or preventable, human error or deliberate attack, CDC fights disease and supports communities and citizens to do the same. CDC increases the health security of the United States. As the nation's health protection agency, CDC saves lives and protects people from health threats. To accomplish its mission, CDC conducts critical science and provides health information that protects the nation against expensive and dangerous health threats, and responds when these arise. (CDC, 2020)

U.S. Department of Agriculture (USDA)

USDA provides leadership on food, agriculture, natural resources, rural development, nutrition, and related issues based on public policy, the best available science, and effective management. Its vision is to provide economic opportunity through innovation, helping rural America to thrive; to promote agriculture production that better nourishes Americans while also helping feed others throughout the world; and to preserve the United States' natural resources through conservation, restored forests, improved watersheds, and healthy private working lands. (USDA, 2020)

U.S. Office of the Deputy Assistant Secretary of Defense (DASD) for Health Readiness Policy and Oversight (HRP&O)

The DASD for HRP&O is the principal staff assistant and advisor to the Assistant Secretary of Defense (Health Affairs) for all medically related readiness DOD policies, programs, and activities. The office is responsible for force health protection, global health engagement, U.S. military assistance in global pandemic containment, international health agreements, deployment-related health policy, joint theater-of-operations information systems, humanitarian and health missions, and national disaster support. (MHS, 2020)

U.S. Department of Defense Office of the Under Secretary of Defense for Policy

The mission of the Office of the Under Secretary of Defense for Policy is to consistently provide responsive, forward-thinking, and insightful policy advice and support to the Secretary of Defense, and the Department of Defense, in alignment with national security objectives. (U.S. DOD, 2020b)

U.S. Department of Health and Human Services (HHS), Office of Global Affairs (OGA)

Global health diplomacy—the intersection of public health and foreign policy—is the core of OGA's work. Through relationships with multilateral organizations, foreign governments, ministries of health, civil society groups, and the private sector, OGA creates and maintains the pathways for HHS to apply its expertise globally, learn from our overseas counterparts, and advance policies that protect and promote health at home and worldwide. (U.S. HHS, 2020a)

U.S. Department of State Biosecurity Engagement Program (BEP)

BEP was first funded in FY 2006 and is part of the Nonproliferation, Anti-Terrorism, Demining and Related Programs Global Threat Reduction programs account managed and implemented by the U.S. Department of State Bureau of International Security and Nonproliferation Office of Cooperative Threat Reduction (ISN/CTR). BEP's mission is to engage life scientists and to combat biological threats worldwide by providing assistance to improve biosecurity, biosafety, pathogen surveillance, and infectious disease surveillance and response. (U.S. DOS, 2019)

U.S. President's Emergency Plan for AIDS Relief (PEPFAR)

PEPFAR is the U.S. government's response to the global HIV/AIDS epidemic and represents the largest commitment by any nation to address a single disease in history. Thanks to American leadership and generosity, alongside the work of many partners, PEPFAR has saved millions of lives, averted millions of infections, and changed the course of the epidemic. (U.S. HHS, 2020b)

INTERNATIONAL GOVERNMENTAL EFFORTS

Bureau of International Health Cooperation, Japan

The Bureau of International Health Cooperation provides various kinds of supports in order to improve healthcare in developing countries. It assists developing countries mainly in the fields of maternal and child health, infectious disease control, and health system strengthening in order to protect the people from life-threatening diseases. It dispatches experts to technical cooperation projects in developing countries, trains health personnel domestically and abroad, and conducts health research; and in addition, it dispatches medical relief teams in many parts of the world in response to natural disasters and epidemics of communicable diseases. (NCGM, 2020)

Centre for Biosecurity, Government of Canada

The Centre for Biosecurity (the Centre) comprises four different offices, which administer and enforce the Human Pathogens and Toxins Act, the Human Pathogen and Toxins Regulations, and certain sections of the Health of Animals Act and the Health of Animals Regulations. Each Office contributes to the Agency's ongoing efforts to anticipate and respond to public health challenges and protect the health, safety, and security of the Canadian public against the risks posed by human pathogens and toxins. (Government of Canada, 2017)

Enabel, Belgium

Enabel is the Belgian development agency. Its mission is to implement and coordinate the Belgian international development policy. It seeks to develop an efficient and sustainable health system that ensures quality healthcare for all. (Enabel, 2020)

Korea International Cooperation Agency (KOICA)

KOICA, established by the Ministry of Foreign Affairs of the Republic of Korea, is mandated to contribute to the advancement of international cooperation through various projects that build friendly and collaborative relationships and mutual exchanges between Korea and developing countries and support the economic and social development in developing countries. KOICA established the Health Mid-Term Strategy (2016-2020) and is striving to provide quality healthcare services and to ensure universal health for residents in beneficiary countries. (KOICA, 2020)

Ministry of Foreign Affairs, Japan

The Ministry of Foreign Affairs sets Japanese health policy. Japan's development assistance for health includes public and private sources of funding. (Llano et al., 2011; Ministry of Foreign Affairs of Japan, 2019)

National Institute of Health, Italy

The institute plans, implements, and evaluates training activities designed to address the needs of the National Health Service. The topics addressed include health service management and evaluation, epidemiology and biostatistics, training methods, laboratory techniques, diseases control and priority public health issues, and health promotion. The institute also plans international health projects. It actively promotes cooperation at three different levels of involvement: scientific partnerships with industrialized countries; scientific and development projects in partnership with economies in transition; and development partnerships in Africa and countries in turmoil, where humanitarian and technical assistance is provided to monitor the National Health Service and safeguard the nation's health. (IANPHI, 2020; ISS, 2020)

Department of Health, Australian Government

The objectives that frame the Department of Health's international engagement are viewed by the Department as inter-linked. None can be achieved in isolation. Collectively, they position the Department to align domestic and international agendas, address shared challenges with valued partners, and provide Australian leadership where appropriate. Its objectives are: (1) protect the health of Australians; (2) keep Australia's health system at the forefront of international best practice; (3) promote evidence-based international norms and standards to support robust health systems and better health in Australia and internationally; and (4)

contribute to Australia's foreign, development, trade, and economic policy goals. (Australian Government, 2020)

U.K. Department for International Development

The Department for International Development leads the United Kingdom's work to end extreme poverty. It tackles the global challenges of our time including poverty and disease, mass migration, insecurity, and conflict. It works to build a safer, healthier, more prosperous world for people in developing countries, and in the United Kingdom as well. (Government of the United Kingdom, 2020)

U.S. ORGANIZATIONS AND IMPLEMENTORS

Emory University's Environmental Health and Safety Office (EHSO)

The mission of EHSO is to provide and support comprehensive environmental, health, and safety programs and services in support of the University's mission to create, preserve, teach and apply knowledge in the service of humanity. (Emory University, 2019)

MRIGlobal

MRIGlobal is a world leader in technology and science. Formerly known as Midwest Research Institute, MRIGlobal has a vast history of working with government agencies, commercial businesses, and academic institutions every year to help further unbiased research and innovative development. (MRIGlobal, 2020)

Nuclear Threat Initiative (NTI)

NTI | bio is working with stakeholders around the world to mitigate the misuse of tools and technologies to carry out biological attacks and to reduce the risk of a laboratory accident that could result in a high-consequence or catastrophic biological event. (NTI, 2020a)

Navy Medical Research and Development Laboratories

The Navy's Medical Research and Development Laboratories are engaged in a broad spectrum of activity from basic science in the laboratory to field studies at sites in remote areas of the world to operational environments. The capabilities and the geographical locations of the laboratories reflect

the broad mission of Navy Medicine's Research and Development Enterprise. (U.S. Navy, 2020b)

Sandia National Laboratories

For more than 70 years, Sandia has delivered essential science and technology to resolve the nation's most challenging security issues. Sandia National Laboratories operates as a contractor for the U.S. Department of State's Bioengagement Program and supports numerous federal, state, and local government agencies, companies, and organizations. (Sandia National Laboratories, 2020)

Center for Global Health Engagement (CGHE)

The CGHE's mission is to provide operational support to DOD's Global Health Engagement enterprise to meet national security objectives. (Uniformed Services University, 2020)

INTERNATIONAL AND REGIONAL ORGANIZATIONS

Biological Weapons Convention (BWC) Implementation Support Unit (ISU)

BWC ISU provides: administrative support and assistance; national implementation support and assistance; support and assistance for confidence-building measures; support and assistance for obtaining universality; administers the database for assistance requests and offers and facilitates associated exchanges of information; and supports States Parties' efforts to implement the decisions and recommendations of the review conference. (UN, 2020d)

CEPI

CEPI is an innovative partnership between public, private, philanthropic, and civil organisations launched to develop vaccines to stop future epidemics. (CEPI, 2019)

European Union (EU) Chemical, Biological, Radiological and Nuclear Risk Mitigation (CBRN) Centres of Excellence

The EU CBRN CoE was launched in response to the need to strengthen the institutional capacity of countries outside the European Union to mitigate CBRN risks. (European Union, 2020)

Food and Agriculture Organization of the United Nations (FAO)

FAO is a specialized agency of the United Nations that leads international efforts to defeat hunger. Its goal is to achieve food security for all and make sure that people have regular access to enough high-quality food to lead active, healthy lives. With more than 194 member states, FAO works in more than 130 countries worldwide. (FAO, 2020a)

Global Health Security Agenda (GHSA)

GHSA is a group of countries, international organizations, nongovernmental organizations, and private sector companies that have come together to advance a world safe and secure from infectious disease threats. Under GHSA, nations from all over the world make new, concrete commitments, and elevate global health security as a national leaders-level priority. (GHSA, 2020)

Global Partnership Against the Spread of Weapons and Materials of Mass Destruction

The Global Partnership is an international forum for coordination of projects to prevent CBRN terrorism and proliferation. (GPWMD, 2020)

Institut Pasteur International Network

The Institut Pasteur Department of International Affairs is responsible for animating and developing the Institut Pasteur International Network, particularly by coordinating major programs that meet current global health challenges. It is also in charge of developing new corporate and scientific partnerships to boost the worldwide presence of the Institut Pasteur and help to address human health challenges. (Institut Pasteur, 2020)

International Plant Protection Convention (IPPC)

IPPC is an intergovernmental treaty signed by more than 180 countries, aiming to protect the world's plant resources from the spread and

introduction of pests, and promoting safe trade. The Convention introduced International Standards for Phytosanitary Measures as its main tool to achieve its goals, making it the sole global standard setting organization for plant health. IPPC is one of the "Three Sisters" recognized by the World Trade Organization's (WTO) Sanitary and Phytosanitary Measures Agreement, along with the Codex Alimentarius Commission for food safety standards, and the World Organization for Animal Health (OIE) for animal health standards. (FAO, 2020b)

Middle East Consortium on Infectious Disease Surveillance (MECIDS)

MECIDS seeks to advance the capabilities of early infectious disease detection, control, and response between its member countries of Israel, Jordan, and the Palestinian Territory, with plans to expand the network to all countries in the region. Its primary health concerns are food-borne illnesses, avian influenza, and Leishmaniasis, a disabling and disfiguring disease. (Connecting Organizations for Regional Disease Surveillance, 2020)

Organization of Islamic Cooperation (OIC)

OIC endeavors to safeguard and protect the interests of the Muslim world in the spirit of promoting international peace and harmony among various people of the world. The domain of health is an important sector among the various areas identified for joint Islamic action in the Ten Year Programme of Action (TYPOA). The TYPOA, Islamic Summit Conferences, Islamic Conferences of Health Ministers, and the Council of Foreign Ministers, place special emphasis on programs and activities, with the involvement of WHO and relevant international organizations, for combating diseases and epidemics, strengthening child health, and eradication of polio. (Organisation of Islamic Cooperation, 2020)

United Nations Office for Disarmament Affairs (UNODA)

UNODA supports multilateral efforts aimed at achieving the ultimate goal of general and complete disarmament under strict and effective international control. The mandate for the program is derived from the priorities established in relevant General Assembly resolutions and decisions in the field of disarmament. Weapons of mass destruction continue to be of primary concern owing to their destructive power and the threat that they pose to humanity. The Office also works to address the

humanitarian impact of major conventional weapons and emerging weapon technologies. (UN, 2020b)

United Nations Office of Counter-Terrorism (UNOCT)

UNOCT provides UN Member States with necessary policy support, and provides in-depth knowledge of the United Nations Global Counter-Terrorism Strategy, and wherever necessary, expedites delivery of technical assistance across four pillars. (UN, 2020e)

United Nations Security Council Resolution (UNSCR) 1540 Committee

Resolution 1540 (2004) imposes binding obligations on all States to adopt legislation to prevent the proliferation of nuclear, chemical, and biological weapons, and their means of delivery, and establish appropriate domestic controls over related materials to prevent their illicit trafficking. It also encourages enhanced international cooperation in this regard. (UN, 2020a)

Virtual Biosecurity Center (VBC)

The VBC, founded in 2011, is a global multi-organizational initiative spearheaded by the Federation of American Scientists committed to countering the threat posed by the development or use of biological weapons and the responsible use of science and technology. The VBC is the "one stop shop" for biosecurity information, education, best practices, and collaboration. (VBC, 2020)

World Health Organization (WHO)

WHO works worldwide to promote health, keep the world safe, and serve the vulnerable. Its goal is to ensure that a billion more people have universal health coverage, to protect a billion more people from health emergencies, and provide a further billion people with better health and well-being. (WHO, 2020c)

World Organisation for Animal Health (OIE)

OIE is the intergovernmental organization responsible for improving animal health worldwide. It is recognized as a reference organization by the WTO and in 2018 had a total of 182 member countries. The OIE maintains permanent relations with nearly 75 other international and

regional organizations, and has regional and sub-regional offices on every continent (OIE, 2020a).