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Placing Global Biosecurity Engagement Programs under the Umbrella of Global Health Security

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Executive Summary

Global biosecurity engagement programs designed to prevent misuse of biological agents and pathogens internationally have increased dramatically under the National Strategy for Countering Biological Threats (NSCBT), which outlined the commitment of the United States Government towards advancing health security .[1] But it is difficult to measure the effectiveness of these programs in improving biosecurity given that there have been relatively few attempts to misuse the life sciences. Current metrics that focus on outputs (what was done) as opposed to outcomes (the impact of what was done) have not been helpful in determining how these efforts might be improved in the future. With these metrics in mind, the goals of the programs have traditionally been more quantitative in nature – for example, increasing the number of agents secured and number of scientists engaged. Broadening the scope of biosecurity engagement metrics can help align program goals with a more qualitative approach that prioritizes the international partner's global health security. Such an approach will be more efficient and successful in improving global and U.S. national biosecurity.

To understand how biosecurity engagement (BE) is currently being conducted and evaluated, interviews were carried out with more than 35 individuals in the United States (including government officials and their non-governmental partners) and abroad (scientists and policymakers engaged through BEs).[i] Over the course of these interviews, the need for restructuring the biosecurity portfolio became increasingly apparent. Many scientists and policymakers agreed that "we need to change the whole program of engagement" to focus more on the "hearts and minds" of our engagement partners (EP). Most programs currently focus on quantifiable outputs: "guns, gates, guards," numbers of workshops held, and scientists trained in biosafety techniques. New programs should emphasize global health security benefits and consider qualitatively-measured outcomes to broaden the scope and effectiveness of the engagements. As resources become limited, the need for a more streamlined, efficient interagency approach to these programs is stark. Ultimately, designing engagements that directly improve global health outcomes will indirectly address biosecurity. More importantly, prioritizing the health and wellbeing of the partner will facilitate global trust and good relationships, thereby more effectively reducing threats to the United States.

This issue brief analyzes information derived from experts to provide: (1) a proposed strategy to support integration of biosecurity within global health security, and (2) a working framework that outlines specific objectives to utilize when designing engagement projects to improve upon global biosecurity.

Proposed Strategy

This strategy provides a framework to support the establishment of a strong, well-functioning global health system that simultaneously advances biosafety, biosecurity, and a culture of responsible scientific research.[2] In order to integrate biosecurity with global health security, the United States government (USG) should:

1. Adopt a more cohesive system of metrics that capture long-term public health goals;

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[i] U.S. government entities – Departments of State (DOS) and Defense (DOD), US Department of Agriculture (USDA), Office of Science and Technology Policy (OSTP), Department of Energy's Sandia National Laboratories, non-profit organizations – the American Association for the Advancement of Science (AAAS), the National Academy of Sciences (NAS) and private organizations – CRDF Global and Metabiota, as well as their international collaborators; both policymakers and scientists from the Former Soviet Union (FSU), the Middle East (ME), Europe, Africa, and South East Asia (SEA).

2. List objectives that will restructure how programs are designed, prioritized, and carried out;
3. Think in a region-specific way when developing and operationalizing projects;
4. Apply these new metrics to past projects in order to identify ways in which future projects can be improved.

The conclusions of this study point to the need for a paradigm shift in the way BEs are designed, enacted, and evaluated. Each project should begin by clearly articulating the benefit towards global health security. Implementing this vision across the collection of projects funded by the USG and non-governmental partners will develop the entire scope of biosecurity engagement. This portfolio-based approach will allow for greater communication among all stakeholders and provide greater efficiency. A Middle Eastern scientist interviewed for this study had reportedly attended thirty-seven biosafety and biosecurity workshops in the last seven years, many sponsored by different agencies, which "asked similar, if not identical questions." Unifying BEs under one strategy allows each agency and partner to address specific pieces that together work towards the common goal, which can help to prevent this kind of overlap and duplication.

EPs are prioritized based on the presence of naturally occurring and endemic pathogens, a burgeoning biological sciences/biosecurity field, and the presence of terrorists in a given region. However, the way in which each region, and even each country, fits into these priorities is drastically different. The strategy described here covers four regions with distinct characteristics to help guide planning of future BEs in order to garner monetary and conceptual buy-in from governments and citizens alike.

It stands to reason that metrics used to determine the success of past programs should inform the development of new programs. Current BEs are designed to meet certain metrics of success and are evaluated accordingly. However, USG engagers across the suite of programs admit that these metrics are often a "formality" and are rarely used to inform subsequent engagements in any measureable way.[3] Examples are presented below of how to apply new metrics to old projects, which can help stimulate innovations towards future projects. To further illustrate, several projects designed by EPs themselves to be most beneficial to their respective region, are also described below along with indicators of their success.

Global Biosecurity Challenges and Possibilities

Since the demise of the former Soviet Union (FSU), scientific engagement efforts have been needed to ensure biosecurity. The initial framework that guided these engagements was modeled after the Nunn-Lugar Cooperative Threat Reduction program, which was primarily established to assist the FSU in dismantling its nuclear and biological weapons and realigning its weapons scientists.[4] While this program enjoyed many successes, there are stark differences in ideal engagement models for countries like those in the FSU, which possessed weapons programs, and those that have no history of biological weapons programs- which is where most biosecurity engagement efforts take place today.

Many comprehensive documents have since been drafted that list metrics tailored for evaluating and improving modern biological engagement programs.[5,6] There are two main problems with these metrics and, therefore, the ability to use them effectively. First, the focus tends to be primarily on quantitative metrics, achieved by "applying U.S.-based life science regulations internationally," instead of the more qualitative indicators that would speak to the establishment of sustainable and trusting relationships that unite life scientists from different countries. Without addressing the human element, programs aimed simply at building institutional capacity will fail at achieving their goals. Second, these metrics are not currently being utilized to define and refine goals to ensure successes; ideally, as one interviewee described, there would be "communicators in place, ideal metrics to measure, and a set-up operationalized and carried out" effectively.

To begin, developing a comprehensive strategic understanding of global biosecurity will help foster the creation of individual projects that contribute to this greater goal. While there is no single definition of biosecurity, it is possible to define important components. At the most basic level, biosecurity is a "biorisk management framework" that encompasses the traditional definitions of biosafety and biosecurity. Biosafety entails "protecting the individual from pathogens," usually by standardizing facilities, equipment, and procedures to ensure safe practices in terms of handling, securing, and disposing of bioagents. Biosecurity extends beyond these basic laboratory practices to "develop codes of conduct" that provide instruction for guarding pathogens and biological agents from misuse. This requires accounting for the more human aspects of security. As it is often said, "you can put a lock on a door" that guards a pathogen, but it is useless if the "human doesn't know to lock it." To that end, training is crucial to help scientists and others who support their work understand what scientific information has risk potential.

Internationally there is "poor recognition of the potential hostile use of life science knowledge or skills," which in many instances carries a greater potential threat than the agent itself. Scientists and technical experts are the "first line of defense against misuse of biological agents" and also play key roles in mitigating biological threats by investigating biological agents, developing bio-sensors, and producing medical countermeasures. Thus, establishing a "sustainable culture" of biological research, marked by career opportunities and funding possibilities as well as international forums that enforce a global concept of responsibilities, makes life science a "harder target for misuse." However, as one interviewee explained, while there is generally a willingness and openness in the international scientific community towards discussions on biosecurity, this same congeniality is not guaranteed at the political level where such discussions can seem to carry "accusations and blame."

Therefore, another crucial component of global biosecurity is a legal framework, which codifies and harmonizes institutions internally and also protects international treaty regimes that work to ensure a culture of scientific responsibility. While more difficult, working towards government buy-in of international laws and norms should be an "overarching goal of every engagement." Political investment promotes sustainability of individual programs by deferring some of the long-term costs and by encouraging feedback and cooperation. As one expert put it, positioning "the whole biosecurity concept in a much larger [global health] program" that addresses the needs of the EP will facilitate government participation.

Therefore all components of biosecurity can tie into the larger framework of global health security, which works to prevent, detect, and respond to infectious diseases. Biosecurity deals with prevention of man-made health risks. Global health security includes endemic diseases, which also threaten the security of the United States. Important components of global health security are functioning biosurveillance systems and a public health infrastructure with the ability to detect and respond to all types of biological threats. But biosecurity is currently "talk[ed] about as separate from the health system." With the current funding limitations, "public health and global health systems need to take [biosecurity] on as an integral piece" to ensure the functioning of all three.

While the NSCBT lists promoting global health security as the top objective, in reality, most BEs functionally separate biosecurity from global health by focusing narrowly on basic biosafety outputs through pathogen and select agent containment. .[7] Engagement programs have recently extended to discussions on biosecurity and bioethics. Broadening the scope of the programs is a step in the right direction, but these goals are only indirectly related to global health security. When designing new programs, outcomes should directly improve global health security by addressing local and regional diagnostic and biosurvellience capacities, the public health infrastructure, and the capacity to respond to endemic disease load. Broadly improving the EPs ability to respond to disease will indirectly improve their capacity to respond to the U.S. select agent list. Restructuring the programs in this way will address the goals of the USG and prioritize the needs of the EP, thereby promoting trust and engendering good will internationally.

Strategic Framework

The strategy that follows adopts a cohesive, goal-oriented framework to articulate higher-level outcomes as they relate to global health security. Instead of simply including the goals of the EPs, the BEs must instead prioritize their public health and research needs. A USG official described the current process as beginning with a "U.S. set of objectives" that are then "fit together" with the priorities of the EP. But very few countries, if any, would define their public health, and subsequent research priorities, in the same way as the United States. For example, according to a USG official who works in biodefense, the United States is very "risk intolerant" whereas other countries might say "we are okay with 90% confidence [in our safety]." Further, the United States has one of the "biggest risks for biosecurity threats so we need to be sure with 99.9% confidence that we are going to be safe." Accordingly, the United States is one of the only governments to have regulations in place that comprehensively address facilities and personnel working with bioagents, an outcome of risk intolerance.

But a U.S.-first approach in designing and implementing BEs has led to inefficiencies in funding allocations. A project designed to combat hemorrhagic fever (VHF), a U.S. objective, funded a VHF-specific ward in a West African hospital. Yet, the U.S. non-governmental contractor who managed the project detailed how this better staffed and equipped ward "sees only 1% of the patients" at the hospital, while the capacity of the rest of the hospital that deals with the highest health priorities, such as malnutrition, dehydration, and endemic diseases like malaria, is "abysmal."

For similar expense, projects could greatly enhance the public health of the broader population by instead enacting improvements to general diagnostics and disease surveillance capabilities. The U.S. contractor said "if [local doctors] could diagnose all the normal [bacterial and viral] cases it would be very easy for me to find the VHF cases," thereby directly tackling the priorities of the EP and indirectly addressing the disease-specific objective of the United States. Overall, to maximize effectiveness, programs must prioritize the needs of the engaged country over the specific considerations of the USG, with the understanding that our long terms goals will only be ultimately realized under this larger "portfolio-based approach."

What follows is a framework that supports the establishment of a strong functioning global health system that advances biosafety, biosecurity, and a culture of responsible scientific research. The framework is comprised of four objectives and sub-objectives. To show how this framework might work, an implementing strategy is developed and applied to several region-specific contexts.

Objective 1: Improve the public health system in order to prolong life and promote overall health and well-being
- 1.1: Identify gaps in public health system
- 1.2: Improve disease diagnostic and surveillance capabilities and electronic health recording
- 1.3: Provide a framework and infrastructure for disease response

Objective 2: Foster capacity building of global scientists and a culture of responsibility
- 2.1: Human resource development

2.2: Responsible life science enterprise

Objective 3: Improve the safety and security of scientists and bioagents
3.1: Improving the laboratory infrastructure
3.2: Biosafety integrated into the enterprise

Objective 4: Develop policy and codes of conduct that support international biological weapons treaties
4.1: Encourage enactment of national legislative framework
4.2: Encourage development of implementing regulations

Objective 1: Improve the public health system in order to prolong life and promote overall health and well-being

Positioning biosecurity underneath the umbrella of public health is beneficial for two reasons: (1) it places the focus of the program first on the engaging partner, which facilitates good relationships, trust, and buy-in from the local government; and (2) global health is a larger mission for more programs, which, according to a USG official, gets "more people and money at the table to work on [integrated] biosecurity."

Sub-Objective 1.1: Identify gaps in public health system

The World Health Organization (WHO) restructured its International Health Regulations (IHR) in 2005 to address increasing globalization coupled with the complexity of the infectious disease landscape. Eight core capacities were identified – national legislation, coordination, surveillance, response, preparedness, risk communication, human resources and laboratory – that needed to be up to standard by June 2012.[8] However, as of February 2013, 110 of 195 State Parties had filled for a two-year extension, and surveys documented large gaps in the ability to ensure public health surveillance and respond to zoonotic, food safety, chemical, and radiological hazards worldwide.[9] Importantly, before a country can improve upon its public health it must assess the system as a whole in order to identify weaknesses. For example - a project is currently being developed with the USG and the WHO to "enable countries to know holistically where the issues are . . . and how much it will cost to fill the gaps." Continuing to fund these types of engagements that enable countries to "assess their own gaps" will improve global health security across the board.

Sub-Objective 1.2: Improve disease diagnostic and surveillance capabilities and electronic health recording

The main focus of the 2005 IHR was the establishment of local surveillance systems that communicate and report information globally to rapidly detect disease outbreaks. As biological threats can be released and transmitted anywhere, the point of origin, at least from a public health perspective, is "not really important," says a USG official who manages BEs. He believes the most crucial aspect when it applies to human health is the time it takes to "detect [an outbreak] and then act to mitigate consequences." In the United States, the Robert Wood Johnson Foundation prepares an annual report that assesses public health preparedness based on 10 specific indicators, ranging from vaccination rates to the chemical capabilities of state public health laboratories.[10] Recommendations in the latest report included modernizing biosurveillance to a real-time, interoperable system to better detect and respond to problems.

Expanding upon this national objective to improve global electronic health information systems would have a major impact on biosecurity. For example, existing online systems like ProMED (Program for Monitoring Emerging Diseases) which is dedicated to rapid global dissemination of information on outbreaks of infectious diseases would benefit from increased international governmental participation and support. The importance of these networks is underscored by the creation of Connecting Organizations for Regional Disease Surveillance (CORDS) in 2009, which "was designed to serve as a platform for a global disease surveillance network."[11] Continuing to improve upon this type of disease reporting system from local to international levels to facilitate rapid dissemination of easily understandable information will allow for epidemiologists, public health experts, scientists, and physicians to visualize and detect outbreaks faster.[12]

Sub-Objective 1.3: Provide a framework and infrastructure for disease response

Equally important to the ability to detect is the potential of the EP to respond to their own disease burden. This objective builds off the ability to detect and diagnose a disease outbreak. Achieving it calls for hospital and building infrastructure, vaccine stockpiles and production capabilities, and a research community that understands the risk areas and is working towards developing countermeasures.

Objective 2: Foster capacity building of global scientists and a culture of responsibility
Individual (and not laboratory) capacity building was the need highlighted most often by international EPs. As one put it, it is "not enough to give a workshop on [standardized biological techniques] and call it capacity building." Instead, it would be more valuable to create programs that educate scientists at all levels of their careers in order to provide a path for sustainable employment. According to a high-level USG official, producing biologists with the "capacity to address the disease burden" of the country positively impacts public health while also allowing for the "development of a culture of responsibility."

Sub-Objective 2.1: Human resource development

International scientists and policymakers provided numerous ideas on how to strengthen the development of individual scientists in their regions. For example, an EP in Pakistan wrote children's books on biotechnology and scientific articles in Urdu as a way to reach a more diverse audience. In addition, a U.S. engager makes a point to hire primarily local employees when staffing international labs and institutions. Priorities should be the establishment of a national science curriculum, maintaining a sustainable job market for scientists, and creating a sense of national and international scientific community. A scientist in Thailand described how being a physician is preferred in her country due to better pay and job security, whereas a scientist must rely on the renewal of annual grants to support themselves and their work. She noted that there is "not a sense that science is a priority" in many partner countries, and accordingly there are only a "handful of government jobs" in biology. In contrast, certain Southeast Asian (SEA) countries, like the Philippines, are "investing heavily in biotechnology" and therefore local government support for scientists and USG support for SEA BEs increased accordingly.

In countries where the benefits of science are not fully appreciated by government officials, it makes sense to connect BEs to public health goals because improving health outcomes is more obviously politically valuable. Providing medical countermeasures and disease outbreak support can demonstrate the advantages of life scientists and improve the prestige of the field in partner countries. This long-term outcome can be addressed in the short-term by continuing to support research partnerships and collaborations between scientists in the United States and those abroad, especially those with public health impacts. Efforts should be made to also enhance regional collaborations. According to an EP who contracts with the USG, "link[ing] regional elements together [provides] more potential for an ongoing relationship to be established." Ideally, these partnerships would provide opportunities for expansion of scientific techniques and allow for coordination of resources across a region. Furthermore, funding for travel to international conferences and research institutions helps foster the development of a global scientific community bound by shared ideas concerning the responsible conduct of science.

Sub-Objective 2.2: Responsible life science enterprise

Government buy-in for BEs, both monetarily and philosophically, is a crucial component of long-term success. Metrics should account for this. BEs that work with government and public health officials to prioritize research and funding have better opportunities for investment. For example, focusing the research system on public health (such as improving vaccine production and disease response capabilities), would have great possibilities for impact. Ensuring the bioethics of these research projects and clinical studies is essential. International funding agencies and scientific journals requiring bioethical forms for supported grants and published projects have lead to some confusion in countries that do not internally consider bioethics. A scientist from Tunisia cited that a common problem is when researchers only consider bioethics "at the end of their work because they want to publish," which undermines the concept. Bioethical regulations are an important component of a research system and she believes BEs can provide a framework for each country to initiate "their own procedures and programs and legislation for bioethics."

Objective 3: Improve the safety and security of scientists and bioagents

This traditional biosafety objective of securing biological agents and pathogens with laboratory and security upgrades has been the main output of BEs. These engagements have been primarily agent-focused and would benefit from greater integration with efforts to combat disease. It is worth noting that many USG agencies that do not work primarily on biosecurity – for example USAID, CDC through PEPFAR, and others – still fund and build laboratory capacities. However, according to a USG contractor who has spent more than 10 years carrying out BEs, these labs are "not designed with cooperative threat reduction principles in mind." However, once the U.S. agency leaves, local constituents may utilize this space in ways that were not originally intended thereby compromising biosafety. Uniform guidelines to address safety and security issues across the suite of U.S.-funded laboratory projects would help. In addition, the possibility, if not the likelihood, that laboratory uses will change over time underscores the importance of both coordination among USG agencies that engage life scientists abroad and sustaining those engagements to help integrate research, public health, and CTR priorities.

Objective 4: Develop policy and codes of conduct that support international biological weapons treaties

In order to be effective, biosecurity regulations must exist at all levels. International agreements and guidelines put forth by the UN must be legislated at a national level and then operationalized through translation into codes of practice at the local level. Various international bodies exist to maintain the Biological Weapons Convention (BWC). The Australia Group (AG) monitors exports to ensure that they do not contribute to biological weapons.[13] The European Committee for Standardization (CEN) produces voluntary standards for international biorisk safety management.[14] The WHO maintains a directory of core publications guiding regulations for transport of infectious substances, laboratory biorisk management, and responsible life sciences research for global health security.[15]

A national legislative framework that strictly enforces biosecurity is a relatively new concept, the beginnings of which were realized in the United States in the late 1980s with the passing of the Biological Weapons Anti-terrorism Act of 1989.[16] This legislation, initially enacted to support the implementation of the BWC, has been modified and updated numerous times since its inception. Ultimately it now defines and implements restrictions on eighty Biological Select Agents or Toxins (BSAT) and further restricts research on thirteen of them, which have been labeled Tier 1 Agents.[17]

As "biology equals information," according to a science journalist, it is not simply the agents themselves that need to be controlled. Instead of simply policing the "finite [BSAT] list," an FBI agent in the Biological Countermeasures Unit believes engaging with scientists may be a better way to "gauge what is of concern." Recently, the FBI has made strides to do this at the local level by connecting universities and research institutions with regional Weapons of Mass Destruction (WMD) coordinators who themselves are connected to both local and national law enforcement officials. By creating these points of contact to "bridge law and science," the entire spectrum of issues, from the select agents to "intellectual property threats" is addressed. The success of these programs is now accepted nationally but the continued expansion of these collaborations internationally is necessary to globally "develop the idea of biosecurity awareness."

Sub-Objective 4.1: Encourage enactment of national legislative framework

The United States legislates biosecurity under the Patriot Act of 2001, the Public Heath Security and Bioterrorism Preparedness and Response Act of 2002, and Executive Orders 13486 and 13546, which were directives to strengthen laboratory biosecurity and optimize security of the BSATs, respectively.[18] These laws require all persons possessing, using, or transferring agents on the BSAT list to register either with the HHS Secretary or the USDA Secretary and meet biosafety and security standards and procedures established by those entities. They also restrict access to agents and define further regulations for those agents with the most bioterrorism risk, the 13 Tier 1 Agents. Communicating the legislation to the life sciences community, through individuals like the WMD coordinators, is crucial to ensure their efficacy. For example, after the anthrax attacks in 2001, many researchers destroyed their strains of *B. anthracis* fearing prosecution under the Patriot Act. That harmed the investigation by making it difficult to trace the relevant strain and possibly compromised future anthrax-related investigations as well as scientific advancements on the bioagent.[19]

As mentioned, very few countries other than the United States have regulations in place that comprehensively address facilities and personnel working with bioagents. For example, countries in the European Union typically possess stricter regulations on genetically modified organisms (GMOs) when compared to pathogenic organisms or biological agents, reflecting the region's history of activism against genetically modified food.[20,21] Japan provides another example. It utilizes a select agent list for human disease but not zoonotic disease agents. Although zoonotic diseases are not endemic to the region – only one of 58 disease outbreaks (a Schmallenberg virus) in the last year affected animals – legislation should still be in place due to potential for viral spread.[22] Also, in contrast to the U.S. system, which until only recently had just one tier to the BSAT list, Japan possesses 4 tiers of regulated agents.[23,24] This step-wise approach "may allow for more flexibility" when developing codifying regulations as opposed to an on/off system and "accounts for the real variability in risk associated with these agents." A potential trade-off is that this greater complexity may be harder to enforce, particularly in resource-limited countries. Since the IHR 2005 updates, 79% of member countries have evaluated their legislation and 58% have implemented changes.[25] For example, Australia introduced two new bills into parliament in 2012 that outlined a new risk-based approach to biosecurity and appointed an Inspector-General of Biosecurity to oversee state and local laws.[26,27] While this type of legislative overhaul is beyond the capacity of many current BEs, conversations should be facilitated between regional government officials and policymakers about the types of regulations that are essential for maintaining biosecurity.

One area in which BEs could provide an immediate legislative impact is through discussions that define EP national scientific priorities. The United States has an extensive legislative framework, mainly contained in Title 42, that establishes science funding and research goals.[28] This body of law is diverse – it ranges from entire legal chapters like Chapter 16, which supports the National Science Foundation (NSF) and the National Institutes of Health (NIH), to specific bills, like H.R.842, which was introduced to the House in February 2013 to "expand the research activities of the [NIH] with respect to functional gastrointestinal and motility disorders."[29] An EP from Kuwait highlighted the lack of a concordant system in the Broader Middle East/North Africa (BMENA) region as an area of weakness, noting that in many countries "there are research institutions and funding agencies but no broader national or political institution for guiding national scientific priorities," which leads to an "everyone for themselves" mentality. U.S.-lead BEs could assist as in many instances "scientists and policymakers working together internally is difficult" and it would "help to have outside people on the side of the scientists to give a model [of collaboration]".

Sub-Objective 4.2: Encourage development of implementing regulations

In response to national regulations, agencies and institutions write implementing regulations locally that are more flexible and allow for change over time. Coordination between the legislative and regulatory framework is important to allow for modifications and to prevent inhibitory restrictions. In the U.S., the Centers for Disease Control and Prevention (CDC) is one regulatory body that establishes regulations for legislated select agents.[30] Developing an international model for implementing regulations that incorporate best laboratory standards and practices would be a "valuable addition" to the biosecurity sphere. These regulations, which could be "targeted to an organization like the International Organization for Standardization (ISO)," would provide a non-compulsory, yet standardized protocol, to allow for accreditation of international laboratories and research practices. Achieving these standards are not typically priorities for U.S. labs, but they are valued by international labs, especially in developing countries, as a way to communicate "function[ality]," says a USG affiliate who implements USG BE programs internationally. Scientists "want to do the right thing" but they need a target for achievement, like an ISO accreditation. By providing an international roadmap of policies and procedures scientists would be able to voluntarily enact "continuous improvement practices" and work towards institutionalized regulations.

Implementing Strategy

Implementing the strategy described above should utilize a cohesive portfolio-based approach modeled after business strategies to allow for improved investments into global biosecurity. This working framework views EPs as consumers and builds in components to ensure that the product, the subsequent BE, utilizes past initiatives to tailor to demand.[31] Metrics are outlined that reflect the strategic objectives in order to continue to feedback upon subsequent and current BEs, thereby improving the programs and the outcomes. Later in this document, this strategy will be applied to several regions of interest, providing specific context for the framework.

General working framework

1. Understand biosecurity challenges on a country-by-country or region-by-region basis
    a. Understand differences between U.S. and country of engagement
    b. Identify largest gaps to public health and research infrastructure
2. Develop clear goals based on country- or region- specific public health challenges
    a. Identify threat/risk factors based on identified gaps to public health (1b)
    b. Design projects with goals to address risk factors
    c. Tie projects into the broader portfolio of engagement programs
3. Gather and organize relevant data necessary to operationalize goals
    a. Identify who needs to be involved in the country of engagement for success: human resources on both sides are key to successful EPs
    b. Determine what material and knowledge resources are needed
    c. Identify who possesses those resources
    d. Discover what additional support those who possess these resources need to be effective engagers
4. Monitor and evaluate the results
    a. Continue to reference goals and subsequent metrics during project implementation
    b. Assess program outcomes immediately after completion and again 6 months to 1 year after completion
    c. Work with engaging partners to develop metrics and evaluate results
5. Use results to inform future engagements

Metrics

Metrics for engagement will vary from program-to-program and region-to-region. Instead of tying success to short-term accomplishments (which tend to be more quantitative in nature), attempts should be made to measure things that represent enduring benefits. In other words, goals and programs should also be designed with the long-term outcomes in mind. The programs themselves would benefit from lengthening the duration of engagements, as according to a USG-contractor, the United States currently "expect[s] the local governments to do things in one year that would take the United States 10 years" to complete. While there are constraints due to funding cycles and the inability of many organizations "to commit to 3-5 year strategies," adopting this comprehensive intra-agency approach to the problem of biosecurity should allow for more flexibility in timing.

Indicators that suggest long-term successes include:

1. Maximized modern diagnostics and minimized pathogens and endemic viral load
    a. Improved public health system
    b. Ability to respond to health challenges
2. Influenced next generation of scientists
    a. Changed/improved curriculum
    b. Policy changes
    c. Utilized and improved local capacity
3. Created or expanded regional network[s] of individuals and groups
    a. Number and qualifications of people involved
    b. Broadening of involved people and programs
    c. Grants funded and renewed
4. Secured government buy-in

    a. Accepted some financial responsibility
    b. Implemented at national level
    c. National policymakers at table
5. Formed effective partnerships
    a. Sustained communication across global networks
    b. Ability to hold honest and fruitful discussions
    c. EPs initiate conversations about both successes and failures
    d. Sense of building communities of trust

Three main factors drive the direction and focus of biosecurity engagement programs: (1) naturally occurring and endemic pathogens, (2) burgeoning biological sciences and biotechnology capabilities, and (3) presence of terrorists in a state or region. The state of each of these factors in a given country will shape the nature of the engagements. Traditionally, projects were centered in the FSU but now regional priorities have shifted to BMENA, Central Africa and SEA.

The "General Working Framework" has been applied to each region below as an example of how this model might be utilized in future engagements. Additionally, possible future projects as suggested by EPs are outlined with metrics for measuring success of those specific projects.

Regional Application

Former Soviet Union

Many FSU BEs were successful in their goals to realign former weapons scientists and account for and secure select agents, yet there have been recent challenges with continuing engagements along with a general regional distrust of the USG. To date, 47 Cooperative Biological Engagement Laboratories were secured, and between 1994 and 2009, 73,000 scientists were engaged in international projects and meetings through the revolutionary Moscow-based International Science and Technology Center (ISTC), which has since been closed.[32,33] A scientist in the FDA who in the past collaborated with scientists in Ukraine noted that when he formerly traveled to the region, locals "used to be excited to see Americans [but] now all this has disappeared." He believes a contributing factor is that compared to Europe, the United States is "far away and expensive" so education and collaboration frequencies have declined. Also challenging, according to a USG engager who specializes in the region, is a difference in the overall value system between the United States, which "has a premium on high-tech, non-human" values and the FSU, "which didn't always have the money or resources to put confidence in devices." Funding and priorities for biosecurity will therefore be different. The biggest gaps to public health as determined by the WHO are human resources and laboratory qualifications.[34] Projects aimed at developing human capacity, the scientific infrastructure, and research projects are therefore priorities.

To combat an increasing climate of distrust in the region that appears to be "sliding back [towards a] cold war mentality," it is important to create BEs that engage young scientists in the global science community. As described by a Russian EP, if the young generation can "participate in global science and know the way the research system works, there is no way Putin or people like him can turn them around to go back and develop biological weapons." Due to the negative political attitudes in the FSU towards the United States government, these scientific collaborations should be funded through universities (which are "very trusted" in the region), instead of directly through U.S. agencies like DOD or DOS. Although the funds still originate from the USG, the name on the contract is an American university, which, according to a Russian scientist, is a "totally different game" and makes it "very easy [for FSU scientists] to receive money, buy equipment and pay graduate students."

- Potential projects:
  - Facilitate research collaborations
  - Promote travel between the regions
  - Encourage and broaden communication between scientists here and abroad
  - Provide funding to strengthen research institutions and technology centers
- Long term effects:
  - Increase career opportunities for young FSU scientists
  - Create a network of scientists who can influence FSU policymakers to enact laws that positively affect biosecurity
  - Engender good-will towards the United States

While maintaining and creating new relationships with scientists inside the FSU will be more difficult due to the political climate and closing of the ISTC, it is important to continue to develop capacities that will fuel a young generation of scientists. Regardless of the political climate, one Russian-American EP reported that his colleagues in the region are "dying to work with us." One example of a potential new collaboration was developed by a senior scientist at the Microbiology Institute in Uzbekistan and submitted to the DOS for consideration. If funded, this project would establish a National Center for Biosafety and Biosecurity, establish a national culture collection, provide equipment and training, and attempt to coordinate the efforts currently housed in many Uzbekistani entities in one institution. This EP noted that the limited number of ministries in the country that attempt to regulate or enforce biosecurity and biosafety do so without coordination from laboratories or research institutions. This results in fragmentation of the system and leaves people "unconcerned about what they are doing because they do not have enough vision to see the linkages between all [biosecurity] issues." He believes that this large gap in the research infrastructure could be addressed with the formation of such a center.

Markers specific to the success of this project could include:

1. Government buy-in – if supported by the United States, there will be money from local government entities to support discussions of biosecurity in government forums (e.g. measuring discussions had by government officials from local to national level).
2. Increase in research capacity – evaluating types of research being carried out in Tashkent, as well as in other areas of the country. Research will begin with plant pathogens as the region has major pathogenic loads affecting their cotton crop. Eventually research will expand to animals and humans with a goal of the center being the study of cross border movement of viruses and bacteria. Assessing if center has regional subsidiaries outside of the capital.
3. Raising "level of understanding of biosecurity beyond just bioweapons" – for example, making food safety and contamination part of the national dialogue. An increase in food testing, a goal of the center, will help prevent gastrointestinal disorders, which is a measurable, public health-related outcome.
4. Adoption of laws – such a center could hold "studies on international regulations" and aim to "adopt necessary framework to carry out these [biosecurity] activities."

U.S.-FSU Cooperation in Combatting Plague

The DOD indirectly funded an exemplary collaboration between Russia and the University of Texas to bypass Russian distrust of governmental agencies. This collaboration on the plague bacterium utilized blood samples provided by FSU public health workers who were vaccinated with a live, attenuated plague vaccine no longer used in the United States. Using this unique serum, scientists were able to identify biomarkers of plague exposure as well as determine novel protective antigens. Scientific partners that build off of these common interests are ideal, as the American scientist described, "I will never find any human donors that have been exposed to plague vaccine; they will never find the expertise or technology to develop the [assays necessary to complete the research]."

Indicators of success for such a project:
(1) Joint publications (the 3-year plague study produced eight);
(2) Presentations at meetings; and
(3) Facilitating research collaborations.

The U.S.-based scientist now trains four graduate students in Russia, and says this is "how I see my task." The young generation will soon be "ruling in science" and it is "very important to have them not isolated but be part of the global science – they should see how we collaborate and enjoy this."

Broader Middle East/North Africa (BMENA)

Initial engagements began slowly approximately seven years ago with a focus on laboratory capacity and biosafety.[35] A continuing terrorist presence coupled with endemic pathogens, such as anthrax, has moved this region to the forefront of many engagement projects. Thus, the suite of projects funded by the USG and NGOs would benefit from increased coordination, and therefore efficiency. The region faces possible saturation of biosafety and biosecurity workshops and training sessions and future projects should have more long-term goals. In addition, BMENA EPs repeatedly noted the sensitivities in the region related to biological weapons, namely the incorrect assumption that they have negative motives simply because they live and work in a region with a high presence of terrorism. Engagers should be aware that understanding of common U.S. terminology, like biodefense and biosecurity, is more complex here. A policymaker from Kuwait believes partnerships would benefit from "being very transparent from the beginning" and tackling these "issues head on" to reassure EPs that they are not under suspicion.. Also noted were divides within the BMENA region; Gulf States have no real need for monetary incentives when compared to North Africa. Additionally, some countries like Afghanistan have "almost no basic research facilities or institutes" which was a complaint from the same Kuwaiti policymaker as it "dilutes discussion." While these previous workshops involved the whole region, she believes it may be more effective to "adopt a more narrow [geographic] focus" moving forward.

As cited by EPs, the lack of coordination between various levels of the scientific infrastructure is a real concern. While the USG and its funding agencies have uniform and international guidelines to enforce ethical codes, streamline research, and advance national scientific goals, such a system is lacking in the region. EPs adopting standardized uniform policies would make both regional and national implementation easier; for example Kuwaiti scientists are currently trying to incorporate guidelines or metrics into grant proposals in order to systemize biosecurity. In addition, the general BMENA public does not "understand biosecurity" beyond the discussion of physical security of agents and self. Furthermore, a scientist from Tunisia said most believe "religion will stop us" from misusing those agents. This type of ethical sentiment is important, however a functioning moral compass is insufficient without real knowledge of all the various risks and threats. Instead of focusing on smaller aspects of the topic, a way to mitigate the larger risk factor is to broaden the ideas of biosecurity into legislative policies and public health discussions, which will positively impact the culture of scientific responsibility across the life sciences community.

- Potential projects:
    - Facilitating research collaborations within the region, particularly those with public health outcomes
    - Facilitating discussions between scientific institutions and governmental agencies
    - Involving policymakers and public health officials, not just top-level scientists, in biosecurity discussions
    - Developing projects that expand the biosecurity/bioethics curriculum
- Long term effects:
    - Merged interests of public health officials and scientists to unify research goals and increase funding
    - Expanded biosecurity legislation
    - Involvement of younger citizens and non-scientists in discussions regarding biosecurity

In the past, scientists and engagers in the BMENA region were invited to meetings and workshops "because they applied" – a standard that, as a scientist from Pakistan bluntly stated, "is not good enough." Instead, regional champions, usually top-level scientists and heads of scientific institutions who believe in the importance of expanding the dialogue and understanding of biosecurity should be identified. Members of the BMENA Biosciences forum, a group formed after the AAAS meetings to facilitate discussion on "international collaboration and responsible science," are a great resource.[36] These champions understand the regional dynamics and therefore can identify the essential officials, both in health and government, whose participation will be necessary to ensure research becomes a national priority. An EP in Kuwait worked with the Department of State (DOS) to implement a surveillance system that employs a mathematical model to predict spread of diabetes and cancer. These are health issues currently affecting Kuwait; yet, as a scientist she faced challenges engaging with policy makers. Input from DOS was useful to get everyone at the table and demonstrate the importance of these issues. In order to develop a "real policy and organization" in this region, she believes people are "needed who have political will and vision and power."

Continuing to facilitate these types of conversations with different entities within BMENA EPs should be a priority. In addition, scientists pointed out that it is "easier to get partnerships with Americans or Europeans" than it is to form collaborations inside the region. This isolation leads to BMENA scientists "not knowing what is happening next door and what facilities could be shared." BEs, therefore, should also focus on developing partnerships within the region.

Improving Biosecurity Policy in the BMENA Region

A cooperative grant funded by DOS through AAAS between scientists at Georgetown University and the University of Tunisia Faculty of Scientists aimed to review national policies and legislations as they pertained to biosecurity in order to provide suggestions for improvements. Thirty Tunisian scientists and policymakers worked with U.S. counterparts over a two-day-summit in the spring of 2012 to devise recommendations for research priorities and ethics. Conclusions were to increase the funding climate through engaging with government officials. According to a Tunisian scientist who attended the summit, "productivity in research and innovative projects" has great potential to attract interest from national legislators from a revenue potential perspective, especially since the country lacks "other economic things like [oil reserves]". The potential fiscal benefits of scientific investment should therefore be transmitted to the local government.

Indicators of success for such a project:
(1) Broadening of the engagement – the recommendations were submitted to the President of the University of Tunisia, the Dean of the Faculty of Sciences, the Director of the Pasteur Institute, the Minister of Higher Education and Scientific Research, and the Minister of Health.
(2) Change of the research infrastructure – a research collaboration was formed to study inflammatory breast cancer, which allowed for the formation of an Institutional Review Board (IRB) at the Tunisia Faculty of Sciences, a crucial component that works to ensure bioethical research.

Central and Eastern Africa

There are three main challenges in this region: (1) high prevalence of naturally occurring pathogens and select agents as defined by the United States, i.e. viruses that cause viral hemorrhagic fevers, (2) generally poor research infrastructure intensified by electrical supply issues, and (3) a huge foreign aid market that has the potential for misuse both by the funders and the recipients. However, these challenges also provide opportunities for BEs to tie into larger international aid programs aimed at public health and possibly utilize larger resource pools.

Basic biosecurity concepts have been discussed in this region for a long time under an ad hoc definition of global health security. A USG official currently working on implementing new policy on global health security believes that building an effective CTR strategy in the region could be as simple as "just add[ing] the piece of biosecurity to what currently exists." Projects that work to improve basic health infrastructure would make huge differences towards improving biosecurity. As pointed out by a USG contractor who works in the region, "if [local doctors] could diagnose all the normal [bacterial and viral] cases it would be very easy for me to find the Lassa fever cases," where Lassa fever was used as an example for those agents that are more relevant towards the CTR-mindset of the United States.

Even though the regional prevalence of these select agents is a main component of why funding exists, promoting disease-specific projects is ineffective. Specific technology, equipment, or services will not be used on a day-to-day basis by the EPs who typically encounter only a few yearly cases of VHF compared to daily instances of malaria, parasites, dysentery, and dehydration. In addition, the historical abundance of foreign investment in the region has created an "aid mentality," which, according to an engager who works closely with Ugandan scientists, should be a "thing of the past." He believes that projects that establish cooperation through "contractual relationships" will also forward trust and the mentality that "we are all equal."

- Potential projects:
  - Setting up mobile laboratories for disease surveillance
  - Implementing transport logistics for pathogens and samples from the field to centralized research laboratories
  - Establishing protocols and systems for working with pathogens and agents
  - Improving infrastructure; especially roads and electricity
- Long term effects:
  - Enhanced ability to diagnose diseases across the region
  - More robust frameworks for disease response; i.e. establishing protocols and systems for producing recombinant proteins today that could one day function as a vaccines
  - Buy-in from local governments - collaborations with Ugandan scientists working on Foot and Mouth Disease (FMD) achieved this metric of success – the ministry of agriculture is working to implement the program on the national level.

Programs that embed scientists, infectious disease specialists, and public health officials in the region for long periods of time will be the most effective. According to the engager in Uganda, this could be done with a "trial balloon" of infectious disease scientists who would create a "pilot program of mobile labs to survey for viral diseases." There already exists a model of this working partnership between biosecurity and global health, as Department of Defense (DOD) components are embedded within the CDC country office in Uganda. However, programs are currently "focused at lab level and at disease detection response." He believes that these need to be expanded into the "field [to] allow Ugandans to make decisions about what is important" for their health security. Again, this move away from disease-specific projects will allow for greater understanding of the risks we face – he advocates getting more "people on the ground to [understand] the pulse of the population."

Developing Creative Solutions to Achieving Infrastructure Improvements

One engagement between scientists at a national laboratory in West Africa involved basic improvements to the science infrastructure with long-term biosecurity outcomes. A U.S. engager carried out an assessment and found the largest gap in their ability to perform good science was a weakness in their cold chain. He spent minimal funds to renovate the electrical system and install a nitrogen generator, which he said other engagers deemed "crazy." Then, with the director of the institute, he established contracts to sell the excess nitrogen as a way to pay for the overhead, building costs, as well as maintenance of the liquid nitrogen system. This type of contractual relationship provides incentive for EPs to utilize and maintain the system. This project was not designed with disease-specific biosecurity goals, but instead prioritized the need of the EP, and in that way was able to end up with even greater biosecurity successes.

Indicators of success for such a project:

(1) Development of a trusting relationship – the director called the U.S. engager during the last Ebola outbreak and he was able to mobilize teams, arrive on the ground, secure samples and, according to him obtain an "incredible amount of data that wasn't there before."

Southeast Asia

BE expansion to SEA has occurred more recently and transitions into the area have been streamlined as the region has an endemic research infrastructure and culture. Many institutions already possess advanced laboratory capabilities and technical abilities similar to the FSU and the United States. EPs are looking for BEs that develop collaborations between scientists and expand biosecurity principles into legislation and policy. On the whole, USG engagers currently working in the region say, "concepts of disease surveillance and dual use research are understood," so engagers do not have to work to "sell the concept of health security." Some countries however, are resistant to share samples based on "political and economic" reasons rather than a lack of appreciation for public health benefits.

In many countries, the legislative component to biosecurity is in its infancy and law enforcement officials have little or no capabilities to respond to threats. Across the board, getting scientists and law officials to come together requires real compromises because scientists tend to resist anything that they view as having the potential to harm research advances and law officials aim to prevent risk at all costs. Getting both at the table to "engage in discussions of responsible conduct of research" – the goal of a project headed by a USG official working in Indonesia – will allow for the ability to "come to an understanding [and a] middle place."

- ❖ Potential projects:
  - Facilitating discussions between biosafety associations, scientific institutions, and governmental agencies
  - Training law enforcement officials and develop their contacts to scientists
  - Analyzing the capabilities of the various health agencies and departments in order to operationalize a flow of interactions
- ❖ Long term effects:
  - Changes in legislative infrastructure.
  - Intra-agency approach to the problem.
  - Spread of ideas beyond the core group of engagement – from the biosafety association to the government

In SEA, as well as other regions, there are only a "handful of people [or] one principal organization" who have the potential to "deal with biosafety" in any government. Identification of these people is necessary, as they "would have to be in the room in order to get something done." A USG official working in the region says that to date this "hasn't happened" on a larger scale although she noted that many biosafety associations have been stood up in the region, which possess "deep subject matter expertise on biosecurity." She managed a BE that worked on training the rotary club in the Philippines to repair hospital equipment, and eventually expanded the skillset to repair lab equipment. This rotary club, headed under a larger Biosafety Association is currently working with the government to "make changes on how biosecurity is implement[ed] in government labs." The program could expand to other organizations, e.g. universities, and therefore achieve the spread of important biosecurity concepts. New projects should address curricula development projects and overall increase the research community in the region.

Connecting the Research Community with Law Enforcement

The FBI is beginning to expand its previously national biosecurity efforts to international markets, namely Southeast Asia, which a U.S. official said would "protect the region's [large] investment in biotechnology." This program would aim to establish international points of contact, similar to the national WMD coordinators, and connect law enforcement agencies with scientific institutions in order to prevent criminal activity and potential for misuse of biological agents or information. In addition, setting up a roadmap of action in these partner countries will allow for faster detection and mitigation of possible harm if misuse does occur. While initial meetings were just occurring at time of contact, a U.S. official who has worked in the region on previous projects as well as this current effort believes implementing these types of programs require "less technical requirements [than past engagements]." So far the program has been met with approval by local government officials.

Indicators of success for such a project:
(1) Establishment of international WMD coordinators and webs of contact between science and government
(2) Frequency with which the WMD coordinator is contacted by scientists

Conclusion

Representatives from all engaging entities should come together at one table to develop a cohesive portfolio-based approach to global biosecurity. Shifting project goals to focus more on qualitative public health outcomes instead of quantitative security outputs has the potential to create programs that cost less and are more effective. It takes a "more creative, long-term approach" to effectively incorporate biosecurity into the public health sphere. Instead of spending the majority of funding on fences, buildings, equipment, and holding workshops for a large cohort of scientists, resources should be dedicated towards broader, more sustainable, results. Training influential people from diverse disciplines more thoroughly and continuing to support them as local consultants on the ground, developing contractual arrangements, funding cooperative research proposals, and working towards achieving government buy-in, is ultimately a better use of resources.

To achieve a cost-effective strategy, we must outline global health security goals and delineate individual tasks. We should dramatically increase the length of the engagements wherever possible and diversify the portfolios – not in location or even immediately in numbers – but in types of activities. Replacing workshops and training seminars in favor of longer project-based programs that address broader global health goals will efficiently integrate biosecurity principles and practices into diverse sectors such as health, legislation, medicine, and ethics. This means applying metrics not as pass/fail measurements, but instead as indicators to allow for more successful current and future investments. In addition, enhancing communication with EPs, before, during, and after engagement, to provide and receive feedback will again enforce trust and establish true partnerships. EPs should be directly and actively involved in metric development.

As an engager summarized, securing a pathogen or preventing a disease "no matter how bad" should never come at the expense of "winning over hearts and minds," as this positive mentality provides the largest contribution towards reducing threats to the United States.

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Author's Note: Considering Funding Priorities

I asked the following question to a spectrum of U.S. individuals currently working on the problem of biosecurity: If you had 1 million dollars to spend on biosecurity where would you spend it? The question was designed to be open-ended but also restrictive. While I am not attributing any answer to a specific agency or individual, I believe the suite of answers points to the diversity of viewpoints and also illuminates some priorities. It is also interesting to note, depending on who was answering this amount ranged from "a drop in the bucket" to "a lot of money:"

- Building a culture of responsibility through training and workshops that forge connections among participants, especially through a uniform systems approach across all entities working on biosecurity.
- Internationally increasing disease surveillance systems without geo-prioritizing in order to avoid creating vulnerabilities.
- Biosecurity upgrades in the Middle East.
- Research collaborations in the FSU.
- Improving how we disseminate disease outbreak information.
- Developing one international comprehensive biosafety curricula.
- Enabling countries to assess their own global health security risks and the costs of filling those gaps.
- Instead of training 30 people for 1 year, hiring and training a few local consultants and experts in a region of priority and keeping them on retainer for 3-5 years.
- Attracting and training people who have experience working in an international community – nonproliferation does not have enough people from different backgrounds.
- Training on leadership, responsibility, and management skills for our international partners.
- Training on international (primarily Middle Eastern) cultures, languages, and sensitivities for U.S. policymakers.
- Enhancing health infrastructure.
- Funding scientists and policymakers who live and engage in the country of interest full-time.
- Developing international standards for best lab practices.
- Training on biorisk management for a laboratory that has samples that are particularly pathogenic.