BRIEFER

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Key U.S. Initiatives for Addressing Biological Threats Part 6: The Defense Advanced Research Projects Agency (DARPA)

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INTRODUCTION

"The world becomes the future because of DARPA." [1]

COVID-19, the disease caused by SARS-CoV-2, has clearly demonstrated that the United States is vulnerable to biological threats of pandemic scale. This awareness has come at exceptionally high cost when calculated in lives lost and the severely compromised welfare of American citizens. [2] More Americans have died from COVID-19 than in any war involving American troops—more than 745,000 at the time of writing. COVID's impact thus far on the U.S. economy is estimated to be in the trillions of dollars. [3] The pandemic continues to rage, similarly impacting every other country in the world.

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[1] Annie M. Jacobsen, *The Pentagon's Brain* (Boston, MA: Little, Brown and Company, 2015), 8.
[2] For examples, see W.J. Hennigan, "The U.S. Spent Billions of Dollars on Biodefense. COVID-19 Was the Attack it Never Saw Coming," *Time*, October 9, 2020; and Christine Parthemore and Andy Weber, "Op-Ed: COVID-19 May Be Teaching the World a Dangerous Lesson: Diseases Can Be Ideal Weapons," *Los Angeles Times*, November 12, 2020.
[3] Terrie Walmsley, Adam Rose, and Dan Wei, "The Impacts of the Coronavirus on the Economy of the United States," *Economics of Disasters and Climate Change*, No. 5, 2021.

Yet the pandemic has also reinforced the aphorism that necessity is the mother of invention—shining a light on numerous examples of governments making the impossible possible. Consider vaccine development as an exceptional achievement. Historically, it has taken 10–15 years for a vaccine to proceed from research to deployment. The rapid research, development, testing, and production of a COVID-19 vaccine was accomplished in a single year.[4]

An ounce of prevention may be worth several tons of cure, but this value can only be actualized if sufficient investments are made in prevention capacities. The U.S. Defense Advanced Research Projects Agency (DARPA) is such an investor, focusing on funding the development of breakthrough technologies with national security aims.[5] For example, DARPA's Defense Sciences Office (DSO) invested tens of millions of dollars in 2012 in a program called ADEPT:PROTECT, a project that explored using messenger RNA (mRNA) as a platform to deliver "antibody-making instructions," conferring protection against a specific disease.[6] This investment is a salient case where DARPA took the long-range view and developed technology for future use cases that were unspecified, but intuitively anticipated.

In the midst of COVID-19, it is clear the program paid off. The success of the nearly $40 billion Operation Warp Speed (OWS) which led to the creation, testing, production, and distribution of safe and effective COVID-19 vaccines around the globe has saved countless lives and mitigated worse economic damage. This success would not have been possible without earlier investments in bleeding edge technologies made by DARPA, such as vaccines using nucleic acid vectors.

As government agencies evaluate lessons from the ongoing pandemic, it is important to consider how to best leverage DARPA to address future biological threats. Further, it is important to delve into the organization itself in a bid to optimize its performance against rapidly-evolving biological threats of the future from natural and anthropogenic sources.[7]

This briefer provides a short background on the Department of Defense's Defense Advanced Research Projects Agency (DARPA). It also provides recommendations for DARPA as the organization grapples with addressing biological threats, both natural or synthetic, within the 21st century's increasingly complex, dynamic threat landscape. Due to its proven potential to impact U.S. national security threats, it is imperative for DARPA to operate at peak efficiency with maximum flexibility to pivot as the biological threat landscape changes abruptly and dramatically.

Further, this briefer provides key points and considerations to help define DARPA's role in the updated National Biodefense Strategy—a fundamental step towards clearly establishing DARPA's position in the biodefense infrastructure. This also helps define a clear lane for DARPA to fully utilize its capacity to address future pandemics and other biological threats for which the character is uncertain.

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[4] Congressional Research Service, "Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccination Materials," March 1, 2021.

[5] DARPA, "About DARPA."

[6] For examples, see DARPA, "ADEPT:PROTECT Vignette," 2021; "Preventing Pandemics," January 29, 2021; and "COVID-19," March 19, 2021.

[7] See United States Congress, "The William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021," January 3, 2020; and The White House, *National Biodefense Strategy*, 2018.

Finally, it is important to note that in this briefer, we employ COVID-19 as a use case that exemplifies DARPA's mission, operations, and security contributions. However, this is only one example of the panoply of advanced work that DARPA conducts on a daily basis to meet its mission of preventing (and creating) strategic surprise across a wide threat domain.

DARPA: AN OVERVIEW

Created by Congress in 1958, DARPA functions as the central research and development organization of the U.S. Department of Defense.[8] The genesis of its mission dates to the launch of Sputnik in 1957, and a commitment by the United States that from that time forward it would be the initiator and not the victim of strategic technological surprises.

The focus of DARPA is to strive for transformational change. It funds a host of "performers" to achieve these advances, with a constant focus on and collaboration with the nation's military services—DARPA's primary "customers." DARPA strives to take on high-risk, high-reward projects, oftentimes with a magnitude of risk too high for others within and outside the federal government. The term "DARPA hard" has been commonly used to describe efforts it funds.

DARPA has achieved its mission through funding technology development at a variety of organizations within government, academia, and the private sector. In doing so, it has transformed revolutionary concepts into practical capabilities. High-profile outcomes of DARPA-funded research include precision weapons, stealth technology, the Internet, the Global Positioning System, and artificial intelligence (AI) technologies that have been used to make commercially available voice recognition products.

The broad category of concepts and capabilities that DARPA works on all share a few characteristics that make DARPA intrinsically a unique organization. First, DARPA funds highly impactful projects—rather than looking to make incremental changes, it seeks to introduce transformative, positive changes in the U.S. strategic landscape. Given the U.S. role in the international community, most will likely have global impact.

Second, DARPA approaches its mission, and the projects it chooses to fund, from a perspective of high risk/high reward. This perspective does not mean that DARPA takes a reckless approach; rather, high risk/high reward in this context refers to the idea that transformation does not happen through piecemeal efforts in existing and well-understood technologies and capabilities. While DARPA attempts to mitigate certain risks by bringing in highly talented experts across multiple disciplines, the organization approaches projects with the understanding that innovation failure rates are exceptionally high in a way that not many other organizations will tolerate. There is an acceptance that failure can and will happen.[9]

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[8]Annie M. Jacobsen, *The Pentagon's Brain* (Boston, MA: Little, Brown and Company, 2015), 5.
[9] Steve Andriole, "Why Innovation Almost Always Fails," *Forbes*, February 20, 2015.

Third, this unique ethos of accepting failure makes DARPA an incredibly unique entity across academia, industry, and government. Even other "ARPAs" do not have the funding levels necessary to pursue projects with the level of risk and reward of DARPA.

Finally, DARPA contains both deep internal expertise on technical matters, as well as an impressive network of experts and innovators that span the globe. This enables DARPA to build unique global teams that seek to develop transformative concepts and capabilities. The unique way these multidisciplinary groups can interact and conceptualize problems allows DARPA to visualize and discern vulnerabilities that most other groups may not see. This capability is of particular importance given the complex ways in which emergent and perennial phenomena create strategic changes in the global security arena, including at the intersection of climate change, ecological degradation, and biological threats.[10]

Risks to DARPA's Success

The agency is not without its challenges, however, in terms of fulfilling its ambitious mission. As input to the development of this briefer, experts at the Council on Strategic Risks (CSR) interviewed multiple subject matter experts highly familiar with DARPA through their experiences working at or for the agency. Based on these extensive discussions, CSR found multiple potential risks to DARPA's organizational success as it moves forward. Four key areas of concern included:

1) Insufficient biological expertise among leadership within the Director's Office (DIRO) given the potentially catastrophic scale of biological threats;

2) Increased risk aversion within the agency overall;

3) A tendency to regularly move the technical goal posts of DARPA-funded efforts during disruptive times and in disruptive ways; and

4) A lack of stability in biological threats being prioritized.

DARPA Today

DARPA's office directors and their deputies are responsible for setting their offices' technical direction, hiring program managers, and overseeing program execution. The DARPA Director, a politically appointed position, has discretionary authority over direction and use of DARPA's roughly $3.6 billion annual budget. They are responsible for initial or renewal appointments of program managers, approving new programs, reviewing ongoing programs, and setting agency-wide priorities.

DARPA program timelines, which produce novel technologies, are usually about 3–5 years, which is very temporally aggressive by traditional research standards. This serves to both reinforce the acuity of need

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[10] R. Schoonover, C. Cavallo, and I. Caltabiano. "The Security Threat That Binds Us: The Unraveling of Ecological and Natural Security and What the United States Can Do About It." Edited by F. Femia and A. Rezzonico. The Converging Risks Lab, an institute of The Council on Strategic Risks. Washington, DC. February 2021.

for program outcomes, while also placing stringency upon performers to maintain a rapid pace to achieve desired outcomes.

These programs are conceptualized and developed into an approved "program" within DARPA by its Program Managers (PMs). These PMs are subject matter experts in their respective fields, ranging across multiple fields including physics, chemistry, materials science, computer science, molecular biology, epidemiology, genetics, and engineering. These experts and leaders come from academia, industry, and government agencies for limited terms, usually in the range of 2–6 years, based on initial 2-year terms with the potential for 1- or 2-year renewal. The short time spans for programs, and Program Manager tenures, fuels the urgency to achieve success in less time than might be considered reasonable in other agencies.

Program Managers report directly to DARPA management. DARPA Program Managers are, critically, also supported by technical experts hired as government contractors and known as science, engineering, and technical associates (SETAs), as well as other experts in security, legal and contracting issues, finance, human resources, and communications. These important support staff are tasked with helping program managers succeed in their brief time at DARPA.

DARPA has been exceptionally successful in the past, and continues to operate in new and surprising ways that strengthen U.S. security capabilities, as well as address anticipated global threats. Yet our conversations indicate that several challenges are affecting DARPA's prospects of meeting its potential, including in addressing biological threats. First, many experts indicate a concern that there is too much bureaucracy and attention to minutiae. Second, the rapid turnover of Program Managers introduces harmful churn. Relatedly, there is inadequate respect for and independence of Program Managers. They are often directed in ways that make success more challenging for performers. It is also clear that the inherently short timelines tend to create unneeded volatility, and put program success at risk. And finally, there is a recognized need for greater focus on coordination with the interagency.

Moreover, the global security environment DARPA faces is becoming significantly more complex. A prominent example of this is noting how, despite the availability of safe and effective vaccines, misinformation campaigns have significantly undermined our ability to vaccinate the entire U.S. population. In parallel, phenomena such as gray-zone warfare, borderless disinformation campaigns, and a renewal of strategic competition in the international arena often further complicate the biological threat space. On a global level, biological threats are changing and interacting with other systemic phenomena such as climate change and ecological degradation, resulting in significant downstream effects on planetary health, pathogen evolution, spillover, emergence, and disease transmission among humans, animal hosts, and vectors.

Between these dynamics and the internal challenges DARPA faces, the organization is at risk of losing its dominant role in the biological sciences. To meet such complex and interconnected challenges, DARPA must maximize its efficiency and flexibility to prepare for abrupt changes in the threat landscape. DARPA should continue its inclination toward high-risk/high-reward research and development (R&D) efforts, but do so while implementing several recommendations as given in the remainder of this briefer.

RECOMMENDATIONS

The stakes are high for addressing these challenges. It is time to reignite the transformative spirit of DARPA so that it may continue to drive breakthroughs against biological threats on the scale witnessed in the advancement of mRNA vaccines— and even more transformative work.

Improve Alignment Across Personnel, Resources, and Performers

Culturally, DARPA is meant to be a creative agent of transformation. This requires the confluence of a unique set of organizational and operational traits that enable DARPA to innovate on the bleeding edge. To this end, DARPA can foster these traits on three levels: First, the DARPA Director's Office (DIRO) should provide the overall vision for DARPA— a future-oriented vision that sets a tone and a direction for what DARPA will focus on and prioritize to a) prevent strategic surprise to the United States and b) generate surprise for adversaries by capturing the global strategic technological high ground. Second, the Program Manager, who should be selected for their superlative expertise in a subject area, executes the vision of the DARPA Director's Office at a tactical and/or strategic level. And third, the Technical (Tech) Office Directors, while subject matter experts in their own right, should be selected on the basis of their technical leadership and management skills, with a focus on supporting program managers and programs to execute the vision of the Director's Office within their office.

This section includes recommendations that are general to DARPA but especially important for setting the organization on a strong path for future work in addressing biological threats.

DARPA Director's Office (DIRO)

Recommendation: The Director's Office should implement a vision for DARPA that focuses on high-risk, high-reward research addressing the most pressing threats to national security and Servicemembers.

Given its value as an organization that produces transformational change, the vision of the Director's Office should focus on high-impact projects that set the pace and direction for the technology landscape. It should provide the vision, research, and implementation necessary to lead the pack in terms of the technology landscape. This vision should also be emblematic of the organization's historic high tolerance for risk. DARPA leadership and programs should also embrace a duality of mission: that of support to the military Servicemember, and that of addressing strategic national security needs writ large. That is, it may be critical to design a DARPA program for a national security need instead of focusing primarily on the program's direct benefit to the military Servicemember. Though the "D" in DARPA stands for Defense, DARPA has a very strong brand, and only through continually pushing for high-risk, high-reward, transformative, and rapid outcomes, can DARPA maintain its prominence. It is notable that defending the nation today requires renewed thinking about scope. For example, the fact that climate change is a defense priority evidences the need to widen the aperture of what DARPA can and should address. DARPA projects and programs gain high level attention, and garner interest from the wider performer community; which then serve to reinforce the DARPA brand. The importance of the sequence of these events, and feedback, should be acknowledged and capitalized upon.

Scoping is also an important component of how the Director's Office will arrive at a transformative, yet feasible, vision given the "color of money" of DARPA funding (6.1, 6.2 and 6.3) and typical DARPA program timelines (3-5 years). The Director's Office can apply a framework that provides the bounds of what the vision will focus on, consisting of understanding 1) what are the threats to the Servicemember and/or to national security that are of the greatest concern; 2) how can DARPA specifically address these threats; 3) what technologies could be developed or enabled that would contribute to the solution set; and 4) the ways to implement the scoped vision. Particularly in a world that recognizes both the outsized, detrimental impact of an ongoing pandemic, as well as the potentially accelerated rate of emergent biological threats from natural and anthropogenic sources, it is highly recommended that this vision includes a significant component that addresses biological threats - a vision that works towards rendering biological weapons obsolete as a mass destruction threat through a bio-focused deterrence by denial strategy.[11]

Technical Office Leadership (i.e., Office Director and Deputy Director)

Recommendation: Office leadership should commit to supporting the success of Program Managers and distributing funding in a meritocratic manner.

The Office Director and Deputy Director should work towards supporting the vision as set forth by the Director's Office. Supporting this vision begins by recruiting experts in the related field(s) as Program Managers. Office leadership should also work to create synergies between the Program Managers, and ultimately support those same expert managers in achieving their program success (programs that serve the particular DARPA vision, which in turn serves the DARPA mission of preventing strategic surprise). Program Managers come to DARPA for a short period of time in order to "have a baby" in terms of a scientific breakthrough. Presuming that that scientific breakthrough is something DARPA needs in order to accomplish its vision, DARPA leadership has then only to focus on nurturing that, minimizing interference and roadblocks, and allowing Program Managers and performers to execute on this agreed upon mission and path.

DARPA should further stabilize and empower funding streams for Program Managers by modifying the "wedge" model of funding (allocation) among DARPA Tech Offices— a "zero-sum" type model where a set amount of funding is available on an annual basis to each of the offices.[12] Offices such as Strategic Technologies Office (STO) or Tactical Technologies Office (TTO) often get larger pieces of the pie, while offices such as DSO and BTO get less. These set allocations are determined by the DARPA Director's Office, and each office must work annually within this set amount of funding (i.e., a wedge). This current model, which creates competition for a limited amount of resources across multiple projects, should be modified into a model that is much more meritocracy-based: one in which the best ideas with the greatest impact (from the fresh talent and perspectives constantly flowing into DARPA) get incentivized via greater funding. This is a dynamic that is particularly important to cultivate as there is substantial and increasing competition for talent in the innovation and technology sectors— across

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[11] Christine Parthemore and Andy Weber, "A Deterrence by Denial Strategy for Addressing Biological Weapons," War on the Rocks, 2021.

[12] Erica Fuchs, "Cloning DARPA Successfully." *Issues in Science and Technology* 26, no. 1 (2009): 65–70.

government, academia, and the private sector. Over time, if not effectively addressed, this could result in significant talent loss for DARPA.

Program Managers (PMs)

Recommendation: DARPA should take a bottom-up approach, allowing Program Managers independence in designing and implementing projects.

A well-known and long-serving former DARPA Director had the tendency to directly supervise Program Managers.[13] This contributed to discussions on whether the agency should be bottom-up, or espouse the typical top-down leadership approach. A subsequent DARPA Director later instituted the position of "Office Director," adding a management layer in between the Director's Office and the Program Managers. And, as recent as one year ago, a previous DARPA Director had said that "PMs are the kings and queens of DARPA," emphasizing the need for more of a bottom-up approach, with a strong focus on the Program Managers, and less so on any layers in between the Director's Office and the Program Manager. DARPA directors have had different managerial styles and instituted different reporting chains, leading to confusion regarding the directionality of reporting.

Our recommendation is that the right choice is a bottom-up approach. Program Managers and performers (including sub-performers) are the drivers when it comes to project ideation, conceptualization, design, and implementation. This usually means operating in a fast-paced environment where performers must meet exceptionally difficult goals with very little slack built into the project timeline. Therefore, it should be acknowledged that the Program Managers and performers are those that have the deep knowledge, expertise, and the best understanding of ongoing projects in their portfolio, usually in their own fields of expertise.

Improve Funding Mechanisms and Sources

Recommendation: Program Managers should be given a discretionary budget to fund promising research proposed through office-wide broad agency announcements.

Each Technical Office at DARPA has available, via the DARPA website, a standing, broadly scoped office-wide broad agency announcement (BAA) to which anyone can submit (propose) their "innovative" idea(s). This is, potentially, an excellent method for capturing and developing truly innovative ideas from potential performers that might not otherwise be able to respond to pre-existing and usually announced opportunities. Nonetheless, the current process of the office-wide broad agency announcement needs optimization. Funding for any efforts selected under the office-wide announcements typically comes from program funds within the selecting Program Manager's portfolio (of funds under their control). Therefore, in order to fund a separate effort, a Program Manager is forced to divert resources from their existing programs to take a risk on any appealing technologies that come through this mechanism.

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[13] Patrick Windham and Richard Van Atta, "Introduction: DARPA—The Innovation Icon," in *The DARPA Model for Transformative Technologies: Perspectives on the U.S. Defense Advanced Research Projects Agency*, ed. William B. Bonvillian, Richard Van Atta, and Patrick Windham (Cambridge, UK: Open Book Publishers, 2019), 7.

A solution to this is the provision of a discretionary seedling budget to Program Managers that is outside of program budgets. Thus, without having to "rob Peter to pay Paul," Program Managers could use their discretionary "seedling" budget to explore and de-risk technologies proposed through the office-wide broad agency announcement, without having to take funds from an existing program's budget. Taking funds from an existing program lends to undoing the substantial efforts put into creating that well-considered budget, effectively wasting time and resources.

Further, to enhance this process, along with a discretionary seedling budget for Program Managers, any proposals being reviewed through the office-wide announcement submission process should have higher requirements for consideration, such as the proposer having completed a moderately detailed Heilmeier Question (HQ) document.[14] Prescreening and greater requirements will reduce the reviewing burden on Program Managers for these submissions, and the greater availability of funding, together, will increase the relative rate of selection of these office-wide announcement submissions.

Finally, increased communication or marketing of this process should serve to encourage submissions and increase their overall quality. This is particularly important for the life sciences, where the emergence of the biotechnology revolution and the promise of the bioeconomy are developing a thriving ecosystem of new technologies and platforms. Given the start-up culture of biotech at this stage, applying DARPA's high-risk/high-reward strategy to funding seedling efforts could increase the throughput of potential promising technologies being evaluated - which would serve to cultivate and attract the best and the most innovative start-up companies for DARPA funding opportunities.

Reach Farther and Wider for DARPA Performers

Recommendation: DARPA should ensure that it seeks performers who will produce the highest quality work, including those from outside of the United States.

Researchers funded under DARPA projects are those who do the innovative work of and for DARPA, under the watchful eye of the Program Managers. These researchers are known as "performers." The choice of these performers is vital, and a great deal of time is spent by DARPA staff on selecting, vetting and then managing these performers. Therefore, it is essential to ensure that the right performers are selected for a program or seedling. However, there has been a tendency of some performers to try and "game" the system by knowing how to prepare slides that will appeal to DARPA, or use the right verbiage to sell their technological prowess to DARPA. This has led to the same performer often receiving multiple awards from DARPA, and not necessarily DARPA choosing the best performer for the effort.

A key recommendation is that DARPA better enhance diversity in terms of the participants and their geographies. This wider look, especially for non-U.S. performers, can introduce novel technologies

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[14] Jinendra Ranka, "DARPA: Enabling Technological Innovation," in *The DARPA Model for Transformative Technologies: Perspectives on the U.S. Defense Advanced Research Projects Agency*, ed. William B. Bonvillian, Richard Van Atta, and Patrick Windham (Cambridge, UK: Open Book Publishers, 2019), 310.

stemming from geographies usually not considered by DARPA, and also lead to cost savings—both of strong interest to DARPA and the nation. This can build on the long tradition of the Department of Defense collaborating with allies and other international partners in addressing biological threats, which will be important to both developing the best technologies in this regard and deterring biological weapons activities.

Find Balance in Pacing

Recommendation: Terms of DARPA Office Directors and Program Managers should be extended to improve stability while still maintaining flexibility and agility.

DARPA is an organization that moves rapidly, with exceptionally short timelines. Program Managers and Office leadership terms are also brief. Though this is by design and intended to seek results quickly, it also requires high maintenance and can introduce harmful churn. In order to find balance between the pursuit of impactful results and potentially harmful attrition, some key issues should be addressed.

The short timelines of programs and brief tenures of staff are baked into DARPA culture and serve to maintain a brisk pace of technological development. Nevertheless, Program Managers almost never see the completion of programs they start, and there is always the potential for a new Program Manager or new office leadership to terminate existing programs or seedlings, also leading to wasted taxpayer dollars. Measures should be taken to avoid disruption of these programs and vision as Program Managers and leadership change. While one Director's or Program Manager's priorities might differ from the next, presumably there is still value in both, and especially in the short time spans under consideration. It would be wasteful to abort successful programs simply because new management has less interest in them.

The DARPA Biological Technologies Office (BTO) has had 4 Office Directors in 7 years. The DARPA Director's Office has had a little less turnover, though as the DARPA Director is politically appointed, this turnover is harder to modify. What can and should be addressed are the more regular changes of the Office Director, Office Deputy and most importantly, the Program Managers who are hired and then directed to manage the technology developments that define DARPA's success—and national security outcomes.

Additionally, the rapid turnover of Program Managers can lead to a confusing and inconsistent environment that is detrimental to research, which in turn makes researchers less likely to apply for DARPA funding. This trend has been seen over recent years, with indications that performers might prefer to seek funding from other U.S. government agencies that have similar performance standards because of the reduced managerial and administrative demands. Though the DARPA brand is strong, recent conversations with subject matter experts in the field indicate a reduced desire to seek DARPA funding because of it being deemed onerous to deal with the agency.[15]

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[15] This is based on conversations with nearly two dozen subject matter experts who were consulted by the authors to help define and explore these recommendations on a non-attribution basis.

DARPA Office Director and Program Manager terms should be lengthened in order to foster stability. The current term length of 2 years to start, with 1- or 2-year extensions, is short by design; DARPA staff regularly speak about their "badge date" as a reference to the date when the individual's DARPA term is due to end. The expectation is that a 1- or 2-year term will be extended, but there is no guarantee and this is mainly reliant on the decision of the Office Director, despite the final decision by and signatory being the DARPA Director. These short terms introduce instability that should be mitigated by lengthening the term. With longer terms, such as 4 to 5 years, Program Managers can focus on developing and then managing programs for a greater amount of time, which allows for continuity and stability within Program Manager tenures and careers. All U.S. employees are "at-will" and can still leave at any time. Yet, increasing the term length would allow a Program Manager who wishes to stay for the duration to do so, and thus maintain some stability among his or her programs and vision. This stability is vital given how projects that have yielded such significant results for the United States, such as early mRNA technology research and development, are not done within the span of 3 - 5 years: even the mRNA technologies that formed the basis for COVID-19 vaccines took over a decade to mature. Program Managers come to DARPA to support the nation and make a transformational change in the world through developing novel technology; current 2-year terms do not support this outcome.[16]

Revamp DARPA Processes for Developing Biological Technologies

Recommendation: DARPA should revamp the Biological Technologies Office to better suit conducting biological research and should increase the number of staff with biological expertise in leadership roles.

The Biological Technologies Office (BTO) was spun out of the Defense Sciences Office (DSO) and created in 2014. Per the DARPA BTO website, BTO "develops capabilities that embrace the unique properties of biology—adaptation, replication, complexity— and applies those features to revolutionize how the United States defends the homeland and prepares and protects its Soldiers, Sailors, Airmen, and Marines" and "helps the Department of Defense expand technology-driven capabilities to detect novel threats and protect U.S. force readiness, deploy physiological interventions to maintain operational advantage, support warfighter performance, and focus on operational biotechnology for mission success."[17]

The DARPA BTO was added as a sixth technical office in 2014 and has largely followed the same processes of the other five technical offices. However, it has become increasingly clear that there are some key differences with the other offices that should be addressed moving forward. Such differences surround the content covered by the BTO, specifically that of studying and using biology to develop technologies. Biological technology development is unlike that of abiotic systems; with biological technology development, "speed of development" and "safety" do not go together. DARPA must acknowledge this as it moves forward. Also, with biological technology there is a substantial commercial market, making harder the choice of what to focus on for DARPA as it works to accomplish its mission of preventing technological surprise.

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[16] Paul Sonne, "How a Secretive Pentagon Agency Seeded the Ground for a Rapid Coronavirus Cure," *The Washington Post,* 2020.

[17] DARPA, "Biological Technologies Office."

Branding is something that is incredibly important for any organization that wishes to build a consumer base and let consumers know the products or services the brand provides.[18] Currently, the name and brand of the DARPA BTO may inadvertently be constricting the scope of the office by having the BTO, and DARPA writ-large, be considered only a "tool developer." To address this issue, DARPA should consider changing the name and scope of the Biological Technologies Office to the Biological Sciences Office. This would clarify how DARPA's role is not restricted to only developing capabilities and tools— in reality, DARPA more broadly functions as a biological systems analyst and influencer. Technical areas of interest to DARPA garner attention from other U.S. agencies and other funders (e.g., foundations), and ultimately catalyze overall investment in a specific area. Potentially more than other fields, basic science is needed in biology to develop technologies, and the focus should also be on early technology levels for DARPA. It should be acknowledged that technology development is but one way in which biological systems can be influenced.

Further, given the recent example and acknowledged importance of addressing biological threats, it is necessary to have sufficient DARPA staff that can represent a broad range of biological expertise from molecular to ecological scales, with an emphasis placed on attracting individuals with multi-scale knowledge application and the demonstrated ability to assess R&D feasibility across biological scales. These staff members should also be distributed across all levels of the DARPA organization, ranging from Program Managers to the DARPA Director's Office level— a necessity to make sure that expertise is readily available in this area to both incorporate knowledge of biological issues in-house, as well as make sure that strong advocates continue to exist across the organization to make sure biological threats get the attention that they deserve.

Finally, there is a strong need to constructively address the conflict between DARPA's tight program timelines and the timeframes inherent in biological processes and regulations involving biological research. There are inherent tensions between DARPA's accelerated timeframe and the limitations that are imposed by elements in any life sciences studies, ranging from the molecular and organismal to the ecological scale. Just to name a few examples: sequencing can be inaccurate, transformations may take significant amounts of time to generate the right colony, evolution and characterization of viral quasispecies require time and repetition, and animal models are limited by the number of animals that match the stringent life sciences research requirements. Of particular concern is how DARPA timelines may push performers to work in lower biosafety levels than what may be prudent, based on the potential biological threats present in uncharacterized samples.

To address these issues, DARPA should conduct a review of time-limiting factors, and find ways to address them through novel capabilities or processes such as running portions of a study in parallel. DARPA should also look to organizations that have past experience in issues like this, such as the National Science Foundation and other federal science funders, for lessons learned. Finally, DARPA should enable greater flexibility in milestones for biological research, permitting researchers to pace themselves according to basic safety, animal welfare, and biological process requirements.

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[18] Kristopher Jones and Forbes Agency Council, "The Importance of Branding in Business," *Forbes*, March 24, 2021.

Improve Transitions from DARPA Technologies

Recommendation: DARPA should place more emphasis on identifying transition partners and engaging with them through all stages of program development.

The "Valley of Death" is a well-known concept in technology development that represents the phase between early-stage development and later stage development moving towards commercialization.[19] It is critical at the outset to find appropriate transition partners to facilitate R&D into the commercial space. Oftentimes, DARPA seeks a partner that is a military Service (Army, Navy, Air Force, etc.), but it is also the case that sometimes the military is not the appropriate transition partner.

Transitioning has always received short shrift at DARPA, in part because of the rapid personnel turnover. Since DARPA programs are usually 3–5 years in length, and Program Manager tenures are 2–6 years, it is rare that a Program Manager will conclude or transition a program that they have started. Because of the substantial effort to develop a program and get it approved, transition can often be overlooked as a problem for the future. However, with the aforementioned regulatory concerns, transition is of particular importance for biological technologies, and novel strategies such as those mentioned above should be taken to facilitate and ensure successful transition of DARPA-funded research and development.

The fairly recent addition of the DARPA Embedded Entrepreneur Initiative (EEI) was a strong step toward supporting transition efforts, designed to accelerate innovations to products and help DARPA research teams.[20] The initiative provides funding and mentoring to DARPA performers, and connections to investors and corporate partners. It focuses on the performers and provides entrepreneurial skills, an understanding of private sector market dynamics, and business expertise.

However, there remains the need for addressing transition earlier on in a program timeline. Therefore, we recommend that the U.S. Department of Commerce and U.S. Department of Health and Human Services be better engaged from the start. They could be strong partners to DARPA as DARPA Program Managers develop programs, and through all stages of program development. A group that can "pick up" the technology development (e.g., running clinical trials in humans or animals, moving forward with regulatory processes) at the stage where DARPA is finished is very important and should be identified as early as possible.

In addition, adding a liaison officer (LNO) for identified or likely transition partners would be a key role in optimizing the technology transition process. The liaison officer would provide knowledge of, and reach back capability into, their home organization, and links with DARPA. Liaison officers at DARPA from other agencies could be consulted early on in DARPA program development, and help shepherd programs after the DARPA funded effort to transition efforts. Examples of some key partners could be the Defense Threat Reduction Agency (DTRA), the Joint Program Executive Office for Chemical,

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[19] Defense Advanced Research Projects Agency, "Innovation at DARPA," July 2016.
[20] Defense Advanced Research Projects Agency, "The Embedded Entrepreneurship Initiative," Accessed October 22, 2021.

Biological, Radiological, and Nuclear Defense (JPEO-CBRND), and the HHS Biomedical Advanced Research Development Authority (BARDA). Similarly, liaison officers from key regulatory agencies such as the Environmental Protection Agency (EPA), Food and Drug Administration (FDA) and U.S. Department of Agriculture (USDA), jointly funded, would be very valuable to help with transitioning DARPA funded technologies.

Regulatory Issues

Biological science is understandably much more heavily regulated than other fields. To conduct animal or human studies, important approval processes consume a minimum of four months of program time before work can even begin. Delays caused by this time requirement could be mitigated by having a standard practice of approving "No Cost Extensions" (NCEs) that adjust for the review time period of the Institutional Review Board (IRB), Animal Care and Use and Review Office (ACURO), and Human Research Protection Office (HRPO). Usually following a DARPA program— after preliminary research has been conducted— any product intended for human or animal use requires regulatory approval from the FDA or USDA. This is an approval process that is beyond even DARPA's large budget and accelerated timelines. However, any delays with respect to these timelines could be mitigated by changing the expectation of a product at the conclusion of a BTO program, via the early consultation of a regulatory liaison officer (LNO), and facilitating appropriate partnering with, or transition to, an entity that has the will and resources to complete the regulatory process. This entity might itself be a separate agency, or else DARPA could work closely with the regulatory LNO.

CONCLUSION

DARPA is approaching an inflection point with respect to its approach to biological sciences and technologies. The global epidemiology of the COVID-19 pandemic itself, as well as the continued uncertainty with respect to the origins of SARS-CoV-2 virus, are stark reminders of the complexity of today's world and especially that of the biological sciences. It is hoped that through reflecting on recommendations put forth in this document, DARPA will continue to lead the pack in making transformational changes that address biological threats—be it via disease prevention, detection, or treatment. American lives depend on DARPA's success.

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