Approach for Research, Development, and Acquisition of Medical Countermeasure and Test Products

2022

Chemical and Biological Defense Program

Executive Summary

Rapid development and convergence of disparate branches of science and technology are both expanding the landscape of chemical and biological threats to the Joint Force and demanding a new medical approach for developing products and capabilities to understand, protect against, and mitigate the effects of rapidly emerging threats. To better prepare the Joint Force against future and unknown threats, including naturally occurring emerging pathogens, the Chemical and Biological Defense Program (CBDP) will pivot away from viewing the threat landscape as a defined list of known biological and chemical agents towards removing or reducing the impact of agents' effects. This shift demonstrates how the CBDP will view medical countermeasure (MCM) response as a spectrum that requires investing in the development of broad-spectrum (or non-specific) MCM and test products and establishing capabilities to rapidly develop narrow-spectrum (or specific) MCM and test products. In the case of an unknown threat, this two-pronged approach allows the agent's effects to be mitigated and the Warfighter to remain operational (e.g., combat ready or, worst case, minimally impacted), while allowing for the development of more specific MCM products to protect against the causative agent. The decision to focus CBDP research, development, and acquisition (RDA) investments and activities in both of these areas was informed by lessons learned from the coronavirus disease 2019 (COVID-19) pandemic, new technological revolution, accelerated development of science and technology, and emergence of new and complex threats and their accelerated rate of evolution, which makes the mission even more complex, dynamic, and challenging.

Vision

Eliminate or mitigate the effects of known and unknown high-consequence chemical and biological threats to the Warfighter through the innovation of medical technologies and development of medical countermeasure and test products that deliver a spectrum of protection.

Introduction and Rationale

Historically, with some exceptions, the defensive requirements driving the CBDP investment approach have been based on an understanding of offensive chemical and biological weapons programs from the decades following World War II. And for the better part of five decades, the Department of Defense (DOD) chemical and biological defense (CBD) MCM and medical diagnostic investments have focused on countering a defined list of known biological and chemical agents. This list was generated and updated based on several factors, to include the potential to pose a severe health and operational threat; a limited understanding of adversaries' chemical and biological weapons (CBW) programs, intent, and doctrine; and technological advances that enable CBW. However, the rapid evolution of technology continues to drive the expansion of that threat list and, as the COVID-19 pandemic demonstrated, the threat landscape now also includes the emergence of novel infectious disease pathogens. As such, it may become increasingly difficult to determine the nature and origin of threat agents, yet impacts to the

operational mission will be similar regardless of whether the threat agent is naturally occurring, accidentally released, or deliberately made.

As the number of biological and chemical threats that the Joint Force could potentially face continue to increase, the CBDP's ability to develop MCMs and test products against each and every conceivable threat decreases. Consequently, a new paradigm is needed whereby the CBDP must pivot away from viewing the threat landscape as a discrete list of known biological and chemical agents towards removing or reducing the impact of agents' effects on the Joint Force by viewing MCM response as a spectrum. This requires the CBDP to prioritize and tailor its RDA investments and activities in non-specific products and specific MCM capabilities that can be adapted and scaled to quickly prepare for and respond to unknown threats and address multi-domain operational battlespace challenges.

The capability to remove or reduce the impact of agents' effects will maintain Warfighter lethality, reduce operational risk, and facilitate continuous operations to win in a CB-contested or contaminated battlespace. As shown in Figure 1, MCM responses should be viewed as a spectrum described as two synergistic areas: broad and narrow. MCM response activities within the broad-spectrum area should focus on immediate use of non-specific MCM products that would allow a Warfighter to remain resilient against a wide array of threats in order to maintain combat readiness and reduce the impact on medical systems. In contrast, MCM response activities within the narrow-spectrum area should focus on capabilities that can rapidly deliver specific MCM products targeting the causative agent. This paradigm shift is particularly important in cases when the threat is unknown and non-specific tests and MCM products may identify or treat symptoms, but not target the causative agent or underlying disease. Furthermore, the immediate use of non-specific MCM products will support development of specific MCM products targeting the causative agent after identification and characterization. As a result, CBDP will take a two-pronged approach to RDA investments and activities for MCM products. This two-pronged approach will (1) initially deliver non-specific MCM products to the Warfighter and (2) establish capabilities to allow for rapid development of specific MCM products. Ultimately, focusing RDA investments and activities for MCM products in both the broad- and narrow-spectrum areas will allow for full coverage of the MCM response spectrum against known and unknown threats.

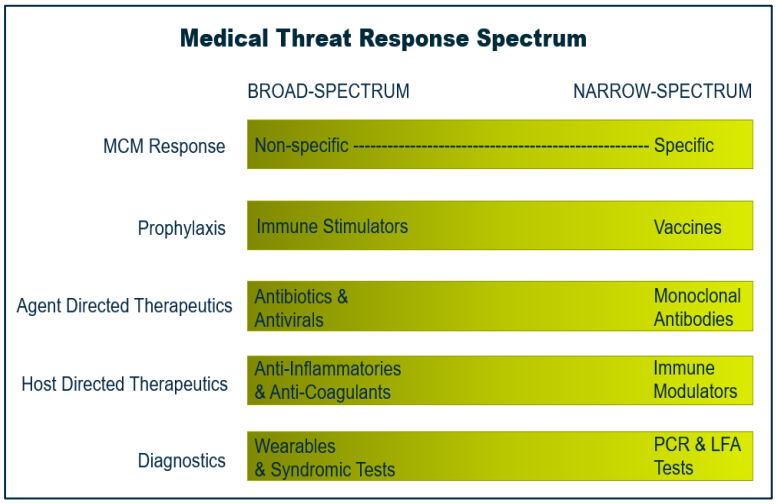

Figure 1. CBDP research, development, and acquisition broad- and narrow-spectrum paradigm showing examples of MCM products across the response spectrum.

The approach going forward involves strengthening current assets, while building a robust pipeline of products and capabilities that provide both broad and targeted coverage. The type of current and emerging threats, the operational risk they pose, and our current capabilities together will guide choices in development of new broad and narrow approaches.

Broad-Spectrum Products and Capabilities

The goal is to mitigate an unknown threat agent's effects, or to target and protect against a wide range or class of possible threat agents. Using broad or non-specific MCM products that supplement or enhance the Warfighter's (host) immune system allows them to remain resilient after exposure to a chemical or biological threat. In addition, this approach includes tests that rely on or measure host biomarkers (physiological response) rather than identifying the causative agent to signal the potential need for rapid administration of non-specific MCM products. The objective is to prevent or limit negative impacts to the Warfighter when the causative agent has yet to be identified or is an unknown threat agent. RDA activities within the broad-spectrum area should focus on characterizing threat agent classes and making available Food and Drug Administration (FDA) approved MCM products or tests that can either be immediately deployed in far-forward settings or provided to the Warfighter before deployment.

Narrow-Spectrum Products and Capabilities

The goal is to identify, prevent against, or neutralize the threat agent by using specific MCM and test products that target the causative agent and underlying disease, which non-specific MCM and test products may not have fully countered. The objective is to protect or further limit negative impacts to the Warfighter and combat operations by designing MCM and test products that specifically target the causative agent. RDA activities within the narrow-spectrum area should focus on establishing capabilities that can lead to pre-positioning and storing products as a prototype;and allow for further development of prototypes into usable MCM and test products for fielding in an operationally relevant timeframe.

Medical Countermeasure RDA Goals

Goal 1: Characterize Threat Agents to Support Broad and Narrow Spectrum Products and Capabilities

- Invest in studies that generate data and information that can support and increase the speed of MCM product development
    - Expand medical-focused threat-agent, disease, and host characterization studies
    - Develop appropriate animal models or novel alternatives to support New Drug Application (NDA) and Biologics License Application (BLA) submissions, including label expansion
    - Expand agent mechanism of action studies
    - Establish an adaptable process that allows for testing of existing MCMs against threats as well as drive the development of novel MCMs

Goal 2: Deliver Broad-Spectrum Prophylactic, Therapeutic, and Testing Medical Products

- Invest in non-specific MCM prophylactics and therapeutics
    - Initiate programs focused on strengthening the host immune system through enhancement or stimulation
    - Develop broad-spectrum MCM products designed to target several threats
    - Develop MCM products that limit or contain agents' effects such as disease progression, transmission, or symptoms
- Invest in non-specific tests that can be used at the point-of-need
    - Develop tests targeting host biomarkers
    - Develop tests that inform of agents' effects such as identifying, discriminating, predicting, or informing on onset of disease or disease severity, asymptomatic vs symptomatic, and contagiousness

Goal 3: Deliver Narrow-Spectrum Prophylactic, Therapeutic, and Testing Medical Products

- Invest in activities that generate data and information or that establish processes to support and increase the speed of specific MCM and test product development
    - Establish capabilities that inform the selection and repurposing of MCM and test products for use at lower roles of care
    - Establish teaming agreements that allow for transfer of MCM and test prototypes, data, or information to commercial companies for further development and manufacturing
    - Establish a sustainable process that allows pre-positioning of MCM and test prototypes for further development or use under informed consent
- Invest in specific MCM and test products that target the causative agent
    - Establish capabilities that allow for development of MCM and test product prototypes on existing commercial company platforms, or in a form factor readily available for transfer to commercial entities for further development and manufacturing
    - Establish capabilities that allow for the storage of MCM and test product prototypes for an indefinite period and will be readily accessible for further development to a usable MCM or test product by a commercial entity in an operationally relevant timeframe

Goal 4: Establish Sustainable, Scalable, and Resilient Public-Private Partnerships for the Access and Acquisition of Medical Countermeasure and Test Products

- Leverage industrial policy to promote the US biotechnology and biopharmaceutical industrial base as preferred performers for CBDP
- Develop contractual relationships with experienced key commercial partners for the development of new and existing products at a rate that ensures continued operation of the desired capability (e.g., 10-30% of annual capacity)
- Leverage interagency partners to mutually support United States Government objectives

- Establish key public-private partnerships with sustainable commercial performers whose manufacturing structure is solvent, have a record of successfully delivering MCM and test products, and can manufacture biodefense products
- Use contractual language to establish rapid surge capabilities beyond current demand for existing and new MCM and test products
- Consider and prioritize supply chain and on-shore production of CBDP MCMs and expand the industrial base for key starting materials (including raw materials, intermediates, reagents, active pharmaceutical ingredients, primary packaging materials for MCM substance, etc.) and finished products to the maximum extent possible
- Design scalability into development plans, when feasible, to rapidly respond to increased demand (horizontal scale-up when possible to keep steady-state production for CBDP products in production throughout the year)
- Leverage contracting authorities to establish priority of access for the production of CBDP products

Conclusion

The COVID-19 pandemic demonstrated the need to alter how we conduct RDA of MCM and test products. COVID-19 was not on any threat list, yet it impacted Homeland defense, the Joint Force, and the DOD's ability to project and generate power. The CBDP cannot simply rely on a discrete list of known biological and chemical agents to better prepare the Joint Force against future and unknown threats. Instead, it must focus on removing or reducing the impact of agents' effects on the Joint Force by developing MCM products and establishing capabilities for use against any potential threat. This paradigm shift requires CBDP investments in RDA activities across the medical threat preparedness and responses spectrum.

To immediately address exposure to an unknown agent or yet to be identified agent, the CBDP will rely on non-specific MCM products that focus on making Warfighters more resilient to a broad spectrum of threats. The use of non-specific MCM products will inform, reduce, or remove the impact of agents' effects on the Warfighter. In cases where non-specific MCM products may not completely eliminate the causative agent or its effects, the CBDP will rely on capabilities to rapidly design and develop specific MCM and test products that target the causative agent for diagnosis and protection or treatment. Together, this two-pronged approach may allow the agents' effects to be prevented, mitigated, or eliminated, so the Warfighter remains operational while characterization of the threat agent continues to enable development of more customized and targeted MCM products over time. Having both broad- and narrow-spectrum MCM and test products and capabilities will better prepare the Joint Force against future and unknown threats.

Abbreviations & Acronyms

BLA	Biologics License Application
CB	Chemical and Biological
CBD	Chemical and Biological Defense
CBDP	Chemical and Biological Defense Program
CBW	Chemical and Biological Weapon
COVID-19	Coronavirus Disease 2019
DOD	Department of Defense
FDA	Food and Drug Administration
LFA	Lateral Flow Assay
MCM	Medical Countermeasure
NDA	New Drug Application
PCR	Polymerase Chain Reaction
RDA	Research, Development, and Acquisition


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BEHIND THE WARFIGHTER. AHEAD OF THE THREAT.