JSTO in the News

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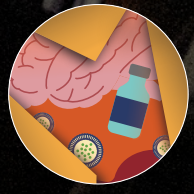
The Benefit of a Calculated Risk



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Front cover: U.S. Navy Lt. j.g. Levi Boland, a nurse corps officer, renders aid to a simulated casualty during a mass casualty response training event. (U.S. Marine Corps photo by Lance Cpl. Jennifer Sanchez)

Inside cover: A U.S. Navy Hospital Corpsman prepares a syringe to aid a simulated casualty during a mass casualty response training event. (U.S. Marine Corps photo by Lance Cpl. Jennifer Sanchez)

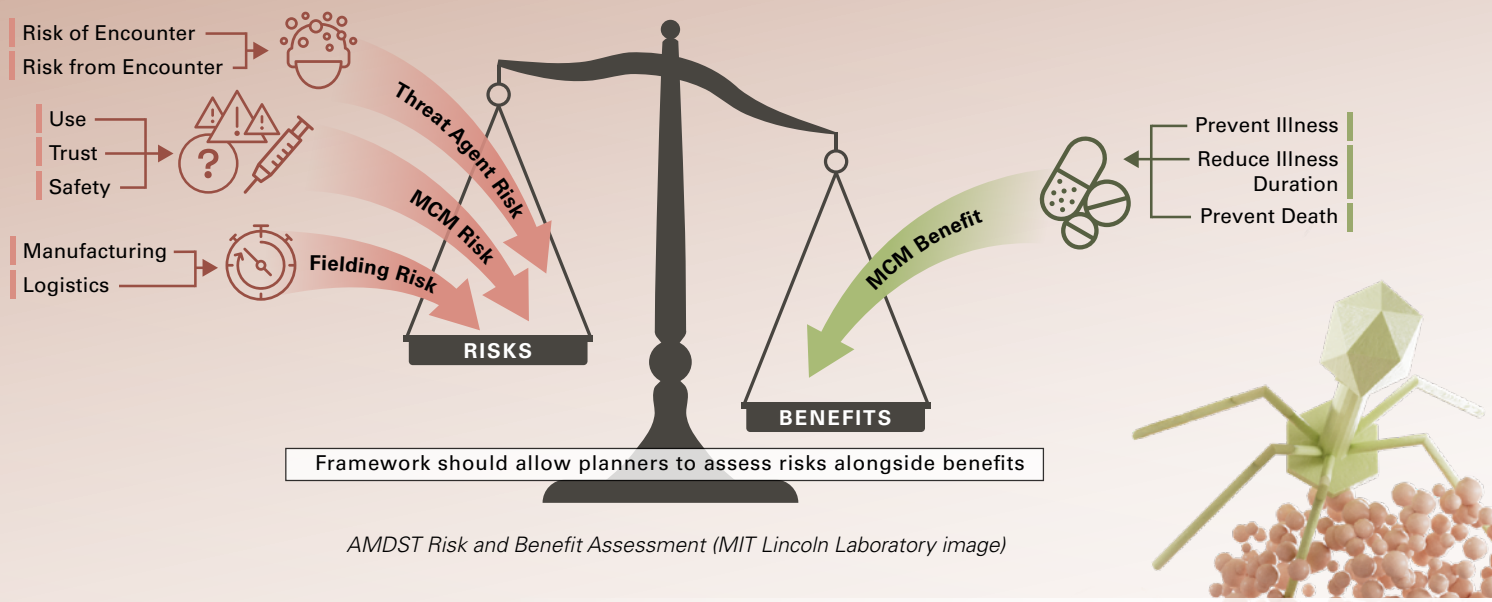
Back cover: U.S. Marines place a simulated casualty on a stretcher during mass casualty training. (U.S. Marine Corps photo by Cpl. Aidan Hekker)

THE **BENEFIT** OF A **CALCULATED**

A powerful framework enables faster, more accurate medical countermeasure decision making when it matters most.

Joint Force medical planners often operate in fast-paced environments with complex and evolving threat landscapes. Solutions for timely treatment of chemical and biological (CB) threats with the help of the Agile Medical Countermeasures Decision Support Tool (AMDST) will allow users to compare various medical countermeasure (MCM) combinations and to present a request for specific investigational or repurposed MCMs to decision makers at the speed of relevance.

The AMDST will also enable the prioritization of MCM plans based on residual risk that meets mission-specific parameters. Overall, this capability will increase the survivability of warfighters by enabling a comprehensive MCM response to persistent CB threats.



AMDST Risk and Benefit Assessment (MIT Lincoln Laboratory image)

The AMDST will also allow a planner to evaluate the risks vs. the benefits ... against a specific threat and operational scenario.

The AMDST is based on a quantitative risk-assessment framework that evaluates four key factors of any mission's medical plan:

- Threat Agent Risk
- MCM Risk
- Fielding Risk
- MCM Benefit

Each of these factors include multi-dimensional underlying components, categories, metrics, and submetrics that are each weighted, scored, and integrated to allow an operational planner a holistic evaluation of CB MCM strategies based on specific mission and threat parameters.

Speed and accuracy are the drivers for the development of this AMDST by the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program (CBDP), in collaboration with the Massachusetts Institute of Technology's (MIT) Lincoln Laboratory.

One of the most powerful aspects of the AMDST is that it takes into consideration the effects of multi-step countermeasure response plans, called layered MCMs. To do this, it quantifies the specific threat agent risks alongside the benefits, safety, and fielding challenges of operational MCMs and provides an overall residual risk score for each potential layered MCM course of action. This score helps define the full risk–benefit ratio to enable informed and efficient decision making through the chain of command.

Not only can the tool be used in real time, but it may also be used for planning scenarios and exercises across the Joint Force to enable it to be ready to fight and win in a CB-contested environment. The AMDST will also allow a planner to evaluate the risks vs. the benefits for the available FDA-approved, investigational, and repurposed MCM types (such as vaccines, pre- and post-exposure prophylactics, and therapeutics) against a specific threat and operational scenario.

In its first year of development, the AMDST technical team examined the risk framework for soman nerve gas and carfentanil opioid analgesic chemical agents; plague, Ebola, and COVID-X biological pathogens; and botulism toxin by weighting and scoring each risk factor component against available MCMs and operational data. In its current development phase, the team is expanding the framework to account for additional categories of threats to move towards a threat-agnostic tool, building capabilities for automated inputs, and further refining the quantitative framework. Additional enhancements include building a graphical user interface to allow users to interact with the tool and operational exercises for additional user engagement and refinement during the critical development phase.

This JSTO tool could join the list of technologies that have successfully provided the Joint Force with critical capabilities. ●

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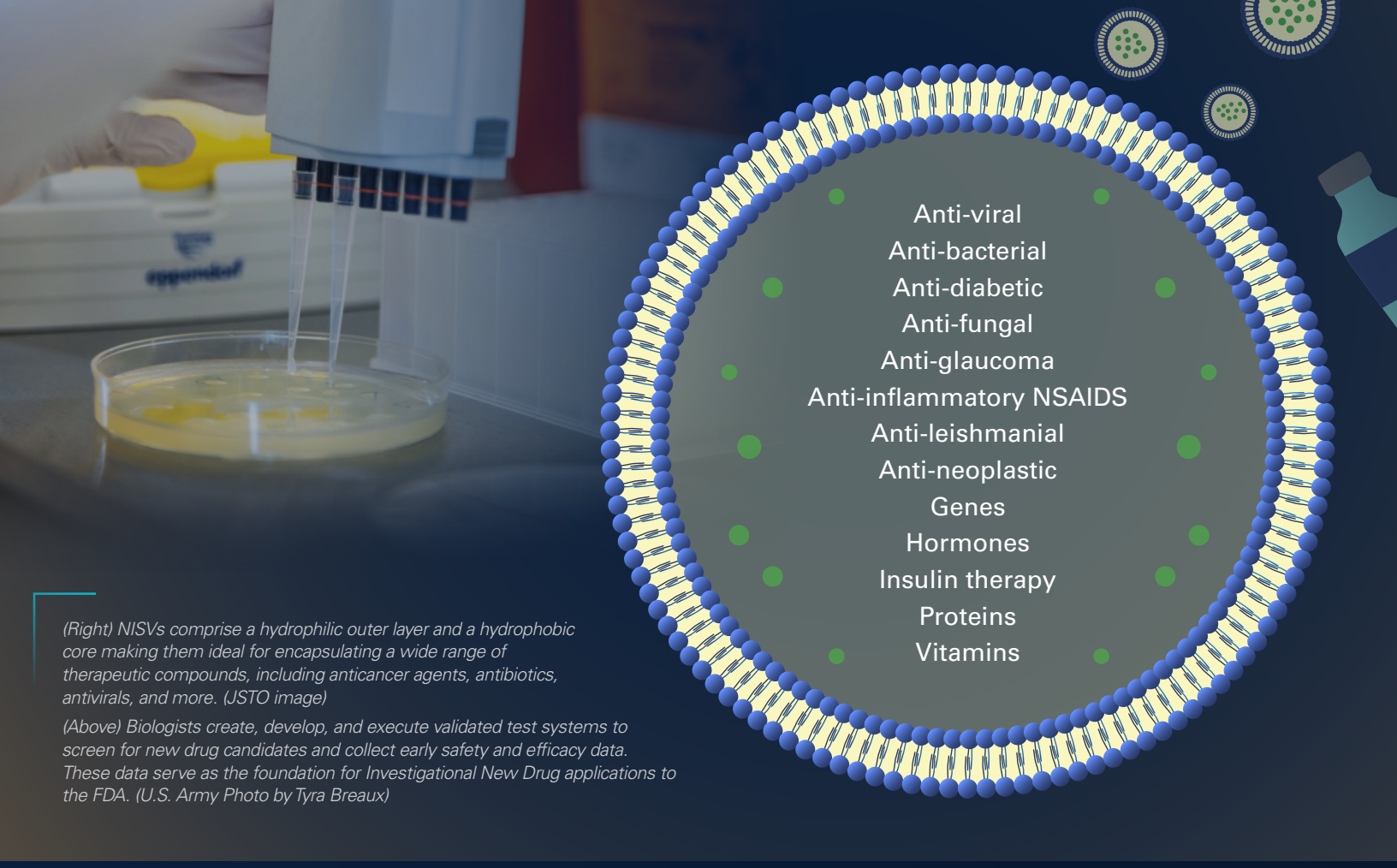
Designed, Sealed, and Delivered

Groundbreaking nanocarriers will ensure battlefield medicine is *effective* and *simple* to administer.

Drug formulation and route of administration are key factors for therapeutic effectiveness and require as much, if not more, consideration as the active pharmaceutical ingredient. For a therapeutic to be highly effective, it must be able to quickly reach the site of infection to deliver agents that either act directly on the pathogen or act on processes that help to rapidly mount host defenses, and this is greatly influenced by drug formulation and administration.



(Right) NISVs comprise a hydrophilic outer layer and a hydrophobic core making them ideal for encapsulating a wide range of therapeutic compounds, including anticancer agents, antibiotics, antivirals, and more. (JSTO image)

(Above) Biologists create, develop, and execute validated test systems to screen for new drug candidates and collect early safety and efficacy data. These data serve as the foundation for Investigational New Drug applications to the FDA. (U.S. Army Photo by Tyra Breaux)

The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program, invested with scientists at the Defence Science and Technology Laboratory (DSTL), an executive agency of the Ministry of Defence of the United Kingdom, to harness the potential of non-ionic surfactant vesicles (NISVs) to transform the field of drug delivery. NISVs, also known as niosomes, are distinct from other lipid-based particles; instead, they are formed from synthetic, non-ionic surfactants, comprising a hydrophilic outer layer and hydrophobic core. These amphiphilic molecules can entrap both hydrophilic and lipophilic molecules, making them ideal for encapsulating a wide range of therapeutic compounds, including anticancer agents, antibiotics, antivirals, and more.

Priority biological threat agents and the diseases they cause bring unique challenges to the development of effective therapeutics and treatment plans. For instance, alphaviruses (a genus of RNA viruses that cause encephalitis) localize to the brain, which makes them inaccessible to most therapeutics that cannot cross the blood-brain barrier, rendering potentially powerful therapeutics ineffective.

NISVs improve upon the concept of conventional liposomes by enhancing stability, biocompatibility, and drug-release duration, while reducing toxicity.

Similar challenges occur in attempts to treat other biothreats when trying to deliver drugs across the gut to reach other specific body sites. It can be difficult to facilitate the movement of some therapeutics across gut tissue resulting in inabilities to reach the site of infection and ineffective treatments. In austere environments, where biothreat scenarios often occur, the route of administration is critical to adequately and quickly address the threat insult. Without access to proper medical equipment, intravenous administration of drugs is unfeasible and, as a result, oral administration is preferred.

NISVs improve upon the concept of conventional liposomes by enhancing stability, biocompatibility, and drug-release duration, while reducing toxicity. The surface of these tiny spherical structures can be easily modified to enhance their targeting ability, enabling drugs to be delivered directly to specific cells or tissues. These features allow NISVs to bypass physiological barriers, such as the blood-brain barrier, that have previously stifled therapeutic development progress. Additionally, this technology ensures encapsulated drugs reach their target sites intact and protected from premature release, which minimizes systemic side effects, and optimizes therapeutic outcomes.

NISVs hold immense promise to transform the definition of an effective therapeutic. With broadened possibilities for more targeted and efficient drug administration, promising drug candidates that have hit experimental roadblocks due to low bioavailability or tolerability may have a second chance. The versatility of NISVs demonstrates a broad range of applicability beyond traditional pharmaceuticals, with great potential for usefulness in other areas like gene therapy for the treatment of genetic diseases.

The path forward for NISV development marks a significant milestone in drug delivery. Work is underway to continue optimizing this promising technology to exploit its full potential via enhancing stability, refining drug release profiles, and improving targeting efficiency. As scientists continue to unravel the entire suite of their capabilities, the application of niosomes in the field of medicine is expected to expand rapidly. With the promise of enhanced therapeutic outcomes, reduced side effects, and improved patient care, NISVs represent a groundbreaking advancement in the pursuit of more effective and targeted drug delivery systems to better protect the Joint Force, our nation, and our allies. ●

A U.S. Navy Hospital Corpsman conducts gas mask IV drills while aboard an amphibious transport dock. (U.S. Marine Corps photo by Cpl. Austin Mealy)

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2024 CBD S&T Conference

SAVE THE DATE

December 2-5, 2024

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The 2024 CBD S&T Conference — hosted by the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO), an integral component of the Chemical and Biological Defense Program — brings together scientists, researchers, program managers, and military personnel to defend our nation and its warfighters against the most pressing chem-bio threats of tomorrow. Hear about the latest groundbreaking research.

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CBD S&T CONFERENCE 2024

Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department performing the role of Joint Science and Technology Office for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program. This publication highlights the department's advancements in protecting the Joint Force, our nation, and allies from chemical and biological threats through the innovative application of science and technology.

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