JSTO in the News

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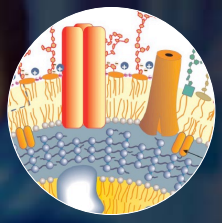
February 2018 | Vol. 8 No. 2



Of Mice to Men: New Melioidosis Vaccine on the Horizon

New Recipes for Decontamination

(Image courtesy of the Army Public Health Center)

Lead DoD science and technology to anticipate, defend and safeguard against chemical and biological threats for the warfighter and the nation.

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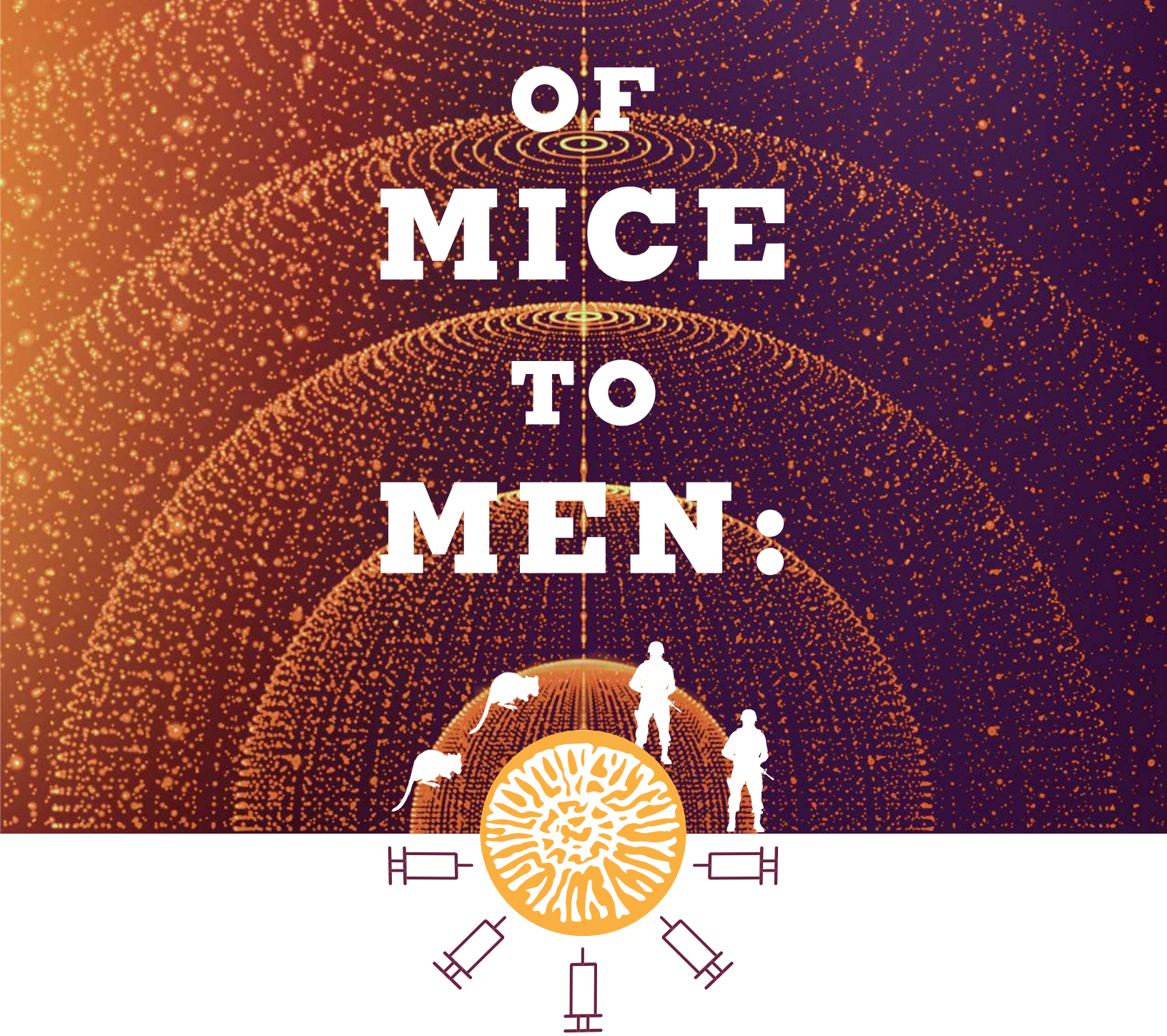
Front cover:
Emily Reinke, Ph.D., and Valerie Adams, Ph.D., read results of the Ames mutagenicity assay for the Army Public Health Center. Toxicologists strive to determine the lethal level of substances using methodologies such as computer modeling, cellular and genetic toxicology, and animal studies. (Image courtesy of the Army Public Health Center)

Back cover:
A warfighter, assigned to 2nd Brigade Combat Team, 82nd Airborne Division, chats with the truck crew before a movement to an advise and assist patrol base in a neighborhood liberated from the Islamic State of Iraq and Syria in Mosul, Iraq. (U.S. Army photo by Staff Sgt. Jason Hull)



First Melioidosis Vaccine on the Horizon

The last case of smallpox in the United States was reported more than 65 years ago, and in 1977 the disease was eradicated due to the development of a vaccine. Vaccinations such as this are critical to protecting our warfighters and the public from biological threats, but many threats still lack countermeasures. Melioidosis, a Centers for Disease Control category B agent, claimed 89,000 lives in 2015 alone, which has prompted researchers from the Defense Threat Reduction Agency's Chemical and Biological Technologies Department to lead development of the first vaccine for the deadly disease.

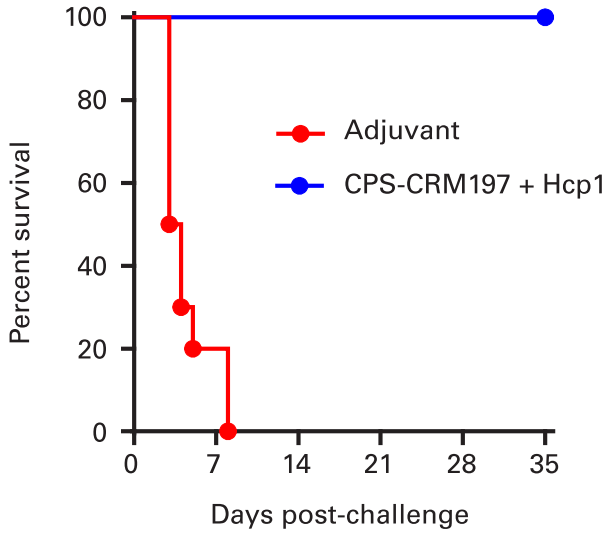
Melioidosis is caused by the bacterium Burkholderia pseudomallei, via inhalation of contaminated dust or water, or contact with contaminated soil, especially through skin abrasions. The signs and symptoms of the disease can vary greatly and may mimic those of tuberculosis or common forms of pneumonia.

Historically, the disease is associated with a high mortality rate due to its quick progression, the difficulty of diagnosis, and the inherent resistance of the bacteria to several antibiotics. Both the intrinsic drug resistance and the intracellular lifestyle make successful antibiotic treatment difficult, lengthy and intensive, often involving intravenous therapy followed by a months-long eradication phase with oral antibiotics.

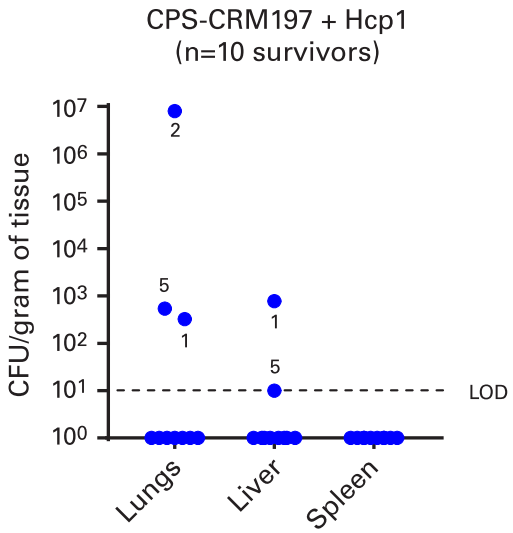
In addition to naturally occurring infections, B. pseudomallei is considered to be a high risk for terrorism use due to the ease of acquiring strains from the environment. The organism is endemic in the soil and water of many tropical areas across Southeast Asia, the Indian subcontinent, northern Australia and parts of Africa, South America and the Caribbean. Given this threat and the lengthy treatment regimen with suboptimal outcomes, there is significant need to develop an effective countermeasure.

Paul J. Brett, Ph.D., and Mary N. Burtnick, Ph.D., Associate Professors at the University of Nevada and the University of South Alabama recently published the research in the Infection and Immunity article "Development of Subunit Vaccines That Provide High-Level Protection and Sterilizing Immunity against Acute Inhalational Melioidosis." Their work found a subunit vaccine candidate that generated sterilizing immune responses in mice.

B. pseudomallei expresses a variety of structurally conserved protective antigens, including cell-surface polysaccharides,

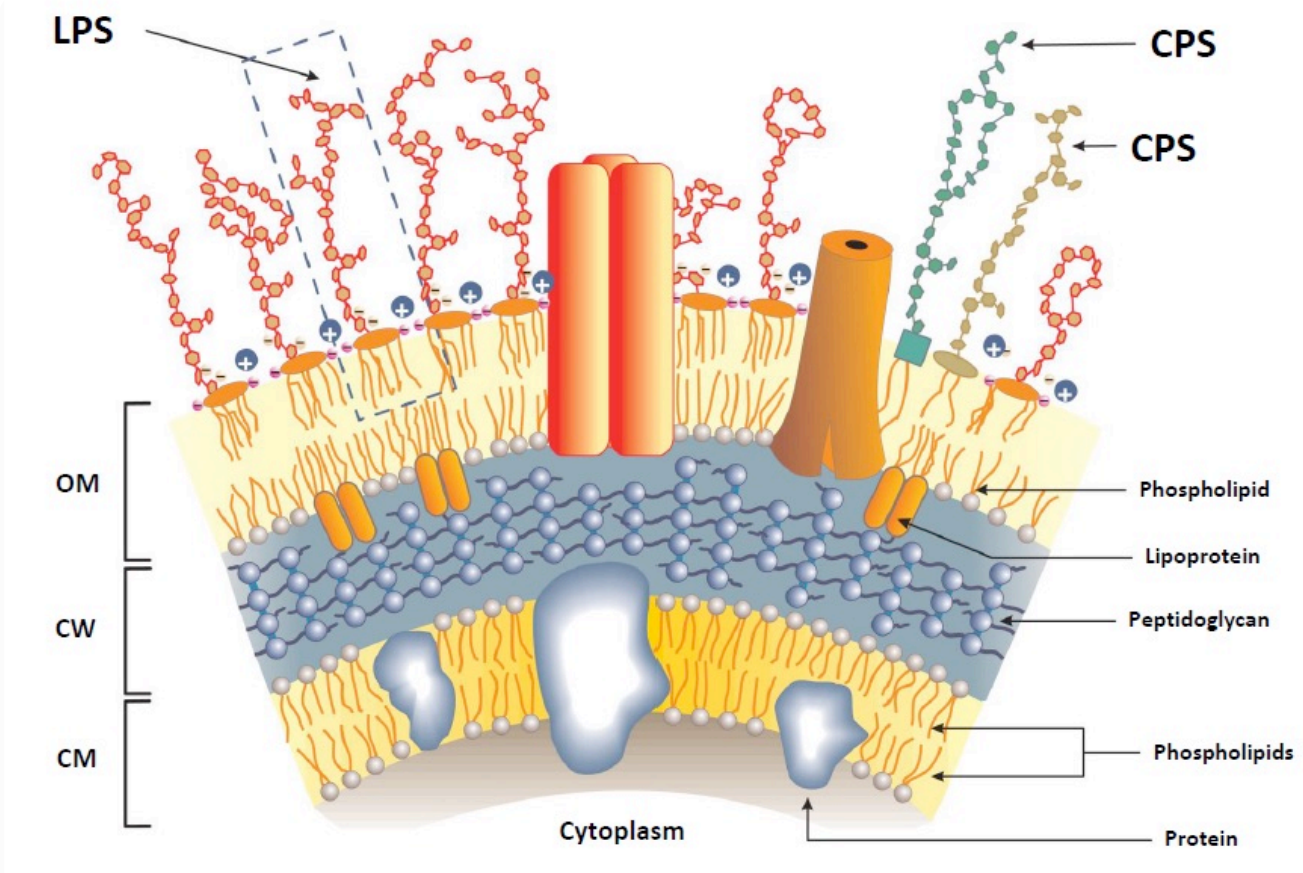


100% Survival



70% Sterilizing Immunity

Survival rates of mice after aerosol challenge with a high dose of B. pseudomallei and amount of culturable bacteria in lungs, livers and spleens. (Image by DTRA CB)



The Burkholderia Cell Envelope

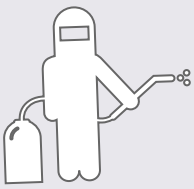
(Graphic courtesy of Dr. Paul Brett)

cell-associated proteins and secreted proteins. The capsular polysaccharide (CPS) is expressed by all known virulent isolates of B. pseudomallei and therefore an attractive antigen for vaccine development.

Researchers tested CPS, in combination with hemolysin co-regulated protecin as a second antigen, because it is highly conserved among B. pseudomallei isolates. Recently tested in mice, this two-part vaccine formulation stimulates both humoral and cellular immune responses to provide mice with a high-level protection and, importantly, sterilizing immunity, against an acute inhalational challenge of melioidosis.

After aerosol challenge with a high dose of B. pseudomallei, 100 percent of the mice immunized with the conjugate vaccine survived the full 35-day study. In contrast, all unvaccinated mice succumbed to disease by day eight. Remarkably, 70 percent of the survivors had no culturable bacteria in their lungs, livers or spleens, indicating that the vaccine formulation had generated sterilizing immune responses. To date, this is the highest level of protection conferred by a subunit vaccine against an acute inhalational challenge of B. pseudomallei.

Collectively, these studies support the rationale for developing multivalent subunit vaccines to immunize against disease caused by B. pseudomallei. Due to the high level of immunity demonstrated during the acute inhalational challenge, DTRA CB aims to develop life-saving vaccines for both the warfighter and public health against naturally occurring and engineered biological agents.



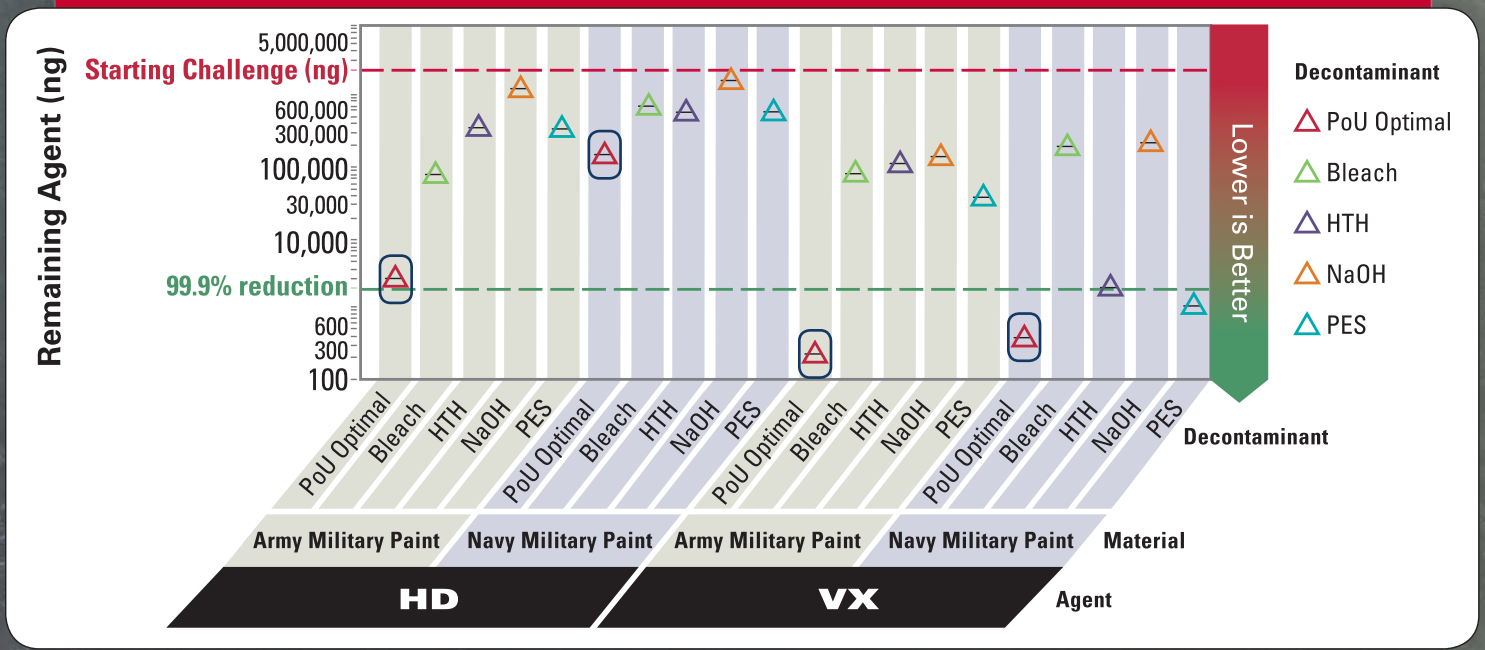
New Recipes for Decontamination

An old adage says that a jack-of-all trades is master of none. Current decontamination methods utilize a one-size-fits-all approach, however due to chemical formulations, this shotgun approach may not achieve sterilization efficacy and toxicology requirements. Utilizing innovative chemistries and point-of-use (POU) approaches, the Defense Threat Reduction Agency's Chemical and Biological Technologies Department and Edgewood Chemical Biological Center is seeking to protect our warfighters from chemical exposure by developing new recipes for adjustable formulations.

In recent years, programs focused on providing warfighters with universal approaches to counteract multiple chemical agents. However, different chemicals require various methods to neutralize them. For example, some agents are better neutralized with low pH levels and others with high pH levels. These variations make the universal-solution too generalized to optimally decontaminate any threat.

The DTRA-ECBC approach enables warfighters to create adjustable formulations based on the agent's properties and contaminated material. It includes optimizing media

Comparison of PoU Program Formulation with Baseline Decontaminants



Starting challenge was 1 g/m^2, so approximately 2 mg. test conditions were 60 min age, 30 min dwell time for the decontaminants, passive water rinse to remove the decontaminants and a 60 min solvent extraction (chloroform for mustard gas HD, isopropanol for VX).

to extract agents from sorptive materials rapidly, investigating chemical agent neutralization options and optimizing surface decontamination performance. Researchers tested paints, coatings and tire rubber as material surfaces as they are common military materials that provide decontamination challenges.

Recently the Defense Science Board (DSB) tested the POU approach to develop optimal recipes. The DSB also compared the effectiveness of the newly developed formulations with five conventional, one-size-fits-all versions. As shown in red on the chart on the previous page, the POU method outperformed baseline decontaminants on both Army and Navy military paint coatings. Further, these POU formulations demonstrated improved efficacy (tables 1 and 2).

With a limited number of ingredients and simplicity of recipes, this proof-of-concept demonstrated an easy-to-use warfighter solution. Additionally, POU decontamination requires less water by volume than universal approaches, reducing the logistical burden. The dual-use system can also be employed in daily operations for cleaning or sanitation, effectively putting the tool in the hands of the warfighter.

Future efforts will leverage findings identified by the POU decontaminant project to tweak additional formulations. Today, this innovative, DTRA-funded research will allow warfighters to have state-of-the-art decontaminants with an enhanced ability to extract harmful chemical agents from military materials.

Agent	Material	Decontaminant	Log Difference	PoU Performance Factor
HD	Navy Military Paint	PoU Optimal	1.26	1
		Bleach	0.59	5
		HTH	0.64	4
		NaOH	0.22	11
		PES	0.61	4
	Army Military Paint	PoU Optimal	2.97	1
		Bleach	1.48	31
		HTH	0.86	129
		NaOH	0.29	475
		PES	0.83	139

Table 1. Baseline decontaminant performance against PoU optimized decontaminate on military coatings with contaminant mustard gas HD.

Log Difference: A normalized response of how much agent remains after the decontamination process, relative to the amount of agent applied. Higher values indicate better removal.

PoU Performance Factor: A normalized response of how the PoU decontaminant performed against the other decontaminants. A value of 1 means the PoU performed the same. Values greater than 1 indicate the PoU performed better than the referenced decontaminant. For example, a value of 100 means the PoU performed 100 times better.

Agent	Material	Decontaminant	Log Difference	PoU Performance Factor
VX	Navy Military Paint	PoU Optimal	3.61	1
		Bleach	1.01	396
		HTH	2.83	6
		NaOH	0.96	446
		PES	3.03	4
	Army Military Paint	PoU Optimal	3.85	1
		Bleach	1.52	214
		HTH	1.09	577
		NaOH	1.04	646
		PES	1.54	202

Table 2. Baseline decontaminant performance against PoU optimized decontaminate on military coatings with contaminant VX.

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Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department. This publication highlights the department's advancements in protecting warfighters and citizens through the innovative application of science and technology research.

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