Warfighter Protection and Acute Care Project Management Office

April 2022 - Volume 2

WPAC NEWSLETTER

& Product Portfolio

Mission: Develop, deliver, and field U.S. FDA-approved preventions, diagnostics, and treatments for infectious diseases and combat wound infections; blood products and blood components; and drugs for battlefield pain management to protect and sustain the Warfighter during far-forward deployments.

U.S. Army Medical Materiel Development Activity

USAMMDA

USAMMDA WPAC PMO PRODUCT MANAGER DISCUSSES THE BROAD SPECTRUM SNAKEBITE ANTIDOTE PROGRAM

By USAMMDA public affairs

The U.S. Army Medical Materiel Development Activity's (USAMMDA) Warfighter Protection and Acute Care (WPAC) Project Management Office (PMO) continually works to leverage partnerships with industry, academia, and other government agencies to develop materiel solutions designed to protect and treat our nation's Warfighters at the point-of-injury and beyond. One of the WPAC PMO's more recent projects involves a broad-spectrum snakebite antidote, which is designed to treat many types of snakebite envenomation, regardless of snake species.

Dr. Lindsey Garver serves as product manager for the BSSA program, and recently she spoke with USAMMDA's public affairs office to provide information regarding the project, and its current and future impact on the health and safety of our Service Members worldwide.

Q: Dr. Garver, please describe your role and responsibilities regarding the Broad Spectrum Snakebite Antidote program.

LG: As a product manager within the WPAC PMO, I manage the cost, schedule, and performance of the entire development process of the BSSA materiel solution, including chairing the Integrated Product Team (IPT), initiating contract requirements, maintaining close communication with the industry partner and tracking their progress, managing risk, identifying opportunities for improvement, communicating with our user community, forecasting the remainder of the lifecycle, managing progress toward acquisition milestones and keeping program documentation current, and reporting all of this information up to USAMMDA leadership.

Q: Please provide an overview of the BSSA program and USAMMDA's role in the project. Who are the significant commercial partners involved?

LG: The BSSA program seeks to develop a shelf-stable treatment for snakebite envenoming that is safe, easy to use by individuals in far-forward austere environments, and is independent of snake species. Right now, traditional antivenom can have some nasty side effects, such as anaphylactic shock. It is often not stable at room temperature, and it is pretty species-specific — which means, you need to know which snake bit you to be treated with the proper antivenom. This also means the military must stock and know how to use multiple types of different antivenom to treat bites from different species. There are some species for which no antivenom even exists, meaning the only treatment is supportive care. This program seeks to provide a solution to all of these issues. The BSSA project is a Defense Health Agency (DHA) program. It was initiated through a Broad Agency Announcement via the Small Business Innovation Research Program (SBIR), and initial efforts were managed by USSOCOM with additional support from the U.S. Air Force. The WPAC PMO picked it up at SBIR Phase 3, when the leading prototype was ready to move into current Good Manufacturing

Practice manufacturing and clinical trials. Throughout the program history, the U.S. Special Operations Command has been a huge advocate, and they are our primary user community.

Ophirex, Inc., a small business entity, is our industry partner on this project. It is a public benefit corporation that is passionate about both the military and global health market. The company is developing our leading prototype, a small molecule drug called varespladib, in oral (both tablet and capsule) and intravenous (IV) injectable form.

Q: Is this BSSA project unique, or are other companies working on similar products?

LG: We have a few other products from other companies in "tech watch." Traditional antivenom has been made the same way for more than a century.

It has the same limitations it had 100 years ago — and it can be very expensive, which is a huge problem for the global health market. All of this has led to the World Health Organization designating snakebite envenoming as a neglected tropical disease. This gap in effective treatment, coupled with worldwide need, has led to a few companies investing in treatment development. As such, they each are developing their technologies in different ways, and using different platforms — so we have them under "tech watch" to monitor the market. However, varespladib is the farthest along in clinical development, and we feel it has the greatest potential to meet military criteria for a safe, effective, easy-to-use solution.

Q: What is the most significant information that people should know about this program? What has been most surprising to you about the BSSA project?

LG: If successful, varespladib will change the way snakebites are treated, for the military and everyone throughout the world. Currently, the military pieces together a protocol for antivenom administration that involves 1) checking matrices to see which product to use based on location and the types of snake that dwell there, 2) obtaining antivenom that may or may not be U.S. Food and Drug Administration (FDA)-approved (although we use it because it is the only product available to treat a specific type of snake venom), and 3) having a medic or other professional reconstitute and inject antivenom into the snakebite victim. Having an FDA-approved broad-spectrum drug in pill form completely changes the game — streamlining and hastening treatment.

Most surprising to me has been how many stories I hear about Service Members encountering snakes. We consider snakebite envenoming a low-incidence but high-impact threat; however, I've heard so many stories of Service Members running into snakes on the job. This really drove home for me the idea that, in addition to being a treatment for bites that occur for a smaller number of men and women, the BSSA also offers a psychological benefit to any Service Member who just sees a snake. They can rest assured that, on the off-chance they are bitten and the snake is venomous, they can stave off even the worst of symptoms just by taking the pills they have in their pocket.

Q: How will USAMMDA's work on this program benefit the health and readiness of our Service Members? Will it benefit the civilian population as well?

LG: Aside from what's already been described, this product is really designed to counter the far-forward threat of snakebites. There is an inverse relationship as one moves into more austere conditions where the threat of snakebites goes up, and access to higher echelons of care goes down. A successful BSSA product extends easy, effective treatment into those austere conditions, supporting the independent maneuver of small teams and widening the window of time needed for evacuation in the event of a bite.

This is a huge product for the civilian population as well. Globally, up to 5.4 million people are bitten by snakes each year, with about half showing clinical symptoms. About 138,000 die each year and 400,000 more suffer permanent deformities or amputations from complications. In the U.S., we do not have a high death rate, but this absolutely will be an important product for farmers, fisherman, hikers, hunters — anyone who lives, works, or recreates in more rural areas. In low- and middle-income countries, this is expected to meet a significant unmet medical need and bring care to a lot of people, especially those who live and work very far from medical resources capable of treating envenomation.

Q: Have you experienced any particular or memorable events during your work with the BSSA program?

LG: Ophirex shared some video with our team of mice that were given either normal care for snakebite or varespladib after administration of a biologically relevant dose of snake venom (a controlled way to mimic a bite, then treatment). The differences in those animals were so stark — the animals that received normal care were huddled, lethargic, and obviously unwell, while the animals treated with varespladib were running around, eating, just like any healthy mouse. As a microbiologist, I'm used to seeing graphs where markers of disease or immune response or pathogen burden tell you if a treatment is working or not — to see it so evident like that by just looking at the animals, this really left an impression on me.

Q: What was the biggest challenge you faced while overseeing this program? How were you able to overcome this challenge?

LG: The technical capabilities we hope to see from any candidate BSSA product make it versatile to use, and should represent a huge leap forward compared to existing antivenom products. This is terrific, but it creates a challenge in thinking about every situation in which it might be used, along with every possible user. Who will use the tablet form and who will use the IV form? The IV form is designed to ease administration if victims experience neurotoxicity and have difficulty swallowing the tablet. Are there situations where we might need the IV form? Will individuals carry it? All individuals or only some? Medics? Which services are interested? Which types of medical facilities across all roles of care will stock it, and how much? What about Continental U.S. facilities for domestic snakebites? What about veterinary use? What about off-duty use?

All of these questions have implications on future quantity requirements, our projected costs, force health protection guidance, and logistics planning. Current antivenom doesn't have the same user flexibility or broad-spectrum applicability, so there's no paradigm to follow. This is a challenge we're still working to overcome, by working with many user community members and documenting assumptions in models that can be adjusted as we accumulate more information. Our WPAC PMO's logisticians have been instrumental in creating a subordinate IPT working group to keep up with this challenge.

Q: Knowing what you know now, would you have done anything differently thus far?

LG: I would have planned many more in-person visits before the pandemic hit, with both our industry partner and with our user community. We started this program mid-2019, and I was lucky to secure a trip out to meet with the Ophirex team in January 2020. However, with conferences canceled and travel restricted, most of the relationship-building with both Ophirex and our DOD stakeholders has been virtual. Luckily, I think we've been pretty successful, but if I had known how the world would change, I definitely would have spent more time face-to-face.

Q: What lies ahead for the BSSA program?

LG: Right now, we're seeing how the first Phase 2b efficacy trial will go. We're already enrolling in the U.S., and India should be set up in the near future. These trials will not only give us our first test

with actual snakebite envenoming scenarios, but they will also provide a wealth of lessons learned regarding our protocol, how varespladib integrates with standard-of-care, perspectives from snakebite victims and healthcare providers, and much more information. All of this data will shape future clinical work including a possible “switch” protocol where different combinations of IV and tablet dosing are given to provide the optimum treatment — for example, a bite that delivered a significant amount of venom may be best treated by an IV infusion followed by maintenance on tablets until total resolution of symptoms.

Q: What is next for varespladib?

LG: We are in a really exciting time for varespladib right now, as we have one trial in progress for treatment of snakebite envenomation and another trial for treatment of Acute Respiratory Distress Syndrome due to COVID-19, both of which are occurring simultaneously. So we are really in data-gathering mode right now, and the answer to “what’s next” really depends on how both of these trials go. But we’re really looking forward to the potential of helping to save the lives of our Service Members and civilians throughout the world.

The FDA Clears the First 510(k) for a COVID-19 Test

On November 1, 2021, the FDA approved BioFire Defense’s COVID-19 Test 2 for analysis of nasopharyngeal swabs (NPS) from symptomatic individuals suspected of COVID-19 by their healthcare provider. USAMMDA’s Warfighter Protection and Acute Care Project Management Office, in partnership with the Defense Health Agency, led the advancement of the regulatory status of BioFire Defense’s COVID-19 test, which has been used under Emergency Use Authorization (EUA) since March 2020. The 510K approval permits this test to be marketed beyond the period of the public health emergency.

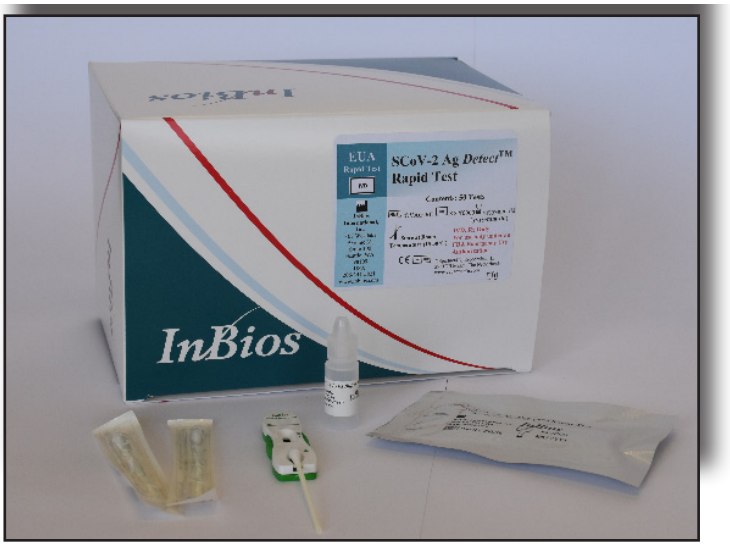
FDA granted Emergency Use Authorization (EUA) for COVID-19 Assays

The WPAC PMO's partner, InBios International, Inc received EUA authorization for their assays detecting SARS-CoV-2 direct antigen and antibodies in human serum, plasma and whole blood, intended to identify prior infection on 6 May 2021 and 24 August 2021, respectively.

In response to the COVID variant, InBios submitted data to the FDAto support the claim that their EUASARS-CoV-2 antigen test can also detect the Delta variant. In July 2021, the CDC estimated up to 83% of all U.S. COVID cases to be the Delta variant. Today, with the Omicron variant making up majority of COVID cases in the U.S., InBios iconducted studies to confirm that their SARS-CoV-2 antigen test can also detect Omicron. These tests are some of the simplest rapid antigen tests to use currently available that have been granted an EUA.

Testing against the Omicron variant is complete; studies showed a consistent level of Positive Percentage Agreement (PPA) between samples collected before the Omicron variant emerged with samples collected after Omnicron emergence. They require no instrumentation or transport media and can be performed on-site with results delivered in less than 30 minutes. The point-of-care test is useful for evaluation of symptomatic and asymptomatic individuals. It can be used for those who are suspected of COVID-19 by their healthcare provider within five days of symptom onset or for individuals without symptoms or other epidemiological reasons to suspect COVID-19 when tested twice over two or three days with at least 24 hours and no more than 48 hours between tests.

The FDA also approved a post-EUA claim on 22 November 2021, expanding the utility of the InBios SCoV-2 Antigen Detect test as an over-the-counter "self-test" using nasal swab specimens collected from individuals age 14 years or older or by adults on individuals aged two years or older. This expanded EUA to include "at-home" use expands the capability of testing for our Service Members, decreasing sample-to-result time and improving return to duty rates. Both testing kits contain 50 tests and swabs, positive and negative controls, can be stored at room temperature, and are now available for purchase from DLA's Electronic Catalog (ECAT).



The Next Generation Diagnostics System (NGDS) Increment 1 Device – Infectious Disease Panel (NGDS-IDP) Available on DLA's Electronic Catalog

The NGDS Increment 1 device is a platform for FDA-cleared, molecular assays for the analysis of clinical samples. It provides health care providers with timely (under 60 minutes) and accurate information to inform individual patient treatment. This platform, known as the BioFire FilmArray, enabled the product launch in July 2021 of the Infectious Disease Global Fever Panel (ID-GFP), a consumable pouch used with samples of whole blood in conjunction with the FilmArray.

Infectious diseases typically result in seven to 14 lost-duty days, prolonged troop performance impacts that may last years, and even, in some cases, death. Historically, for deployed personnel, infectious disease rates occur at 100 cases per 1,000 troops. The ID-GFP, packaged in a kit, provides the capability to detect multiple fever-causing pathogens to include parasites, viruses and bacteria. The NGDS device and ID-GFP kit provides sensitive, specific, and rapid detection of nucleic acids from these fever-causing pathogens, enabling faster and better informed medical decisions. This system supports near-real-time patient treatment and health protection decision-making.

The NGDS ID-GFP kit effort is a collaboration between the Joint Project Manager for Chemical, Biological, Radiological, and Nuclear, Medical; National Institute of Allergy and Infectious Diseases (NIAID); BioFire Defense LLC (contractor), and USAMMDA. Each partner is responsible for funding the development of required assays for their diseases of interest. The ID-GFP kit underwent extensive testing with blood samples obtained in clinical studies performed in the U.S., South America, Africa, and Asia. In 2020, BioFire Defense submitted applications to the FDA for approval of the ID-GFP tests for Chikungunya, Dengue, Leptospirosis, and Malaria as well as an External Control Kit to be used by laboratories to validate their performance of the tests. The FDA approved those applications in November 2020, setting the stage for deployment in July 2021. DOD users may order the ID-GFP kit directly from BioFire Defense and through the Defense Logistics Agency's Electronic Catalog (ECAT). The FDA is reviewing an application to augment the Global Fever Panel by adding NIAID-supported assays for 12 additional pathogens.

First FDA-Approved Treatment for Severe Malaria Now Available Through DLA

The severe malaria treatment drug Intravenous (IV) Artesunate, developed by AMIVAS, can now be procured by DOD Military Treatment Facilities (MTFs) via the Pharmaceutical Prime Vendor (PPV) contract, subsequent to its commercial launch in March 2021. IV Artesunate is available through the Defense Logistics Agency's prime vendor contract for unit ordering. The WPAC PMO executed an initial procurement and distributed IV Artesunate to European Command (EUCOM), Indo-Pacific Command (INDOPACOM), and U.S. Forces Korea (USFK) to ensure medication is available within the eight-hour treatment window.

The IV Artesunate has two package configurations with individual National Stock Numbers (NSNs) assigned: a 2x2 package with two vials of the Artesunate and two diluents, and a 4x4 configuration with four of the Artesunate and four diluents. MTFs must fund and request IV Artesunate through their normal PPV supply channels, but are assured that they will receive the drug in a timely manner to treat patients with severe malaria.

Canine Blood Products – Clinical Study Underway

The Military Working Dog (MWD) is a critical member of the tactical or search and rescue teams. Canine blood products such as Canine Freeze Dried Plasma (CFDP), Canine Freeze Dried Platelets (CFDPlt) address the need to treat MWDs with severe blood loss close to the point-of-injury in an austere environment in order to improve patient outcomes. USAMMDA WPAC PMO, in partnership with BodeVet, Inc., is managing the effort to assess the value of treatment with CFDP and CFDPlt as part of damage control resuscitation. The goal is to obtain results that assist the development of doctrine that is specifically aimed at saving the lives of wounded military working dogs.

In 2020, a USAMMDA-led team awarded BodeVet, Inc. a contract to perform a multiple-site clinical study that will involve wounded dogs that have been brought to veterinary treatment facilities. Very often, such dogs have had unfortunate encounters with moving vehicles or with other animals that bite. With consent of the owners, dogs that meet enrollment criteria are entered into the study on a randomized basis to receive the current standard of care (balanced salt solution), CFDP, CFDPlt, or both freeze dried plasma and platelets. The canine trauma study received regulatory approvals for initiation in April 2021. The first subject was enrolled in the clinical study in August 2021. As of March 2022, the study was under way at Colorado State University, Tufts University, Iowa State University, and Auburn University.

Commitment to the Long-Term Sustainment for the Adenovirus Vaccine

The WPAC PMO manages the Adenovirus Types 4 and 7 vaccine distribution to new recruits across the DOD military training sites and is committed to ensuring long-term viability for this vaccine. WPAC awarded a contract to complete a supply chain gap assessment in FY21. The assessment was completed in July 2021 and the Manufacturing Modernization Working Group team members from WPAC attended an on-site meeting with the manufacturer (Teva) to review and discuss the outcome of the multi-year effort to identify ways to modernize the adenovirus vaccine manufacturing process, and to reduce or mitigate risks to the process and its supply chain, in an effort to assure continuity of supply to the Warfighter.

The Adenovirus vaccine is vital to maintaining the health of all DOD military recruits as it protects Service Members against Febrile Respiratory Illness. Since 2011, 2,348,100 doses have been procured and shipped.

Pfizer's Tick-Borne Encephalitis (TBE) Vaccine received FDA Approval

WPAC PMO's Commercial Partner, Pfizer, announced FDA approval of TICOVACTM Pfizer's TBE vaccine, marketed under the brand names FSME-Immun® and TicoVac™ in Europe, and TICOVAC™ in the U.S. The vaccine was FDA approved on 13 August 2021 for active immunization to prevent Tick-Borne Encephalitis virus (TBEV) in individuals one year of age age. It is the only FDA approved vaccine to help reduce the risk of TBEV for people traveling to TBEV endemic areas. The CDC Advisory Committee on Immunization Practices (ACIP) is expected to discuss recommendations on the safe and appropriate use of the vaccine with guidance publication for TICOVAC anticipated in early 2022.

TBEV poses a high risk to U.S. and allied forces supporting the North Atlantic Treaty Organization (NATO) alliance in Eastern Europe in the absence of countermeasures.

TBEV is the fifth most operationally significant infectious disease in U.S. European Command (USEUCOM). However, U.S. Service Members have no means to counter the threat other than personal protective measures and supportive care. The TBEV vector (i.e., ticks) and virus are highly focal and typically found in wooded areas.

TBEV is a viral infection of the brain and spine. Hospitalization may last from 3 to 40 weeks and life-long disabilities may result in very severe, non-fatal cases. In lethal cases, death occurs within five to ten days of onset of neurologic signs. Case fatality rates vary by subtype, but can be as high as 30% with the Far Eastern subtype, found in Russia and far-east Asia. Up to 46% of TBEV patients suffer from long-term neurological sequelae, leading to significant long-term healthcare costs.

"It's a remarkable achievement for Pfizer and its long-standing history of developing vaccines that meet the goal of FDA approval and provide the capability to the Warfighter. This great accomplishment is a testament to the dedication and reflection of Pfizer's commitment to provide health for all."

WPAC Product Manager, Ryan Adams

WPAC Employee Highlights

Dr. Lawrence Lightner retired after 43 years in March 2022 and Dr. Kendra Lawrence was promoted to Project Manager.

Carmen Sanders was promoted to WPAC's Senior Program Analyst position and Marc Clayton moved into her position as Program Analyst.

Marc Clayton attended Automated Cost Estimating Integrated Tools (ACEIT) training in October 2021.

Dr. Kendra Lawrence completed PMT 4010 at Defense Acquisition University. PMT 4010 is a program management course focused on developing and honing leadership skills for senior acquisition professionals.

Calli Rooney successfully completed Level II of the Acquisition Leadership Challenge Program (ALCP).

LTC Laura McGhee and Michelle Mason achieved Defense Acquisition Workforce Improvement Act (DAWIA) Program Management Level II certification.

MAJ Christopher Morgan earned DAWIA Program Management Level III certification and Army Acquisition Corps membership, respectively.

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