

SUCCESSFUL PARTNERSHIP TESTS NEW MEDICAL COUNTERMEASURES FOR CHEMICAL DEFENSE

Remaining flexible—a necessity in an uncertain scientific research and development environment—was key to the successful completion of the BioScavenger project, as was maintaining constant and open communication between all team members.

AN INVISIBLE THREAT

In addition to obvious dangers, military personnel must also contend with the possibility of unseen threats. Such hazards may creep in, invisible, causing confusion, convulsions and even paralysis within seconds of exposure. They are colorless, odorless and difficult to detect, and can be fatal if not treated promptly. They are nerve agents—the most toxic and rapidly acting of all known chemical warfare agents.¹

Nerve agents are highly poisonous chemicals that prevent the nervous system from functioning properly.² Many nerve agents were initially developed in Europe as pesticides in the first half of the 20th century, but had such hazardous side effects that they were developed by military organizations for use in warfare.³ Organophosphorous nerve agents are similar in composition to pesticides, called organophosphates, though nerve agents are much more potent than pesticides.⁴ These manufactured chemicals include sarin (GB), soman (GD), tabun (GA) and VX, none of which are found in nature.^{5,6} VX is the most potent of all nerve agents, and the least volatile, which makes it a potential long-term threat, in the form of contaminated surface residue, lasting for days or even months on surfaces it has come into contact with. The Centers for Disease Control and Prevention (CDC) reports the possible use of VX or other nerve agents as chemical warfare agents during the Iran-Iraq War in the 1980s, and several countries including the U.S. have known stockpiles.^{7,8}

DynPort Vaccine Company LLC

A CSC Company

64 Thomas Johnson Drive

Frederick, Maryland 21702

+1.301.607.5000

www.csc.com/dvc

Answers for Success



¹ CDC. Chemical Emergencies Overview.

² CDC. Chemical Emergencies Overview.

³ CDC. Chemical Emergencies Overview.

⁴ CDC. Facts About VX.

⁵ CDC. Chemical Emergencies Overview.

⁶ Agency for Toxic Substances and Disease Registry. ToxFAQs for Nerve Agents (GA, GB, GD, VX).

⁷ CDC. Facts About VX.

⁸ Agency for Toxic Substances and Disease Registry. ToxFAQs for Nerve Agents (GA, GB, GD, VX).

DEVELOPING A NEW PRE-TREATMENT

Boosting the amounts of a naturally occurring human enzyme called butyrylcholinesterase can block nerve agents when they enter the bloodstream, preventing the agents from reaching their targets, and negating the danger. Currently, post-exposure treatments (antidotes) are available to treat nerve agent exposure; however, post-exposure treatments are not ideal for combat situations, when it may not be immediately apparent what the soldier has been exposed to, or possible to seek prompt medical attention. Pre-exposure treatment offers several advantages, including giving warfighters exposed to such agents the ability to continue their missions, rather than be immediately evacuated to a medical facility, preventing nerve agent casualties in the field.⁹ The U.S. Food and Drug Administration (FDA) has approved one pre-treatment, pyridostigmine bromide, "to increase survival after exposure to soman 'nerve gas' poisoning."¹⁰

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been researching butyrylcholinesterase for two decades. Nicknamed "BioScavenger," the enzyme works by capturing the nerve agent as it enters the body, before it can reach its physiological target.¹¹ In 2005, the U.S. Department of Defense (DoD) Chemical Biological Medical Systems - Medical Identification and Treatment Systems (CBMS-MITS), building on the work of USAMRMC scientists, awarded a contract to further advance development of human plasma-derived BioScavenger as a pre-exposure therapeutic, or prophylactic, against chemical nerve agents.

Under the contract awarded to DynPort Vaccine Company LLC (DVC), a CSC company, DVC led a collaborative effort with Baxter International Inc., a leader in the development and manufacturing of plasma-derived therapeutics. Baxter completed process development and manufacturing of a candidate therapeutic to be used in a Phase 1 clinical trial conducted by DVC. Baxter developed, manufactured, characterized and preclinically tested the candidate protein used in the trial, and served as the Sponsor.

THE INTEGRATED PRODUCT TEAM

DVC's leadership in government contract management and biopharmaceutical product development, particularly biological and chemical defense countermeasures, provides an advantage to both clients and partners. DVC's matrixed organizational structure is designed for flexibility and efficiency, providing various technical expertise as needed during product development.

⁹ Scienceblog.com. Enzymes interdict nerve agents in 'bioscavenger' program.

¹⁰ FDA. FDA Approves Pyridostigmine Bromide as Pretreatment Against Nerve gas.

¹¹ Scienceblog.com. Enzymes interdict nerve agents in 'bioscavenger' program.

Robust support functional areas provide more than a decade of experience in government contract management, including risk management, finance and contracts/subcontracts administration expertise, which is required to successfully navigate complex contractual and billing requirements. In addition, all DVC program managers and an increasing number of technical staff members are certified Project Management Professionals (PMPs), and have extensive specialized training in government acquisition as well. Companies new to government contracting, or those in which organizational or financial structures prohibit such work can benefit from DVC's long history of success in these areas.

DVC managed the BioScavenger program across four time zones and two continents using its proven Integrated Product Team (IPT) structure. The IPT for each product team is led jointly by a Principal Investigator (PI), who oversees technical development and a Program Manager (PM), who oversees the program budget, schedule, risk management and administrative details. Technical personnel, such as manufacturing, regulatory and quality assurance experts, and support personnel, such as contracts/subcontracts administrators and financial analysts comprise the remainder of the team, along with key representatives from both client and subcontractor personnel. Both CBMS-MITS scientists and Baxter personnel were an integral part of the BioScavenger team from the beginning, and worked in concert with DVC to address program challenges.

"DVC employed an IPT that was well-prepared to address the challenges encountered, and ensure that appropriate steps were taken to protect the safety of volunteers as well as the integrity of the studies," said DVC Program Manager Tracey Senate, PMP.

NAVIGATING UNCHARTED TERRITORY

Every day DVC product teams are doing work that has never been done before. The research and development environment can be unpredictable, with unexpected developments. The IPT must be prepared to address such challenges and adjust the program accordingly, while minding cost, schedule and—most important—human safety.

Throughout the clinical trials, DVC's quality assurance experts ensured compliance to FDA regulations and International Conference on Harmonisation (ICH) guidance, monitored adherence to the clinical trial protocol and study-specific procedures and verified clinical data integrity—all important steps to ensure human safety.



DELIVERING SUCCESS

The BioScavenger clinical trial material was manufactured using Baxter's proprietary commercial plasma fractionation process. Phase 1 clinical trials, or "first-in-human" trials of BioScavenger were conducted, testing both intravenous (IV) and intramuscular (IM) routes of administration. While IV administration provides the more rapid response typically needed for post-exposure treatment, IM administration lends itself more readily to the possibility of self-administration, as might be necessary in a combat setting. Both routes of administration were evaluated at the client's request, to investigate as many uses as practicable for BioScavenger. Trials of both IV and IM administration routes support additional studies with this compound as a potential agent for prophylaxis and treatment of organophosphorous nerve agent exposure.

Remaining flexible—a necessity in an uncertain scientific research and development environment—was key to the successful completion of the BioScavenger project, as was maintaining constant and open communication between all team members. Ultimately, despite some unexpected occurrences, the DVC and Baxter team successfully completed the contract to the client's specifications on time and within budget, illustrating the value of DVC's flexible IPT model to both clients and partners, and providing vital new information for the DoD chemical defense medical countermeasure arsenal.

The safety and efficacy of this product in humans has not been established. This product is under clinical investigation and has not been licensed by the FDA.

This study was funded by the Chemical Biological Medical System-Medical Identification and Treatment Systems (CBMS-MITS), Department of Defense (DoD) Contract W9113M-05-C-D131 and does not represent official DoD positions, policies or decisions.

ABOUT MITS

MITS centrally manages the development, acquisition and fielding of products used for the prophylaxis, treatment and diagnosis of chemical and biological warfare agent exposure, to drugs which will prevent or mitigate the actions of chemical or biological agents. MITS is part of the Chemical Biological Medical Systems Joint Project Management Office (CBMS-JPMO), which is responsible for the development, procurement, fielding and sustaining of premier medical protection and treatment capabilities against chemical and biological warfare agents.



ABOUT DVC

DynPort Vaccine Company LLC (DVC) manages product development programs and provides consulting, technical and program management services to U.S. government agencies and companies in the biotechnology and pharmaceutical industries. The company's portfolio includes vaccines and therapeutics to protect against emerging infectious diseases including biological and chemical warfare threat agents and seasonal and pandemic influenza. DVC is a wholly owned subsidiary of CSC (NYSE: CSC). DVC is part of CSC's North American Public Sector business unit's Civil and Health Services Group. CSC's expertise in providing health services to government agencies has grown over the last five decades to offer commercial best practices integrated to meet federal, state and local healthcare requirements. Services range from optimizing claims processing to operating disease surveillance systems to vaccine development and management. CSC's ideas and solutions are improving the quality of healthcare with better information for better decisions to save lives and money. For more information, visit www.csc.com/dvc.

REFERENCES

Chem-Bio Defense Quarterly Magazine. U.S. Department of Defense Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD). Vol. 6, No. 2; Apr – Jun 2009. Available from: <http://www.jpeocbd.osd.mil/packs/DocHandler.ashx?DocId=2727>

Chemical Emergencies Overview. [Web page on the internet]. Atlanta, GA: Centers for Disease Control and Prevention.; [2006 Mar 9; cited 2009 Jun 17]. Available from: <http://emergency.cdc.gov/chemical/overview.asp>

DynPort Vaccine Company LLC. HuBChE Technical Data Package [internal documentation]. 2009 Mar 24.

Enzymes interdict nerve agents in 'bioscavenger' program. Scienceblog. 2005 Jul 21. Available from: <http://www.scienceblog.com/cms/node/8498>

Facts about sarin. [Web page on the internet]. Atlanta, GA: Centers for Disease Control and Prevention. [2004 May 17; cited 2009 Jun 17]. Available from: <http://emergency.cdc.gov/agent/sarin/basics/facts.asp>

Facts about VX. [Web page on the internet]. Atlanta, GA: Centers for Disease Control and Prevention. [2003 Mar 12; cited 2009 Jun 17]. Available from: <http://emergency.cdc.gov/agent/vx/basics/facts.asp>

FDA Approves Pyridostigmine Bromide as Pretreatment Against Nerve Gas. [Web page on the internet]. Rockville, MD: U.S. Food and Drug Administration. [2003 Feb 5; cited 2009 Jun 17]. Available from: <http://www.fda.gov/bbs/topics/NEWS/2003/NEW00870.html>

JPM Chemical Biological Medical Systems. [homepage on the Internet]. Quantico, VA: Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD). [Accessed 2009 May 11; cited 2009 Jun 17]. Available from: <http://www.jpeocbd.osd.mil/packs/Default2.aspx?pg=180>

ToxFAQs for Nerve Agents (GA, GB, GD, VX). [homepage on the Internet]. Atlanta, GA: Agency for Toxic Substances and Disease Registry. [2002 Apr; cited 2009 Jun 17]. Available from: <http://www.atsdr.cdc.gov/tfacts166.html>

