

# Freeze-dried Plasma

## The Trail Back to the Battlefield

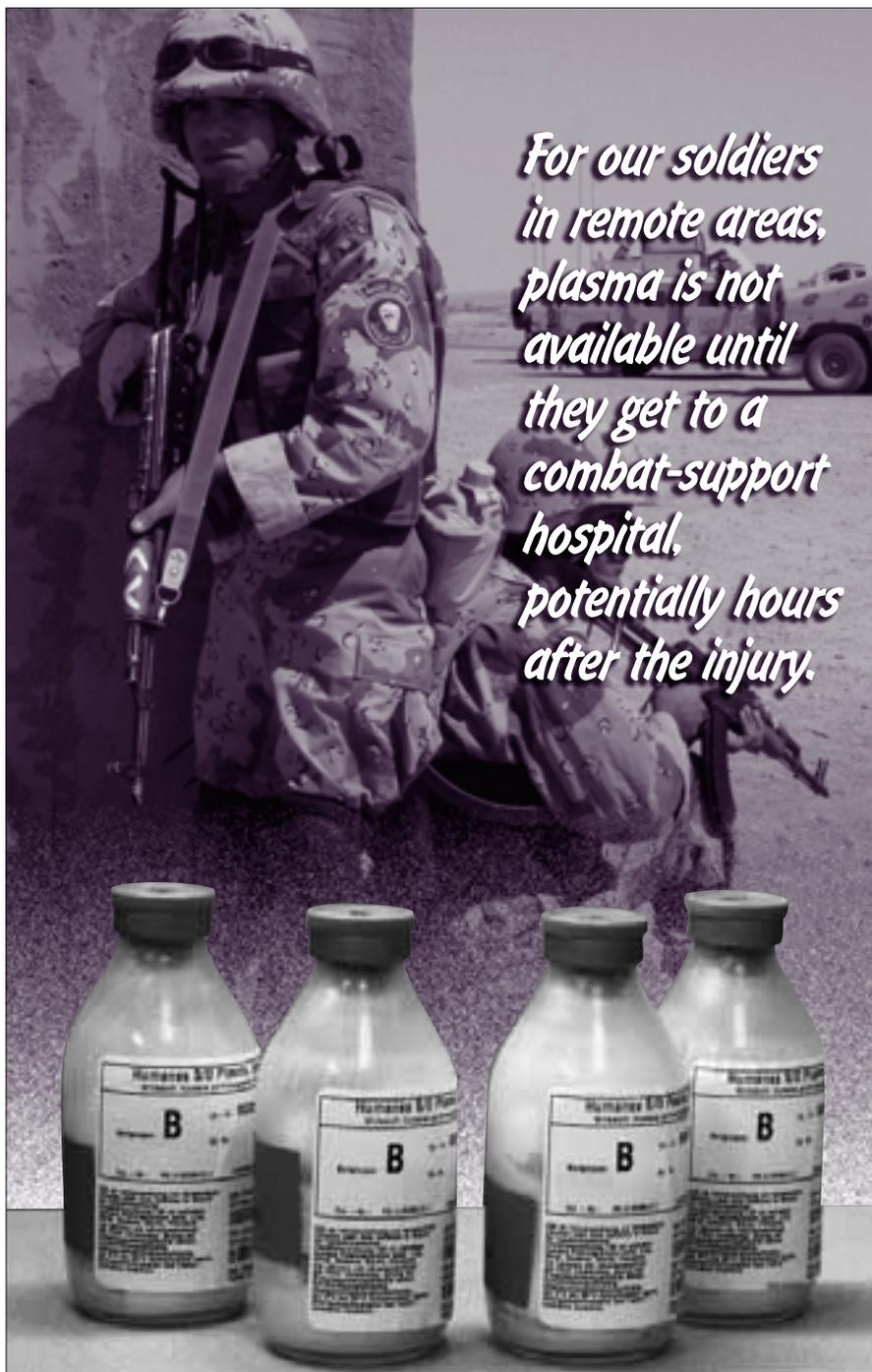
Elizabeth Barrows

I would like to share with you my current view of the path traveled by a product with a long history within the U.S. armed forces: freeze-dried human plasma. I have joined this path in the recent history of the product, and I hope to be part of the team that once again brings freeze-dried plasma to the aid of wounded soldiers.

Whole blood donations are divided into component products to allow more effective storage and more efficient use. Plasma, a clear yellow liquid that contains the clotting proteins needed to stop bleeding in the injured, is a component of blood; in modern hospitals, it is stored frozen at a temperature no higher than -18 degrees Celsius for up to one year before thawing and use. In civilian trauma centers, plasma is often available in the emergency room, but for our soldiers in remote areas, plasma is not available until they get to a combat-support hospital, potentially hours after the injury.

### Early Issues with Freeze-dried Plasma

Ironically, freeze-dried plasma was one of the first blood components identified, separated, and stored for shipment into war zones. That was back in the 1940s, before physicians and scientists understood that within the life-saving fluid, there lurked deadly viruses. To efficiently freeze-dry large quantities of plasma, the individual units were poured into a large pool often containing the plasma from more than a thousand donors. If even



*For our soldiers in remote areas, plasma is not available until they get to a combat-support hospital, potentially hours after the injury.*

**Barrows**, of the Henry M. Jackson Foundation, is a project coordinator specializing in resuscitation and blood product development on contract to the Army's Combat Casualty Care Research Program. She holds a master's degree in biomedical engineering and is a Project Management Institute certified project management professional.

a small fraction of these units contained active viruses, they could easily be transmitted to the entire pool, subsequently infecting hundreds of recipients. The distribution of pooled whole plasma in the United States was stopped in 1968.

When faced with a barrier, humans simply try to overcome it, which is what they did in the late 1980s, when a number of methods for inactivating the viruses in blood products were developed. In 1989, virally inactivated plasma products were brought to the European market; and in 1998, a product was approved for marketing by the U.S. Food and Drug Administration (FDA). The Army saw the opportunity to bring freeze-dried plasma safely back to the marketplace, and initiated a research program in 2000.

I was introduced to the Army's freeze-dried plasma research program when I joined the Army's Combat Casualty Care Research Program as a contracted project coordinator in 2004. At that time, researchers in the Department of Blood Research at Walter Reed Army Institute of Research had already freeze dried the American solvent/detergent-treated product, but that product was no longer in production. They were also working on stabilizing the proteins in single-donor, untreated units of plasma; however, there were significant manufacturing problems that would be difficult, if not impossible, to overcome. Though the researchers in the Department of Blood Research had expanded the science of freeze drying human proteins, there appeared to be no commercially viable way forward for American freeze-dried plasma.

Then suddenly, everything changed—with one e-mail.

## **New Developments**

The major supplier of solvent/detergent-treated plasma in Europe, Octapharma, produces and sells their product as frozen bags, similar to the traditional product. However, the German Red Cross – Blood Service West, Octapharma's development partner, has maintained a license and production facility in Germany for both frozen and freeze-dried solvent/detergent-treated plasma since May 2004.

The medical director for the German Red Cross – Blood Service West contacted the Walter Reed Department of Blood Research by e-mail, describing manufacturing facility upgrades and offering either processing of American plasma or sale of German plasma. Discussions ensued, and in the spring of 2005, the Blood Research Department chief invited Dr. Albrecht Hoburg, the director of blood safety for the German Red Cross Blood Service West, to visit the Walter Reed Army Institute of Research, where he presented the German Red Cross' product, LyoPlas.

## **The Potential of LyoPlas**

Over the following summer, there was much discussion within the Department of Blood Research over the desire to purchase some of the LyoPlas and test its properties in house. Unfortunately, the budgets had already been set, and there was no way to incorporate LyoPlas testing without cutting some portion of the existing research program. It looked as if that path was going to remain unexplored, until I read about the Foreign Technology and Science Assessment Support Program, a small program run by the U.S. Army Research, Development and Engineering Command with the goal of supporting foreign technology testing for transition into U.S. Army projects—exactly what we wanted to do with LyoPlas. With support from the Blood Research Department chief and the research area director for the Combat Casualty Care Research Program, I drafted the Foreign Technology and Science Assessment Support Program application package. After a number of reviews and a presentation by the department chief to the U.S. Army Research, Development and Engineering Command review board, we were awarded \$75,000 to purchase and test LyoPlas.

I started to plan a way forward through advanced development for LyoPlas, assuming that the product is of the quality we believe it to be. The only way for it to enter advanced development without a needless time lag would be to find outside funding to support the transition. I had missed the deadline for the Defense and Foreign Acquisition Challenge Programs, but the Technology Transition Initiative was still a possibility. When the call came for applications, we had been in discussions with the German Red Cross, but we still had not received the LyoPlas and really had no data on the product. I recognized that any application I filed would be essentially six months too early, but maybe some good could come simply from the application process.

With approval from the department chief, I decided it was worth the risk to put this product forward for Technology Transition Initiative funding. It was a mature product produced on a mature product line. The only hurdle from a scientific standpoint would be to complete any additional testing required for FDA approval. This is not a small hurdle but one that is well within the scope of the Technology Transition Initiative program. I figured that putting LyoPlas forward a little early would, at worst, draw attention within the U.S. Army Medical Research and Materiel Command, and perhaps increase the chance of receiving core funding for product development in the next budget cycle.

Projects submitted to the Technology Transition Initiative program have to go through a number of gates, starting at the command level and progressing up to the Office of the Secretary of Defense. The LyoPlas proposal progressed through the U.S. Army Medical Research and Ma-

**What's Fast,  
Up-to-the-Minute, Electronic,  
and Comes to Your Desktop  
Every Month?**

## Defense AT&L *eLetter*

Defense AT&L  
*eLetter*

Acquisition Today for Tomorrow's Transformation



Jim King  
Under Secretary of Defense (AT&L)

January 2006

### Message from the USD(AT&L)

Welcome to the first edition of the AT&L eLetter. This monthly, electronic publication will keep you up on the latest news to help you do your job — supporting the warfighter. I appreciate your hard work and the ethical, professional way you meet the challenges you face every day.

Recently, we announced some stellar performers who have made significant contributions to our mission. I extend my hearty congratulations to the winners of the 2005 Packard Award and the AT&L Workforce Development Awards for their contributions.

I am proud to pin you all in providing our warfighter with the best equipment and services in our interests. Many of you are also providing our warfighter with the best equipment and services in our interests. Many of you are also providing our warfighter with the best equipment and services in our interests.

**B**ringing you the latest AT&L news in a convenient format—updates on acquisition policy and legislation, certification information, news of acquisition excellence, job support tools, special messages from the under secretary of defense (AT&L).

You'll find all that and more, each item summarized to save you time, with a link to the complete article or information online.

And you don't have to do a thing to get it because it's e-mailed directly to you on the second Thursday of every month.

Contact [ATL.eLetter@dau.mil](mailto:ATL.eLetter@dau.mil) for more information.

**Defense AT&L eLetter.  
Acquisition Today  
for Tomorrow's  
Transformation**

Defense AT&L eLetter is not connected with *Defense AT&L* magazine.

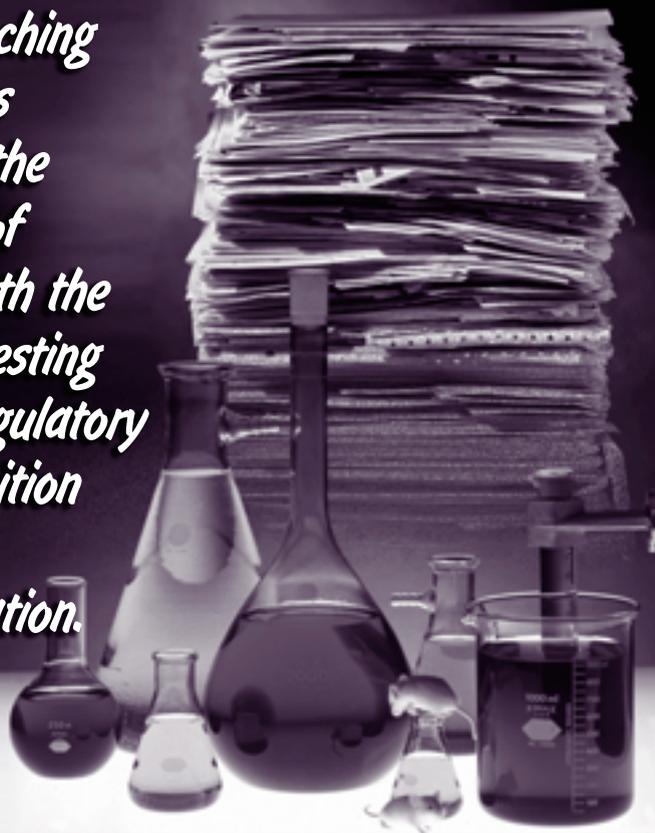
teriel Command meeting surprisingly little resistance. I was pleasantly surprised when the U.S. Army Medical Research and Materiel Command included it as one of the three proposals put forward to the Army Technology Transition Office. Over the next few weeks, the department chief and I fielded numerous questions regarding the application. Through hard work, frantic phone calls, and a bit of luck, we were able to augment and polish the proposal enough that it was the only medical proposal to be forwarded from the Army to the Office of the Secretary of Defense for funding review. At press, I am still awaiting the expected briefing call, and can only hope that this proposal will be successful.

As I mentioned, my main goal in putting this project forward for the Technology Transition Initiative was to gain some attention within the Army Medical Research and Materiel Command. In short, it worked. Planned fiscal year 2006 research budget cuts were recently revised, freeing up a fair amount of FY2006 dollars that needed to be obligated by Sept. 30, 2006. The research area director for the Combat Casualty Care Research Program recommended that the LyoPlas project receive funding to accelerate the transition to advanced development. The commanding general of the U.S. Army Medical Research and Materiel Command concurred and earmarked \$300,000 for the LyoPlas project; the money will be used to evaluate the existing body of data and start preparation of an investigational new drug application, a necessary step in the Food and Drug Administration licensing process.

### Scientific and Financial Challenges

There are many scientific, acquisition process, and financial challenges ahead on the path to return freeze-dried plasma to the battlefield. The scientific challenges are the least predictable because they are the most difficult for the Army to control. The Army does not control the manufacturing line for LyoPlas, so either it must meet the Army's needs and the Food and Drug Administration's requirements without any modifications, or the German Red Cross must be willing and able to make any required modifications. Additionally, the regulatory hurdles will be a reflection of the climate within the FDA at the specific time that this product enters their regulatory review system. The prior solvent/detergent-treated plasma licensed for sale in the United States had a tendency to cause fatal clotting problems when used in large volumes in patients with severe liver dysfunction, leading the FDA to put a black box warning on the label. Though the license was never revoked and the product ceased production for other reasons, there is going to be a burden on the LyoPlas application to demonstrate safety or to drive the decision that use of this product is not appropriate in that situation. The first step in demonstrating that LyoPlas is appropriate for use as plasma is to demonstrate the inherent differences between LyoPlas and the

*The overarching challenge is financial—the challenge of funding both the scientific testing and the regulatory and acquisition process documentation.*



older American solvent/detergent-treated product with laboratory testing. Then the Army and the German Red Cross will need to work with the FDA to design and conduct clinical trials that are appropriate to the indications planned for LyoPlas in the American market.

Compiling acquisition documents, like performing scientific experiments, requires a commitment from a varied team of people. As a contract project coordinator, my ability to garner support rests entirely on my salesmanship and communication skills. I am lucky that this product is already strongly supported by a group of subject matter experts who have been very vocal about the potential benefits access to LyoPlas might bring. The research area director for combat casualty care has also actively supported the return to freeze-dried plasma research by supporting both a science and technology objective in 2000 and an Army technology objective in 2006, and by actively supporting the transition from research to advanced development. Representatives from the U.S. Army Medical Materiel Development Activity have offered support in the form of objective technical reviews, integrated product team support, and expertise in medical product development. As our knowledge of the product grows, I plan to continue to introduce it to other members of the Army and Department of Defense, whose input is required or beneficial within the acquisition chain, including the combat developer and other official user representatives. Navigating the Army medical materiel

development process successfully is contingent on all of their support.

The overarching challenge is financial—the challenge of funding both the scientific testing and the regulatory and acquisition process documentation. For initial funding, I am hoping the Technology Transition Initiative comes through. If not, there are a number of other programs that might be able to assist the transition of this product, though I need to review the program goals to determine which ones, if any, are appropriate for a foreign product produced by a non-profit entity. I am also going to actively work to make sure this product is reviewed on the annual mission area materiel plan, in hopes that it will rank high enough to earn core funding in FY2008, the next available funding year. I have also found that it pays to be ready, so I am planning to continue drafting the acquisition documents and encouraging the development

of the needs and requirements documents that must be staffed in order for freeze-dried plasma to ascend through the acquisition milestones. If money does become available, it usually goes to the one who can make the most rapid use of it. I plan to be ready to make use of any money that falls this way.

At this point I feel that I am standing on the crest of a hill, looking back on freeze-dried plasma's long history and looking forward to what the modern product will look like when I leave this path, after the product has received a marketing license from the FDA and has returned to the battlefield. The initial product purchase funded by the Foreign Technology and Science Technology Assessment Program award is finally in house, and the first set of tests were completed by mid-June.

I am confident that if the briefing call comes for the Technology Transition Initiative program, my department chief will be able to say that this product meets the Army's specifications for freeze-dried plasma, that an investigational new drug application is already under development, and that this project is on track for a Milestone A review in early FY2007. The trail conditions look good from here.

The author welcomes comments and questions. Contact her at [elizabeth.barrows@na.amedd.army.mil](mailto:elizabeth.barrows@na.amedd.army.mil).