The Case for Dried Plasma

Ciaran Flanagan

CCO Velico

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Be Prepared

Accelerate development of both centrally manufactured dried plasma products that can be rapidly procured.

Develop dried plasma manufacturing capabilities through Military Blood Programs to provide provide local self-sufficiency, stockpiling and surge capacity.

Action today will better prepare our military health care system to **successfully resuscitate future casualties with survivable injuries**.

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The NEW ENGLAND JOURNAL of MEDICINE

"**Death from hemorrhage** represents a substantial global problem, with more than **60,000 deaths per year** in the United States and an estimated **1.9 million deaths per year worldwide**, 1.5 million of which result from physical trauma."

25 Jan 2018 Hemorrhagic Shock. Jeremy W. Cannon, M.D.

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By the time I've completed this presentation 60 more people will have died from uncontrolled haemorrhage.

One person every 15 seconds.

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Time to Early Resuscitative Intervention Association with Mortality in Trauma Patients at Risk for Hemorrhage

Andrew-Paul Deeb, et al Journal of Trauma 2023

Among the 1504 patients, every 1-minute delay in prehospital resuscitation was associated with 2% increase in the odds of 30d mortality (p=0.03).

Bleeding patients need resuscitation initiated early

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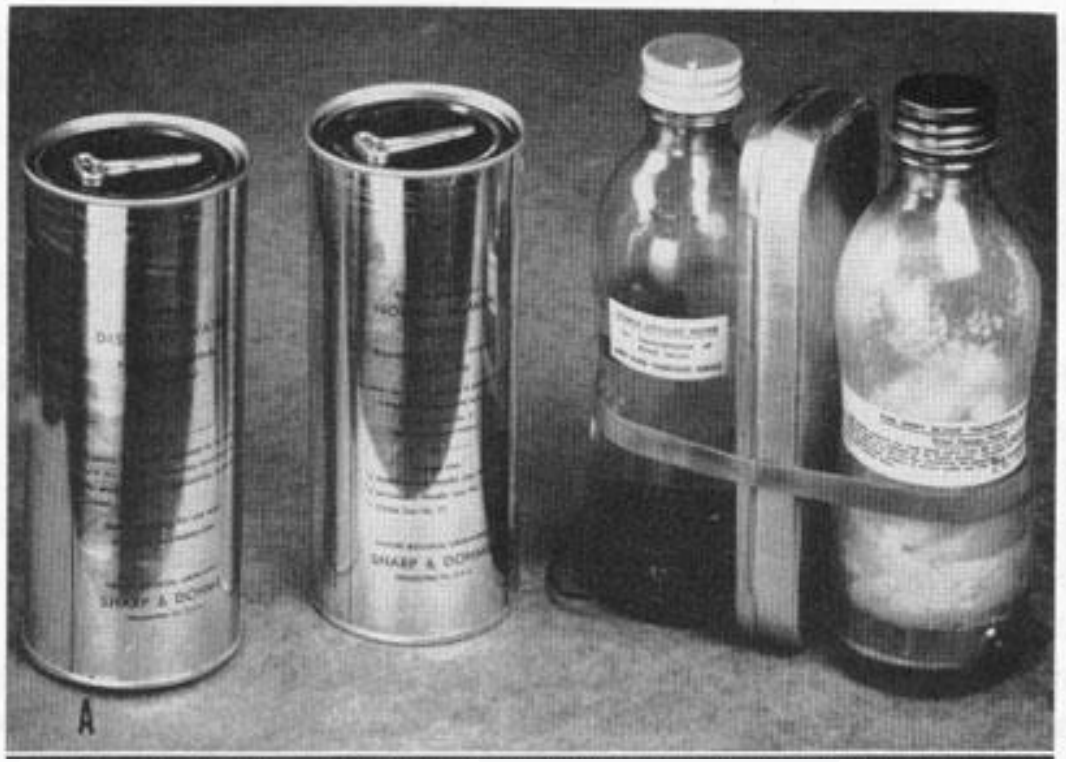
The Quest for Dried Plasma

Dried Plasma has been a holy grail of emergency response medicine for almost a century.

Dried plasma is not a new technology, nor is its use as a biobridge to definitive care and resuscitation a novel approach.

Plasma has a long history and long runway for the development of a dried blood product

WWI and WWII transfusions of whole blood and plasma to treat shock and hemorrhage



WWII British(L) & US (R) Army Dried Plasma Units.

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War: The Mother of Medical Invention

THE PREPARATION AND PRESERVATION OF HUMAN PLASMA*

IV. Drying of Plasma from the Frozen State by Low Temperature Condensation in Vacuo

MAX M. STRUMIA, JOHN J. McGRAW AND JOHN REICHEL

From the Laboratory of Clinical Pathology of the Bryn Mawr Hospital

Drying of biological substances for the purpose of preservation is now accepted as a safe and adequate procedure when properly performed.

Dried plasma has a definite place in modern therapeutic armamentarium, because it permits safe and prolonged storage and transportation under adverse conditions. Furthermore, it may be reconstituted in a concentrated form, for the treatment of certain conditions, particularly edema of the brain.

It has already been mentioned that human plasma and serum, as well as other biologicals, such as guinea pig complement, thromboplastin preparations, and prothrombin, are even better and much more simply and economically preserved by freezing and maintenance in the frozen state.[1c] The preservation of most plasma in the frozen state and a small portion in the dried state will meet all requirements.

Essential points of drying to be considered in order to maintain as many of the original properties of the plasma as possible are:

(1) The original liquid plasma must be fresh, and must meet the requirements set forth in our previous articles[1], and those of the National Institute of Health applicable to the preparation of dried plasma,

(2) Plasma must be prefrozen and dried from the frozen state,

* This research was aided by a fund donated by Mrs. John S. Sharpe, Mrs. Edward Law, the Women's Board and the Social Service Department of the Bryn Mawr Hospital and a grant from the National Research Council.

- 1936 - 1938 Blood components manufacture
- As far back as 1938 Max Strumia was producing dried plasma at Bryn Mawr.
- 1938 - 1940 Preservation of plasma by freeze-drying technology
- Spray dried plasma was produced in Sweden for their defence forces.

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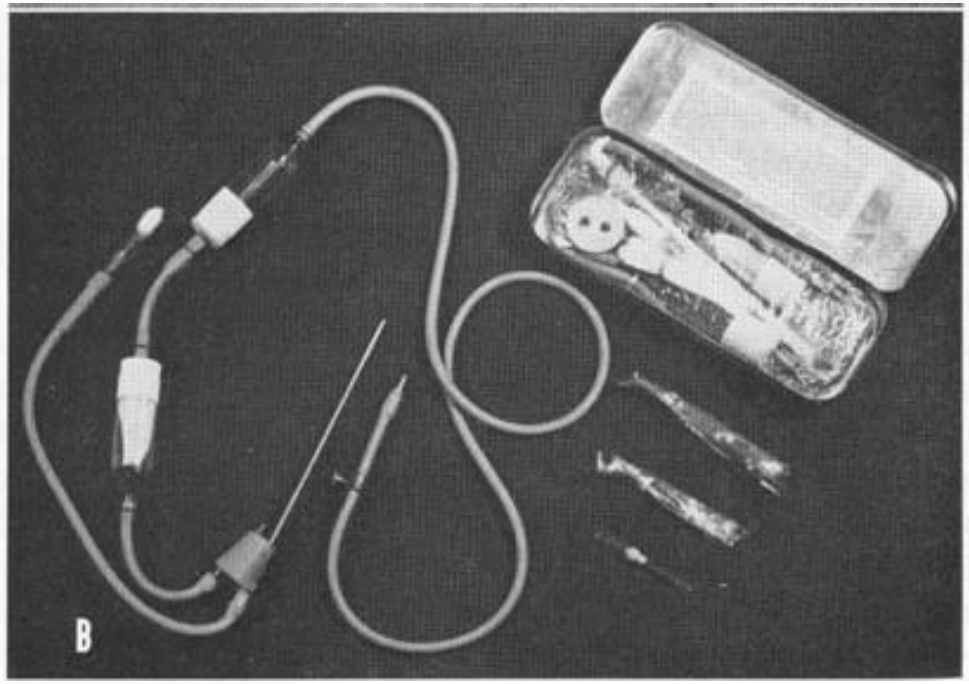
Far Forward

GOAL:

To bring blood products **far forward** to administer to bleeding soldiers. Dried plasma was produced for use by frontline units during World War II.



British Dispensing Unit for Plasma

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Military User requirements:

- Portable
- Easily prepared
- Ruggedized
- Shelf stable not requiring cold storage
- Sterile

FIGURE 159.—Administration of plasma on beach, only few feet from surf, to survivor of landing craft sunk off coast in first days of invasion of Normandy, June 1944.

1950’s-2000’s: **50 Years of Decline**

- Hepatitis from dry plasma transfusions identified by end of WWII; believed benefits outweighed the risks
- Attempts at pathogen reduction including reduction of pool sizes failed
- Discontinued due to risk of HBV contamination from large donor pools
- 1950’s Dry plasma use discontinued by US and Britain
- Serum albumin replaces dry plasma as primary resuscitation fluid for US soldiers

1950's-2000's: **50 Years of Decline**

- Renewed efforts in the 1980's – However, production of French lyophilized plasma ceased as a result of HIV risk

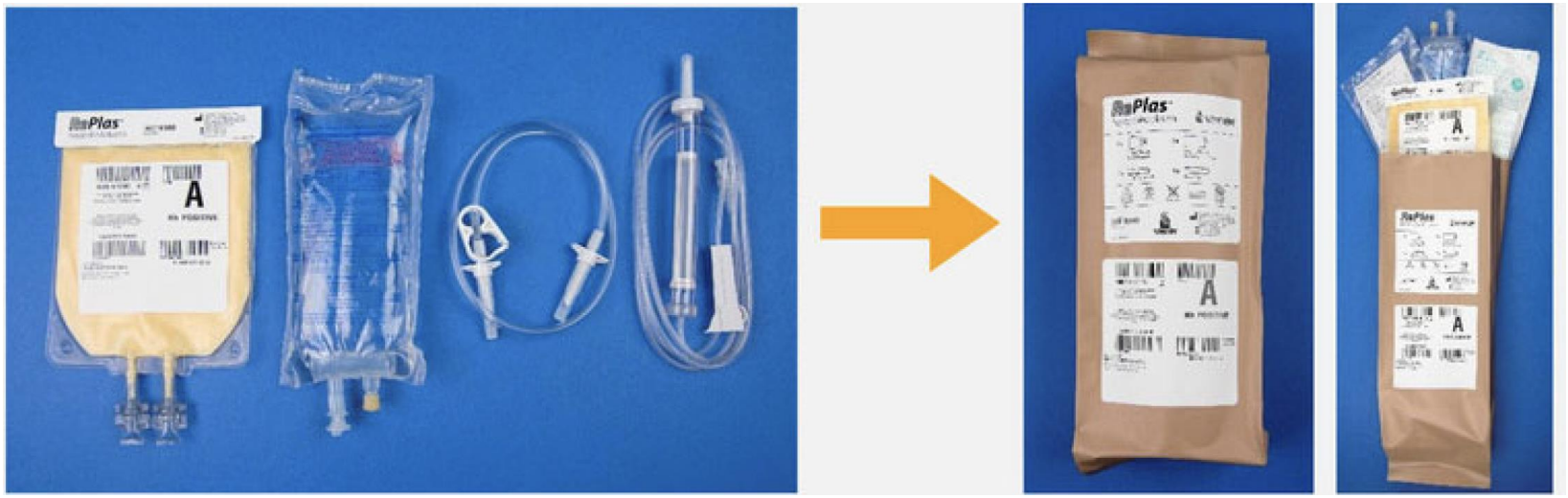
- French, Germans and South Africans produced dried plasma in the 1990's during Desert Storm

- Renewed "modern" effort in to develop dried plasma began again in the US around 2005 with US Army MRMC BAA for dried plasma development

Modern Dried Plasma Products

Non-US	Product	Drying Method	Manufacturing Model	Plasma Source	Pathogen Reduced	Packaging
French	FLyP	Lyophilized	Centralized	Small pools	Yes	Glass
German	LyoPlas N-w	Lyophilized	Centralized	Single-donor	No	Glass
South African	FDP Bioplasma	Lyophilized	Centralized	Large pools	Yes	Glass
Switzerland	OctaphasLG-Lyo	Lyophilized	Centralized	Large pools	Yes	Glass

Modern Dried Plasma Products



US	Product	Drying Method	Manufacturing Model	Plasma Source	Pathogen Reduced	Packaging
Teleflex	EZPLAZ	Lyophilized	Centralized	Single-donor	No	Plastic
Terumo	TFDP	Lyophilized	Decentralized	Small Pools	Yes	Plastic
Velico	FrontlineODP	Spray dried	Decentralized	Single-donor	No	Plastic

Modern Dried Plasma Products

Plasma
Sources: NF, FFP/PF24

Plasma Drying Chamber (PDC)

Veli Dryer

Veli Sealer

Dried Plasma
Unit

US	Product	Drying Method	Manufacturing Model	Plasma Source	Pathogen Reduced	Packaging
Teleflex	EZPLAZ	Lyophilized	Centralized	Single-donor	No	Plastic
Terumo	TFDP	Lyophilized	Decentralized	Small Pools	Yes	Plastic
Velico	FrontlineODP	Spray dried	Decentralized	Single-donor	No	Plastic

Current Dried Plasma Products

Non-US dried plasma

French FLyP

German LyoPlas N-w

South African FDP Bioplasma

Octapharma – OctaplasLG-Lyo

- Glass Bottles
- Lyophilized
- Centralized

US dried plasma

Teleflex EZPLAZ

Terumo TFDP

Velico FrontlineODP

- Plastic
- Lyophilized
- Decentralized

Regulatory

- 2019 Guidance on Development of Dried Plasma Products for Transfusion
  - Initial indication ”where conventional plasma is impractical for use or unavailable”.
  - An expanded indication will be pursued where conventional plasma is available, and will likely require “additional adequate and well-controlled clinical studies would likely be necessary.”
  - Initial indications from the various studies including Velico’s own research, is that reconstituted dried plasma is comparable to conventional plasma products and has similar levels of coagulation factor activities and clotting profiles.

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Research Supporting Prehospital Plasma

- Holcomb, Spinella, Cotton - 1:1:1 for Damage Control Resuscitation (DCR)
- 2013 Holcomb PROMMTT
- 2013 Radwan
- 2015 Holcomb PROPPR
- 2017 Shackelford
- 2016, 2022 Pusateri – Review
- 2019 Zaza – Review
- 2018 Moore HE, Moore EE, COMBAT trial
- 2018 Sperry et. al., PAMPer trial
- 2020 Pusateri – Post hoc analysis of COMBAT and PAMPer
- 2021 Hrebinko – secondary analysis, health economics case

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‘Dried plasma:
An urgent priority for trauma readiness’

The Journal of Trauma and Acute Care Surgery

2023 Aug; 95(2): S4-S6.

Travis M. Polk, MD, FAGS, Jennifer M. Gurney, MD, FAGS, Leslie E. Rigg§, MS, MT, SBB, JeremY. W. Cannon, MD, SM, FAGS, Andrew P. CaP-, MS, MD, PhD, FACP, and Paul A. Friedrichs, MD, FAGS

“As the US military pivots from years of low-intensity counterinsurgency operations to preparation for large-scale combat operations against a near-peer competitor, **the realities of providing medical care to thousands of casualties are sobering.**

Evidence collected during recent conflicts reinforces that **damage-control resuscitation and early hemorrhage control are crucial to survival** for patients with severe injuries. Numerous studies continue to demonstrate the criticality of early lifesaving interventions and the impact of timely and appropriate resuscitation with blood products.”

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PAMPer Study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 26, 2018 VOL. 379 NO. 4

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

J.L. Sperry, F.X. Guyette, J.B. Brown, M.H. Yazer, D.J. Triulzi, B.J. Early-Young, P.W. Adams, B.J. Daley, R.S. Miller, B.G. Harbrecht, J.A. Claridge, H.A. Phelan, W.R. Witham, A.T. Putnam, T.M. Duane, L.H. Alarcon, C.W. Callaway, B.S. Zuckerbraun, M.D. Neal, M.R. Rosengart, R.M. Forsythe, T.R. Billiar, D.M. Yealy, A.B. Peitzman, and M.S. Zenati, for the PAMPer Study Group*

Funded by the U.S. Army Medical Research and Material Command, this was a multi-center study, cluster randomised, phase 3 superiority trial study of 501 patients.

230 patients received plasma while 271 received standard-care resuscitation during air-medical transport.

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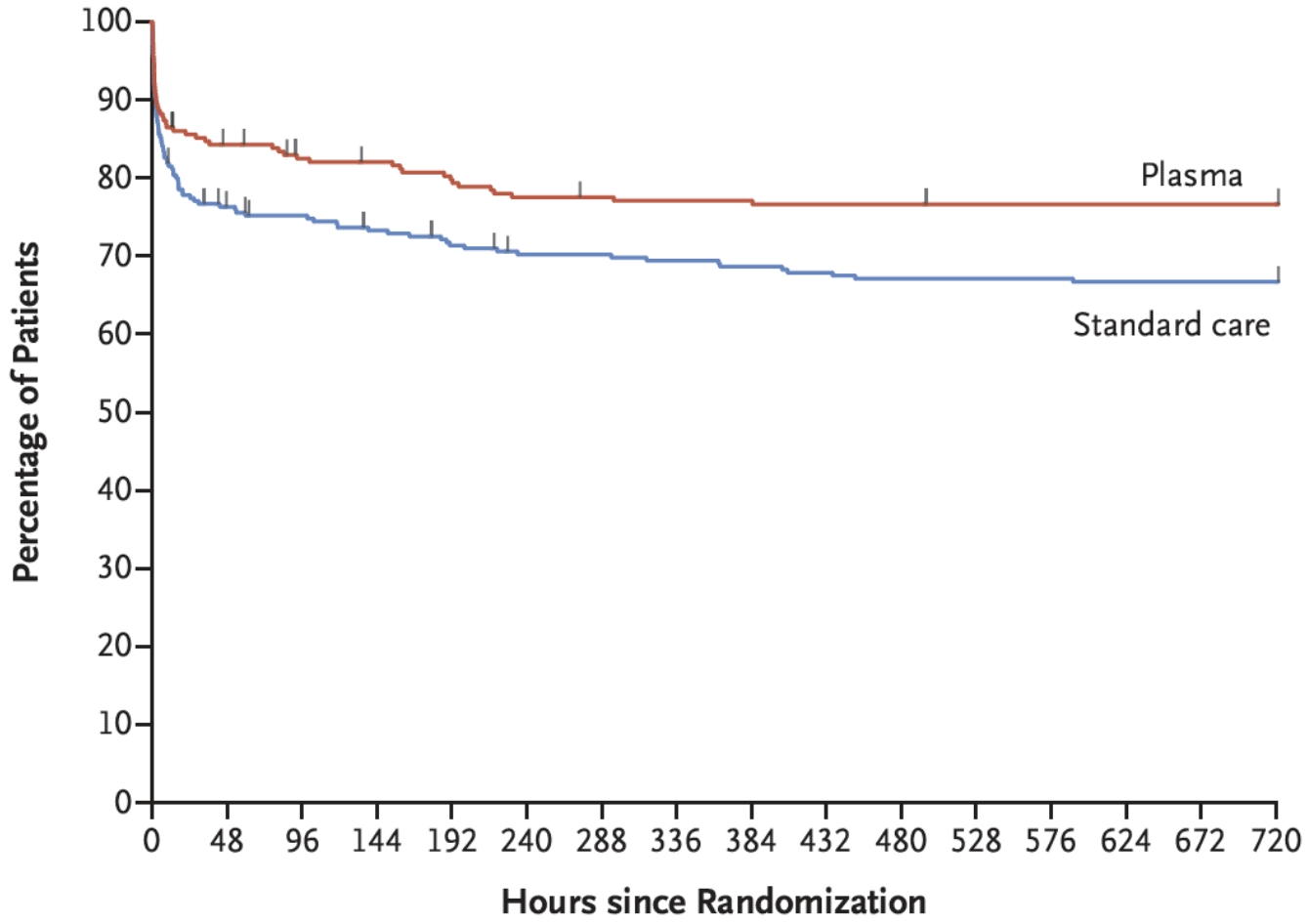
The Case for Plasma First: Prehospital Air Medical Plasma Trial (PAMPer)



No. at Risk							
Plasma	230	183	172	170	169	168	168
Standard care	271	194	181	179	173	172	172

After 30 days, **76.8 percent of the patients who received plasma were still alive,** compared with 67 percent of those who received standard care.

Plasma patients also had lower 24-hour and in-hospital (reduction of 10%) mortality.

Their blood clotted faster, and they received fewer blood components overall than their counterparts who did not get the prehospital plasma.

Sperry, et al : N Engl J Med 2018; 379:315-326 DOI: 10.1056/NEJMoa1802345
Blood plasma during emergency air transport saves lives (medicalxpress.com)

The Case for Plasma First: Prehospital Air Medical Plasma Trial (PAMPer)

"These results have the power to significantly alter trauma resuscitation, and their importance to the trauma community cannot be overstated,"

"This is the first trial in a quarter century to have the potential to alter prehospital care so considerably."

Jason Sperry, M.D., M.P.H., professor in the departments of Surgery and Critical Care Medicine in Pitt's School of Medicine.

Sperry, et al : N Engl J Med 2018; 379:315-326 DOI: 10.1056/NEJMoa1802345
Blood plasma during emergency air transport saves lives (medicalxpress.com)
Medical Xpress - New England Journal of Medicine

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JAMA Surgery | Original Investigation

Evaluating the Cost-effectiveness of Prehospital Plasma Transfusion in Unstable Trauma Patients
A Secondary Analysis of the PAMPer Trial

Katherine A. Hrebinko, MD; Jason L. Sperry, MD, MPH; Francis X. Guyette, MD, MPH; Joshua B. Brown, MD, MSc; Brian J. Daley, MD; Richard S. Miller, MD; Brian G. Harbrecht, MD; Jeffrey A. Claridge, MD; Herb A. Phelan, MD; Matthew D. Neal, MD; Brian S. Zuckerbraun, MD; Mark H. Yazer, MD; Kristina J. Nicholson, MD, MSc

Patients receiving TP required fewer packed red blood cells (4.9 vs 6.9) platelets (0.6 vs 1.2) and plasma (2.3 vs 3.3) transfusions in the first 24 hours post injury, generating an **average transfusion related cost saving of $891.77.**

CONCLUSIONS AND RELEVANCE

Prehospital thawed plasma transfusion for trauma patients in hemorrhagic shock was lifesaving and cost-effective compared with standard care and and its use should become commonplace.

Hrebinko KA, Sperry JL, Guyette FX, et al. Evaluating the Cost-effectiveness of Prehospital Plasma Transfusion in Unstable Trauma Patients: A Secondary Analysis of the PAMPer Trial. *JAMA Surg.* Published online September 22, 2021. doi:10.1001/jamasurg.2021.4529

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The Military Need for Dried Plasma

Future conflicts are likely to include widespread use of artillery and rockets delivering incendiary and thermobaric munitions, resulting in increased numbers of burn casualties, further increasing requirements for plasma.

To meet projected requirements for a future conflict, the allied armies need to develop enhanced, independent and locally self-sustaining blood product solutions.

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The Military Need for Dried Plasma

Logistics challenges for blood products in austere locations

Limited supplies of liquid blood products particularly in the early and most intense phases of conflict.

The use of "walking blood banks;' is a rapid response strategy built on the concept of pre-qualified, emergency blood donors to assist in meeting surge needs.

The Military Need for Dried Plasma

Given the benefits of early plasma resuscitation and the current state of technology, **dried plasma would seem the most proximate, logistically superior and feasible solution.**

Proposed use cases for dried plasma:

1. Immediate resuscitation at the point of injury, until other blood products are available;

2. Initial resuscitation along with red blood cells and other components such as cold-stored platelets;

3. Replacement for liquid or frozen plasma throughout prehospital and early/acute in-hospital continuum of care;

4. Initial resuscitation of burn injuries and related shock.

The Journal of Trauma and Acute Care Surgery

'Dried plasma: An urgent priority for trauma readiness'

2023 Aug; 95(2): S4-S6.

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"As an immediate resuscitation capability for the battlefield that can be safely stored at room temperature, **dried plasma should be available along the entire continuum of combat casualty care.**

This means that the product should be **issued to all field medics and corpsmen, as well as carried on all en route care platforms, including ground ambulances**. "

The Journal of Trauma and Acute Care Surgery

'Dried plasma: An urgent priority for trauma readiness'

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How many units of dried plasma were produced in the US & shipped overseas during World War II?

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Over 10,000,000 Units of Plasma

How many units of dried plasma would a large-scale conflict require today?

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What if …

every military **medic and all military emergency response vehicles, could carry a supply of dried plasma**, that could be **quickly reconstituted and used at a scene to save a life?**

Rapid Rehydration

& Scalability

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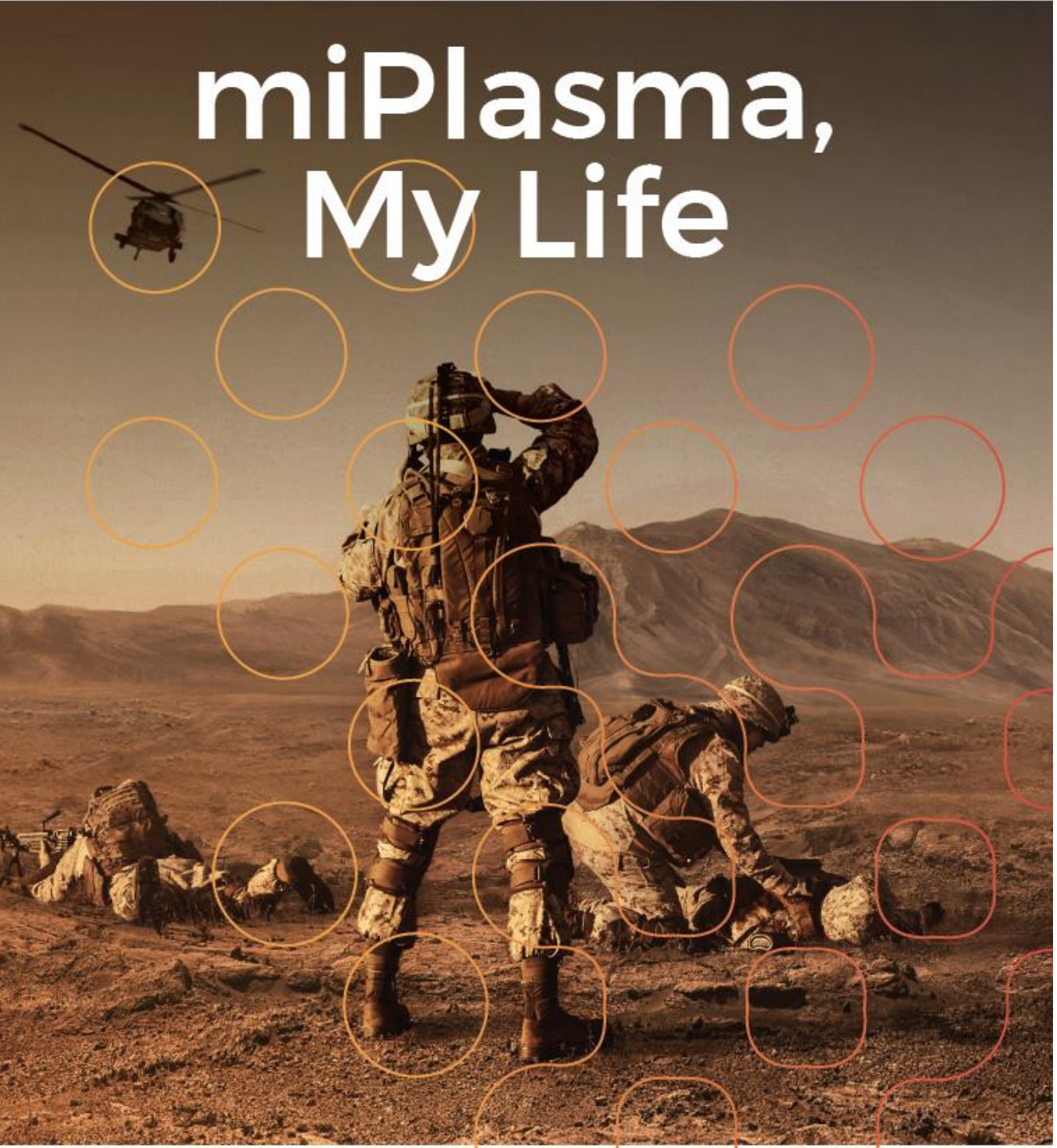

miPlasma
POWERED BY VELICO

What if …

every soldier, could **carry their own autologous supply of dried plasma** in their backpack?

Decentralised

Sovereign Self Sufficiency

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Thank you