

Establishing Prehospital Transfusion with Airlift Northwest and Harborview
Medical Center

Max J Louzon

A thesis

submitted in partial fulfillment of the
requirements for the degree of

Master of Science

University of Washington

2017

Committee:

John R Hess, Chair

Ryan A Metcalf

Monica B Pagano

Program Authorized to Offer Degree:

Department of Laboratory Medicine

© Copyright 2017

Max J Louzon

University of Washington

Abstract

Establishing Prehospital Transfusion with Airlift Northwest and Harborview Medical Center

Max J Louzon

Chair of the Supervisory Committee:
Dr. John R Hess
Laboratory Medicine

Harborview Medical Center (HMC) routinely received patients transferred from outside facilities. These patients would be supported with blood products sent by the transferring facility, and on arrival these products would be discarded due to unvalidated shipping methods. This process put a strain on local blood suppliers and small transfusion services. The local aero-medical evacuation provider, Airlift Northwest (ALNW), also had no blood products to support trauma patients being transferred from the scene of the injury. These patients only began receiving transfusion support upon arrival at HMC.

HMC partnered with ALNW to begin supplying blood products to support the transfer of patients. This process would entail validating a system to ensure the blood products would be kept at a storage temperature between 1-6°C. Since ALNW had six air bases throughout Washington and Alaska, the Credo Series 4 EMT cooler was validated to store the blood products for up to seven days to minimize transport between HMC and ALNW. To ensure an appropriate temperature was maintained in the cooler, a temperature recorder was placed in the

cooler along with the blood products.

HMC also used new blood products, low titer plasma and liquid plasma, to support prehospital transfusion. Low titer plasma (LTP) was defined as blood type A plasma with a titer of anti-B as $\leq 1:200$. LTP was occasionally used in place of the traditional universal type AB plasma due to inventory control purposes. Typically HMC stocks thawed plasma that expires five days after thawing. To support ALNW holding blood products for seven days, liquid plasma was used as it expires 26 days after donation.

All staff at HMC and ALNW were trained in handling the coolers as well as the applicable usage procedures. HMC began supplying blood products to ALNW in May 2015 and since then 24 patients have been transfused. Originally Boeing Field was the only site supported by HMC allowing for quick resolution of the problems encountered with the coolers, temperature recorders, and blood products. Since May 2015, the program has expanded to Olympia with plans to support the other air bases. The program for prehospital transfusion has also gained the interest of the organ transplant team and a separate validation will be taking place.

Table of Contents

1 Introduction	9
2 Literature Review	11
3 Background	17
4 Materials and Methods	20
4.1 Community Resources	20
4.2 Blood Products	21
4.3 Coolers	23
4.3.1 Credo Series 4 EMT Validation	23
4.3.2 Preconditioning	24
4.3.3 Installation Qualification	24
4.3.4 Operational Qualification	25
4.3.5 Performance Qualification	26
4.3.6 Validation Results	32
4.4 Pyxis Refrigerator	32
4.5 Removable Lock	32
4.6 Marathon microDL	33
5 Results	35
5.1 Established Prehospital Transfusion Process	35
5.2 Education	36
5.2.1 HMC TSL Initial Training	36
5.2.2 ALNW Training	38
5.3 Initiating Prehospital Transfusions	39
5.4 Maintenance of blood storage temperature	42
5.5 Data logger usage	47

5.6 Fresh thawed plasma	48
5.7 Inappropriate use of liquid plasma	49
5.8 Wear and tear of credo coolers	52
6 Discussion	54
6.1 Expansion of Program	54
6.2 Transplant support	56
7 Conclusion	57
7 Bibliography	59

List of Figures

Figure 1 - Results from the operational qualification.	27
Figure 2 - Results from the performance qualification: scenario one.	28
Figure 3 - Results from the performance qualification: scenario two.	29
Figure 4 - Results of the performance qualification: scenario three.	30
Figure 5 - Results of the performance qualification: scenario four.	31
Figure 6 - results of the Performance Qualification Scenario Five.	32
Figure 7 - A lock before use on the left and an in-use lock on the right.	34
Figure 8 - Patients transfused by ALNW over time.	41
Figure 9 - Relative usage of RBC and plasma products by ALNW.	42
Figure 10 - An acceptable temperature recording taken over seven days.	45
Figure 11 - A temperature recording with a larger tail at the beginning.	46
Figure 12 - An unacceptable temperature recording.	47
Figure 13 - A data logger both from the front and on its side.	48
Figure 14 - Impact freshly thawed plasma has on the internal temperature of the Credo cooler.	50
Figure 15 - Liquid plasma on the left and a thawed plasma on the right.	52
Figure 16 - Example of LIS warning	53
Figure 17 - Example of a tear in the Credo cooler's VIP.	54

Acknowledgements

I would like to thank Dr. John Hess, Dr. Ryan Metcalf, and Dr. Monica Pagano for all of your help and encouragement with this project. Dr. Lynn Stansbury, this document only exists because of your patience and mentorship. Nina Sen, Erin Tuott, and Roxann Gary your work on this entire process has been invaluable. I'd also like to thank all of the staff at Harborview Medical Center Transfusion Service Laboratory for their hard work and assistance. Finally, I need to think Heather Eggleston and Brenda Hayden for their encouragement and support.

1 Introduction

In 2014 a patient in rural Alaska was injured and had to be medically evacuated to the nearest level one trauma facility, Harborview Medical Center (HMC) in Seattle, WA about 1,400km away. To support the patient in route, the transferring hospital sent two group O negative (O neg) red blood cells (RBCs) with the patient. These products, combined with what the patient already received while being stabilized, exhausted the transferring facility's blood supply. Once the patient arrived at HMC those two O neg RBCs were discarded as there was no way to guarantee they were still acceptable for transfusion. When the transferring facility was notified of this, they wanted to know if there was a way to return the supplied blood to them since without those products, they would be left with none for several days until a new shipment could be arranged.

Situations like this to this were repeated regularly at HMC. Blood products sent by transferring facilities were being discarded because there was no way to ensure the purity, potency, or safety of the blood products when they were received. However, the facilities had to transfer patients with blood products because no other blood products would be available while the patient was in transit and very often these critically ill patients would require transfusion during transport in order to survive. This informal process of patient support arose without coordination between the involved parties which included the transferring hospitals, Airlift Northwest (ALNW), and Harborview Medical Center. While this process was aimed at providing the best possible care for each patient, it was plagued with inefficiencies that led to product wastage.

In addition to increased regional product wastage, patients transported directly from the scene of an accident had no blood products available to them. These patients only received transfusion support after arriving at a medical facility. The lack of blood products to support prehospital transfusion in addition to the loss of blood products sent with transferred patients presented a need for an independent blood supply during aeromedical evacuations.

2 Literature Review

Blood has held a place in the practice of medicine since ancient times. Hippocrates believed blood was one of the four humors that made up all living things and imbalances in the humors should be rectified via methods like bloodletting.¹ Others would consume blood in an attempt to gain strength and bravery leading to the Roman Emperor Septimus Severus banning drinking the blood of dying gladiators in 193 AD.²

The first blood transfusion is often cited as that of Pope Innocent VIII who fell ill in 1492 and received blood from three 10 year old boys.² The Pope never recovered and the donors died of blood loss. This account though may be based on mistranslations and the Pope may have simply consumed the blood of the boys. In February 1665, blood was transfused successfully between two dogs by Richard Lower leading the way for human transfusion.³ Dr. Jean Denis performed the first human transfusion in 1667, transfusing lamb blood into a 15 year old boy. During the transfusion, the boy felt "...a very great heat along his arm," but otherwise felt improved.² Overall blood transfusion though remained a dangerous procedure and fell into disuse until the 1800s.

James Blundell in 1818 noted the dangers of transfusing blood from different species and began transfusing human blood into patients.⁴ While patients reported negative side effects such as fever, backache, and passing "dark urine", the transfusions were well tolerated by at least four of the ten patients infused. Continuing through the 1800s and early 1900s, developments were made in anticoagulants, infusion protocols, blood sources which all led to the development of viable transfusion medicine starting in the 1900s.

Karl Landsteiner's discovery of the ABO blood group system in 1901 marked the beginning of understanding the immunologic underpinnings of blood transfusion. Landsteiner's original paper concludes with the author stating the reaction patterns between the blood groups may explain the previously noted reactions to blood transfusion.⁵ In his original paper, he also noted that none of the individuals tested at serum that reacted with their own cells, one of the first descriptions of self-tolerance.

At first, blood transfusions were direct transfusions: the donors and recipients were joined either by stitching blood vessels together or by using needles. In 1907, early compatibility testing was done at Mount Sinai Hospital in New York when donors and recipients were matched by blood type.⁶ Indirect transfusions, collecting donated blood for transfusion later, were made possible by using citrate as an anticoagulant and gained acceptance in 1915.

During World War I (WWI), the first blood bank was built by Captain Oswald Hope Robertson.⁷ He arranged for blood to be collected from type O donors (who were usually lightly wounded soldiers), stored in glass bottles, transported to the battlefield, and transfused to patients wounded at the front lines. These early transfusions to injured soldiers became the basis for trauma response in later years.

The first aero-medical evacuations have been attributed to the French in September 1870, when King William I of Prussia laid siege to Paris for four months and during that time 160 patients were airlifted out of the city using observation balloons. While this anecdote has ultimately proven false⁸, the use of aero-medical evacuation began gaining traction in military circles starting in the early 20th century. The first documented proposal for transporting wounded patients via air transport was in 1895 by Charles Richet, and in November 1915

became a reality when 13 injured members of the French Expeditionary Force were taken medically evacuated using a Farman F-Vb fighter aircraft.⁹ Aero-medical evacuations were increasingly implemented in World War II, and, with the availability and increased maneuverability of rotary-wing aircraft on August 10, 1950 rotary-wing aircraft were authorized for use during the Korean War. Then starting in 1965, rotary-wing aircrafts began being used to provide medical transport to civilians in the Philadelphia area and in 1968 was a key feature in the opening of the world's first level I trauma center, the University of Maryland's Baltimore Shock Trauma.¹⁰ By 1975 there were 35 civilian rotary-wing ambulance systems and in 2016 there were 302 air medical services within the United States which use either rotary and fixed-wing aircrafts.¹¹

Current use of rotary and fixed-wing aircraft for medical transport of patients is widespread throughout the United States, however the stocking of blood products on aeromedical transports is variable. A survey in 2016 of 235 helicopter emergency medical services (HEMS) showed that only 25.3% independently carry blood products.¹² Of the HEMS that carried blood products 59.3% carried blood on all transports. The remaining transports only provided blood products for select situations. When transporting trauma patients from the field, blood was used 4.9% of the time while interfacility transports used blood on 6.2% of the time. HEMS that serviced less population dense areas were also more likely to carry blood compared to HEMS that focused on urban areas.

The lack of HEMS providing blood is understandable when factors such as blood storage, staff training, and blood product selection are considered. These hurdles are often enough to deter most aero-medical services from stocking blood. Instead, patients are supported with other

forms of fluid resuscitation which tend to focus on maintaining volume and blood pressure at the expense of coagulation capacity. Roughly a third of mortality related to traumas is due to hemorrhage, and of these, up to 56% occur before arriving at the hospital.¹³ The use of blood products during the prehospital period is correlated with improved acid-base status, increased blood pressure, decreased use of blood products over 24 hours, and improved early outcomes.^{14 15}

The type of blood products that need to be provided for early interventions is an area of active debate and research. Some facilities are only offering pRBCs as part of their prehospital transfusion program while others are offering a mix of pRBCs and plasma products. The importance of plasma in particular has been studied when treating trauma patients due to its role in reversing coagulopathy.¹⁶ Plasma typically is made available as thawed plasma which has a shelf life of five days and requires preparation making it unsuitable for immediate use. Liquid plasma requires less preparation and has a longer shelf life making it a more feasible product but its availability is dictated by the blood supplier. Transfusing blood products in a 1:1 ratio has been shown to benefit patients undergoing massive transfusion.¹⁷ Problems do exist for prehospital transfusion of plasma though. Blood group incompatibility is a risk if non group AB plasma is being provided and issues of hemovigilance remain a concern.¹⁸ Anti-A and anti-B present in the plasma of donor plasma has been linked to hemolytic reactions in recipients with the corresponding antigens. The donors of the products that led to the transfusion reaction typically have titers of the anti-A or anti-B as >100 at saline and >400 at antiglobulin.¹⁹ One documented case of a hemolytic transfusion reaction was traced back to a unit of group O whole blood with an anti-A IgG titer of 32,768. The recipient experienced oliguria and hemolysis for two days before recovering.¹⁹ When donors have lower titers of anti-A and/or anti-B, the

transfusions are typically well tolerated. The Special Forces of the Swedish Armed Forces will accept group O donors as “universal donors” if their anti-A and anti-B have IgM titers ≤ 100 and IgG titers ≤ 400 .

In addition to the typically available blood products, researchers have examined the use of more novel blood products with aero-medical transport patients such as freeze dried plasma, whole blood, and cold storage platelets. Freeze dried plasma is currently an EU approved product and has a number of logistical advantages over thawed or liquid plasma. When it was tested as part of a HEMS program in Norway, it was easily integrated into the response process and no adverse reactions to its use were noted.²⁰ Whole blood is also being examined as an alternative to the current practice of component therapy. The military has begun using whole blood as part of massive transfusion protocols and its use may improve patient 30-day survival.²¹ Whole blood has the advantage during trauma resuscitation of providing a physiologic ratio of all three major blood components, RBCs, plasma, and platelets while minimizing the recipient’s donor exposure. Cold storage platelets are also being used as part of the prehospital transfusion protocol for some HEMS programs.²² Cold storage platelets are a combined dose of platelets and plasma and when available allow for further treatment of coagulopathy. However, this product has a shelf life of three days leading to increased risk of the product being wasted.

Implementing blood product use leads to certain logistical challenges for HEMS providers. Blood products can be stored in a refrigerator at the air base and when needed, be moved to a validated cooler and brought on the flight.²² Another option is for blood banks to supply the products in a validated cooler on demand but this process requires a short turnaround time between the request and the provision of blood. Wastage related to these programs can be

minimized by using fresh blood products that are rotated regularly. This allows for blood products that are older to be returned to the blood bank so they may be transfused. These processes also hinge on appropriate validation of the coolers in order to guarantee the storage requirements of the blood products are met and products are not wasted. Interestingly, product wastage does not appear to be much of a concern in published literature. ⁸

3 Background

Prior to the development of a standardized process the availability of blood products for patients being transferred by ALNW was variable. Three conditions needed to be met in order for blood products to be made available: 1) patients had to be coming from a transferring facility; 2) the transferring facility had to have blood products to spare; and 3) the transferring facility had to have some way to ship the blood products.

Taken together, the following clinical and systems problems had to be resolved if blood products were to be made available for all patients who might need them during aeromedical evacuation. These issues included:

- Prehospital transfusion was not available for patients being transferred from the field. Patients involved in traumas leading to hemorrhage had no prehospital transfusion support leading to increased urgency for transfusion upon arriving at HMC ED. This would lead to delays in drawing samples for patient testing leading to increased reliance on emergency release blood products;
- Availability of blood products was inconsistent with regards to when blood products would be supplied and which blood products would be available. Transferring facilities did not have uniform processes for supporting patient transfer; some facilities could not offer any blood products due to a small on site inventory, while others could offer only pRBCs or only plasma;
- Variations in the size and weight of provided blood storage containers led to difficulties with the size and weight requirements with the rotary and fixed-wing aircrafts used with aeromedical evacuation. Space on aircrafts used for patient transfer is limited, and the

blood storage containers at a transferring facility may be in excess of what can be accommodated by ALNW or what is required to adequately store the provided blood products;

- Inability to track transportation temperatures led to blood wastage. Blood products must be transported at a temperature between 1-10°C and this temperature must be demonstrated for each transported product either through temperature recorders or process validation. If the appropriate temperature range cannot be proven, the blood products must be discarded as their safety and potency is no longer ensured;
- Transfusion reaction work ups were complicated by multiple sources of blood leading to issues with traceability and hemovigilance. Transfusion reactions and product recalls can occur long after product transfusion, and the following investigation requires accounting for all impacted products. If blood products were transfused by an outside facility before transfer, patient notification and follow up can be delayed, while if implicated blood products were discarded, the transferring facility could spend time attempting patient follow up when it is not warranted.

In response to a clear community need, the medical director of HMC TSL approached ALNW to begin developing a program to support prehospital transfusion. HMC TSL had been receiving feedback from blood suppliers and community transfusion services requesting blood support for transferring patients. It was also known that other aeromedical evacuation providers, such as University of Maryland's Shock Trauma Center, provide blood transfusion when transporting patients.²³ This allows for a more varied ability to provide care to critically injured patients. Developing this program in partnership with HMC TSL would allow ALNW to adopt

policies and procedures based on a reliable source of blood products. After consideration, ALNW agreed to developing a system to support prehospital transfusion.

As ALNW had no process currently in place to provide their own blood products, an entire system had to be established. This would need to include deciding which blood products would be offered, how the blood products would be stored and tracked, how temperatures would be maintained, and finally, how best to involve, train and support both ALNW and TSL team members in the process.

4 Materials and Methods

Building a system of support for prehospital transfusion required the review and validation of necessary resources. The community resources were already in place to provide patient care but policies and procedures would need to be revised to incorporate prehospital transfusion. Blood products would need to be assessed for use during emergency procedures as well as their viability within a off site cooler. The cooler required validation to ensure the products would remain at blood storage temperature between 1-6°C. Temperature recorders were validated and used to verify storage temperature of blood was maintained.

4.1 Community Resources

Harborview Medical Center (HMC) is a 400 bed hospital based in Seattle, Washington that specializes in emergency medicine, HIV/AIDS care, neuroscience, orthopedics, burns, psychiatric and psychological care²⁴. King County founded and owns HMC while the University of Washington (UW) provides the staffing and management. HMC is the only level 1 trauma and burn facility for Washington, Alaska, Montana, and Idaho; this means that HMC is serving as the trauma center for 25% of the land mass of the United States, and patients are often being transported long distances with serious injuries. Over the course of a year HMC sees about 64,500 patients in the emergency department and has about 17,000 admissions.

HMC has an onsite transfusion service laboratory (TSL) that opened in 2011. Before that point, all transfusion testing was performed by an outside laboratory. In 2016, HMC TSL processed approximately 14,000 patient specimens and transfused 14,471 blood products²⁵. Testing performed includes blood typing, antibody screens, antibody identification, red blood cell (RBC) phenotyping, direct antiglobulin tests, elutions, transfusion reaction investigations,

and antibody titers. As of 2016, the TSL has 30 staff members including medical directors, management, and testing staff. The HMC TSL is accredited by CAP and AABB.

HMC TSL uses Sunquest 7.2 as its laboratory information system (LIS). The LIS is used to record specimen and blood product testing as well as track blood product location. Using the LIS, HMC TSL is able to track which products are currently with ALNW as well as record product inspections when the the units are returned.

Airlift Northwest (ALNW) was founded in 1982 and has provided transport for over 100,000 critically ill patients, adults and pediatric, in Washington, Alaska, Montana, and Idaho.²⁶ Their fleet is comprised of five rotary-wing aircraft and six fixed-wing aircrafts that are distributed across five bases in Washington and Alaska. All flights have two nurses in addition to provide care and a medical director is available remotely. ALNW is accredited by the Commission on Accreditation of Medical Transport Services (CAMTS).

CAMTS was founded in 1990 and provides accreditation to 183 medical transport systems in the United States as well as internationally.²⁷ They provide a set of standards for their members which are revised every 2-3 years while also providing continuing education and training workshops. These standards include processes for infection control: risk analysis, rotor wing operations, fixed wing operations, staff training, equipment maintenance, and pilot qualifications. Some states, including Washington, have adopted regulations requiring CAMTS accreditation for air ambulance services, otherwise accreditation is voluntary.²⁸

4.2 Blood Products

All blood products used by HMC TSL are purchased from FDA licensed blood donation facilities in full compliance with all regulations.

Packed red blood cells (pRBC) are typically between 300-400mLs with a hematocrit between 55-65%. Additive solutions, either AS-1 or AS-3, are included with the pRBCs to increase shelf life. All pRBCs are leukoreduced. Irradiated pRBCs are not typically provided due to the decreased shelf life of the product. The ISBT component codes of the pRBCs are E0336 or E0382. Transfusion with pRBCs is indicated in patients with a critical deficit in oxygen carrying capacity.²⁹ O negative pRBCs are provided to ensure ABO compatibility with all patients and to minimize the risk of D alloimmunization.

Liquid plasma is derived from whole blood donation and has the red and white cells removed via centrifugation. The product is never frozen and may contain viable lymphocytes which could potentially lead to graft versus host disease but which is less of an issue for the majority of patients who need blood product support during aeromedical evacuation. Liquid plasma was originally approved for use up to 26 days after collection, but HMC TSL implemented a policy to only use it up to 18 days after collection due to limited half life of clotting factors. Liquid plasma and thawed plasma show little difference in clotting factors up to seven days of storage but after that show decreased levels of factors II, V, VII, and protein S.³⁰ Indications for liquid plasma include replacing plasma proteins and coagulation factors during massive transfusion and trauma protocols. Either AB or low titer A liquid plasma was provided. Low titer was defined by the collection facility as having a titer of anti-B as less than 1:200.

Due to inventory management concerns, thawed plasma was also used. Thawed plasma could be plasma frozen within 8 hours after collection (fresh frozen plasma) or within 24 hours after collection. After thawing both products were available for up to five days. Thawed plasma is considered acellular and is safe for patients at risk for graft versus host disease. The

indications for giving thawed plasma were the same as for liquid plasma and the same blood types were provided.

4.3 Coolers

To keep the blood products at an appropriate temperature, Credo Medic Pack Series 4 EMT coolers were used. The coolers had an outer dimension of 234.9 x 209.5 x 203.2 mm with a weight of 3.3 kg. They had an internal volume of 2L, sufficient to hold 2 pRBCs and 2 plasma units. The coolers were composed of three parts: an internal thermal container filled with heavy water (TIC), a vacuum pack container (VIP), and an exterior carrying container. The internal thermal container would be frozen before use and as it thawed would maintain a temperature around the melting point of heavy water, 3.82°C. The cooler was originally certified to maintain a temperature between 2-8°C for up to 48 hours.³¹ The Credo Medic Pack Series 4 EMT's small size and weight make it ideal for transport. Its internal use of heavy water to maintain temperature also allows for prolonged storage time of blood products.

4.3.1 Credo Series 4 EMT Validation

ALNW provides services from six airbases throughout the Pacific Northwest, and none of which are directly connected to a hospital in which blood products could be immediately retrieved. Instead, the blood products needed to be stored at the airbase in a monitored refrigerator, and they would then be retrieved when needed. In order to provide this level of service, the coolers used for blood storage needed to be validated to ensure:

- They could contain the necessary supplies. These would include blood products, necessary documentation, and a temperature recorder.

- They could maintain a temperature between 1-6°C for a prolonged period outside of HMC TSL. Blood product storage has strict temperature requirements and for products to be brought back into HMC TSL's inventory after being issued to ALNW, these temperatures would need to be maintained.
- They would be able to maintain temperature during flights in a variety of situations. This would include prolonged flight times and flights occurring during a variety of weather conditions.

4.3.2 Preconditioning

Before use the coolers had to be preconditioned. This involved placing the VIP in a $\leq 18^{\circ}\text{C}$ for at least eight hours. Following that, the VIP had to be left at room temperature for 25 minutes before it could be packed to allow the heavy water within the VIP to begin melting. This step always occurred before the cooler was used.

4.3.3 Installation Qualification

Before using the coolers, the coolers were examined for any rips, tears, or cracks that could interfere with use. At this point they were also assigned a unique identifier that was placed on all components of the cooler. The coolers were also tested to ensure they could contain the two pRBCs and two plasma products as well as the associated paperwork. In addition, a Marathon MicroDL temperature recorder was kept with the blood products to monitor internal storage temperature of the cooler.

4.3.4 Operational Qualification

The initial qualification procedure was designed to determine if the cooler could be stored for five days in a refrigerator, be taken on a mock flight, and would maintain a blood storage temperature between 1-6°C for the entire duration.

On day zero, the cooler was packed appropriately with two previously discarded pRBCs, two previously discarded plasma units, and a temperature recorder. The packed cooler was then stored in the refrigerator for five days. On the sixth day, the cooler was removed from the refrigerator and left at room temperature for eight hours. After this it was placed back in the refrigerator. On day seven the temperature recorder was analyzed. See Figure 1 for a graph of the results.

Analysis of the results showed the cooler maintained a temperature between 1-6°C for the week the cooler was packed. The temperature did rise when the cooler was brought to room temperature but it never exceeded 6°C and when the cooler was returned to the refrigerator following the mock run, the internal temperature began to decrease.

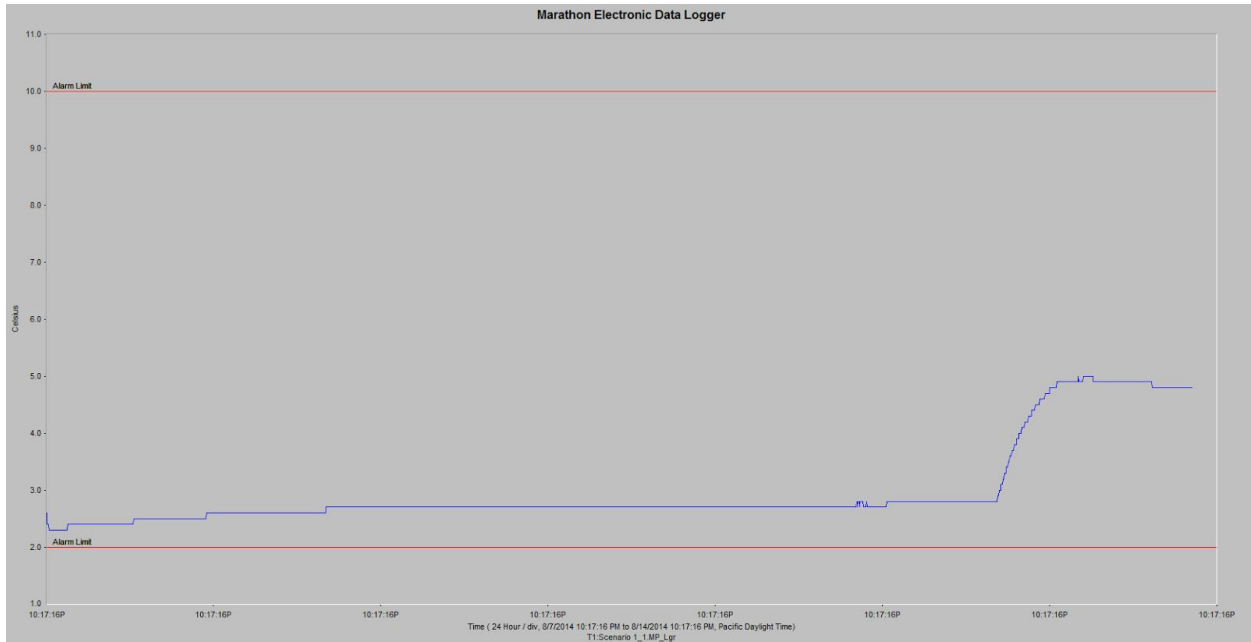


Figure 1 - Results from the operational qualification.

The temperature recording is graphed in blue; the upper limit of 10°C and lower limit of 2°C are marked in red. The cooler maintains a temperature of about 2.5°C until it is placed at room temperature. At that point the temperature rises steeply to about 5°C where it plateaus.

4.3.5 Performance Qualification

To assess the performance qualification the cooler was run through five different scenarios to test its ability to maintain appropriate blood storage temperatures under a variety of conditions.

Performance Qualification - Scenario One

Scenario One was designed to test the cooler’s ability to maintain an appropriate temperature on multiple mock runs.

On day zero, the cooler was packaged appropriately and stored in the refrigerator. On days three and six, the cooler was removed from the refrigerator and left at room temperature for six hours. At the end of this six hour period, the cooler was placed in the refrigerator. On the

seventh day, the temperature recorder was removed and analyzed. See Figure 2 for a graph of the internal temperature recording of the cooler.

Scenario one demonstrated two temperature rises correlated with removal of the cooler from the refrigerator. Internal temperatures were again halted when the cooler was placed back in the refrigerator and to some degree even reversed. Multiple mock runs did not endanger the blood products and the products would be safe for return back into general inventory at HMC TSL.

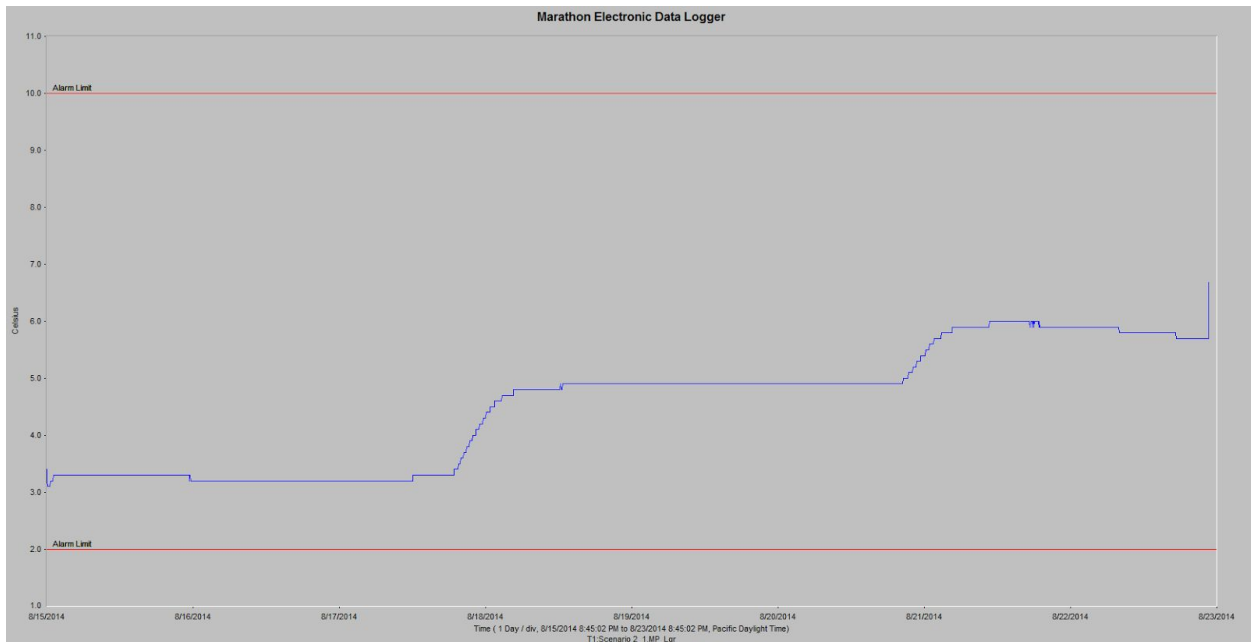


Figure 2 - Results from the performance qualification: scenario one.

The temperature recording, in blue, shows two rises in temperature which correlate to the times the cooler was brought to room temperature. After both mock runs, the temperature stabilized or lowered.

Performance Qualification - Scenario Two

Scenario two tested the ability of the cooler to maintain temperature during a protracted, 48 hour run.

On day zero, the cooler was packed appropriately and stored in the refrigerator for four days. On the fifth day the cooler was removed from the refrigerator and left at room temperature for 48 hours. After this time period, the temperature recorder was removed and analyzed. See Figure 3 for a graph of the temperature recording.

The cooler being left outside of the refrigerator for 48 hours pushed the internal temperature to just below 6°C. Repeated use of the cooler after a longer run could endanger the blood products by pushing the internal temperature above 6°C.

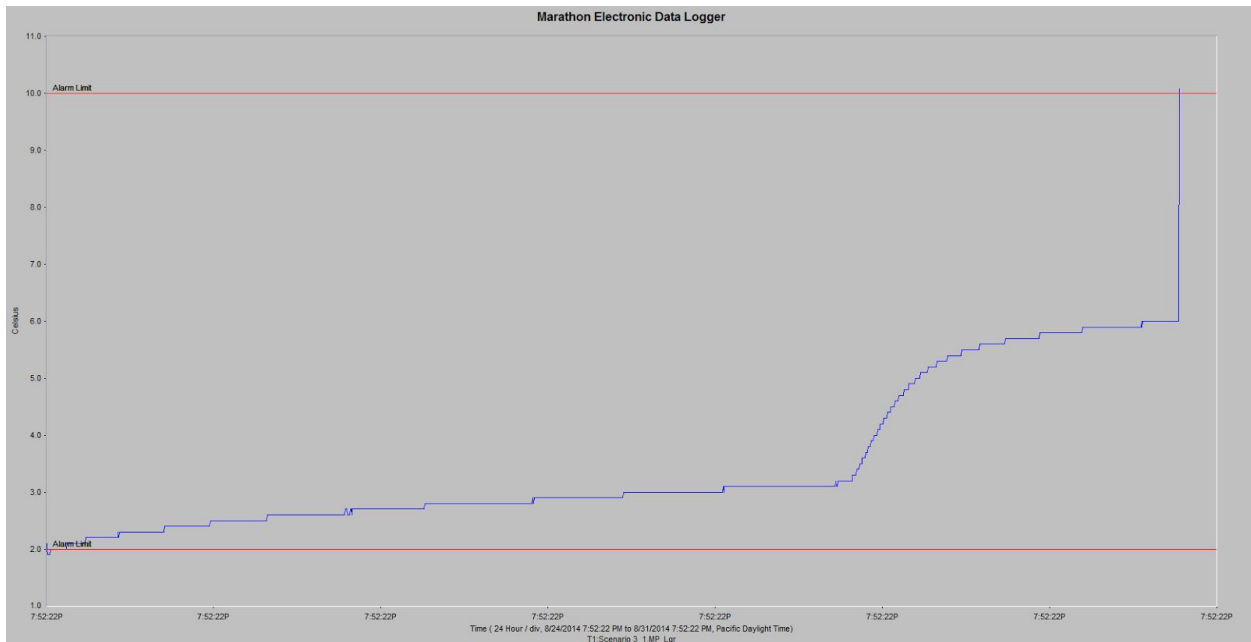


Figure 3 - Results from the performance qualification: scenario two.

The extended 48 hour run ended with the internal temperature just under 6°C, but it was never exceeded. The temperature spike at the very end of the recording is an artifact from unpacking the cooler and handling the temperature recorder.

Performance Qualification - Scenario Three

If the coolers were going to be at the airbase for an extended period of time, the coolers were tested to ensure they would be capable of going on runs a majority of the days they were there.

On day zero, the coolers were packed appropriately and stored in the refrigerator. On days two, three, four, five, and six, the coolers were removed from the refrigerator and left at room temperature for eight hours and then returned to the refrigerator. At day seven, the temperature recorder was removed and analyzed. Figure 4 shows a graph of the temperature recording.

Compared to scenario two, shorter runs appeared to have a lesser effect on the internal temperature of the coolers. The intermittent refrigerator of the coolers may have provided an insulating effect and allowed for an acceptable internal temperature to be maintained.

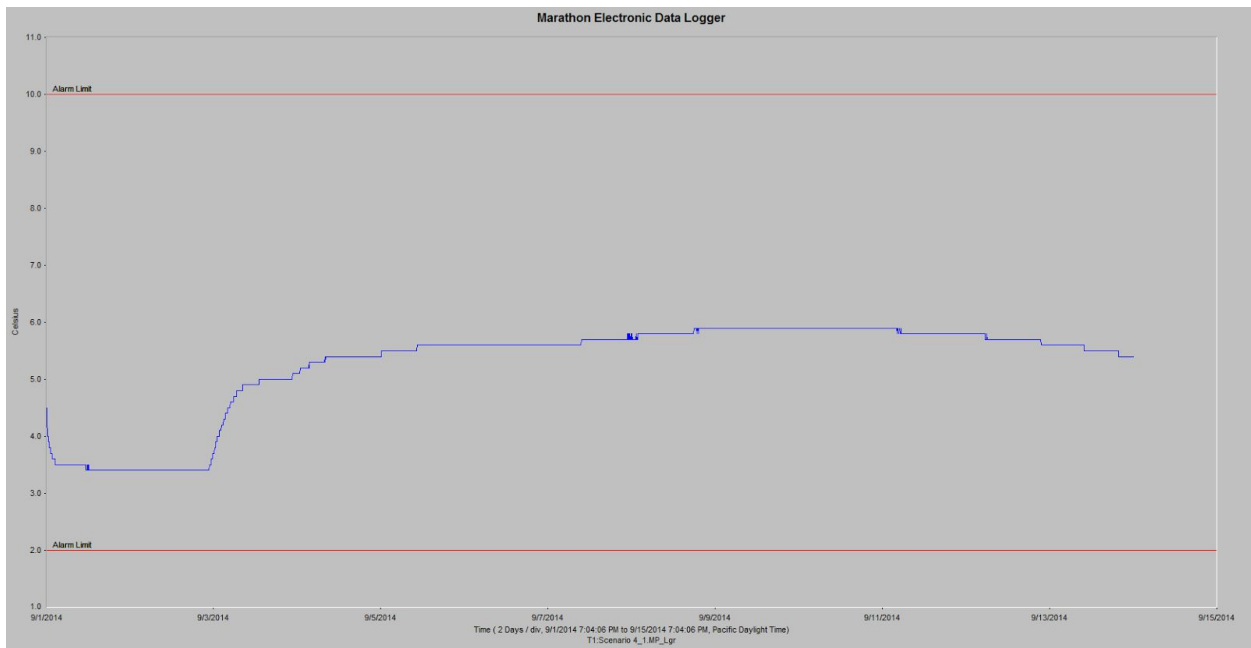


Figure 4 - Results of the performance qualification: scenario three.

Following the initial rise in temperature associated with the first mock run, the temperature stabilized at around 5.5°C for the remaining time. It was again noted that over time, the internal temperature of the cooler began to lower towards the end of the week.

Performance Qualification - Scenario Four

Up until this point, all the mock runs involved using room temperature as a surrogate for the temperature of an ALNW flight. This scenario was designed to test the cooler's ability to withstand higher temperatures and still maintain an appropriate blood storage temperature.

On day zero, the cooler was packed appropriately and stored in the refrigerator for 6 days. On the sixth day, the cooler was placed in a microbiology incubator at 37°C and stored for 24 hours. At the end of this period, the cooler was unpacked the data were retrieved and analyzed. Figure 5 shows the internal temperature recording of the cooler.

A microbiology incubator set to 37°C was used to simulate an extreme temperature in Seattle, WA, but one in which the cooler may be exposed. The cooler was able to maintain an acceptable temperature during the 24 hours it was in the incubator even after being stored for seven days in a refrigerator which began to illustrate how the coolers may be best used in order to preserve the blood products.

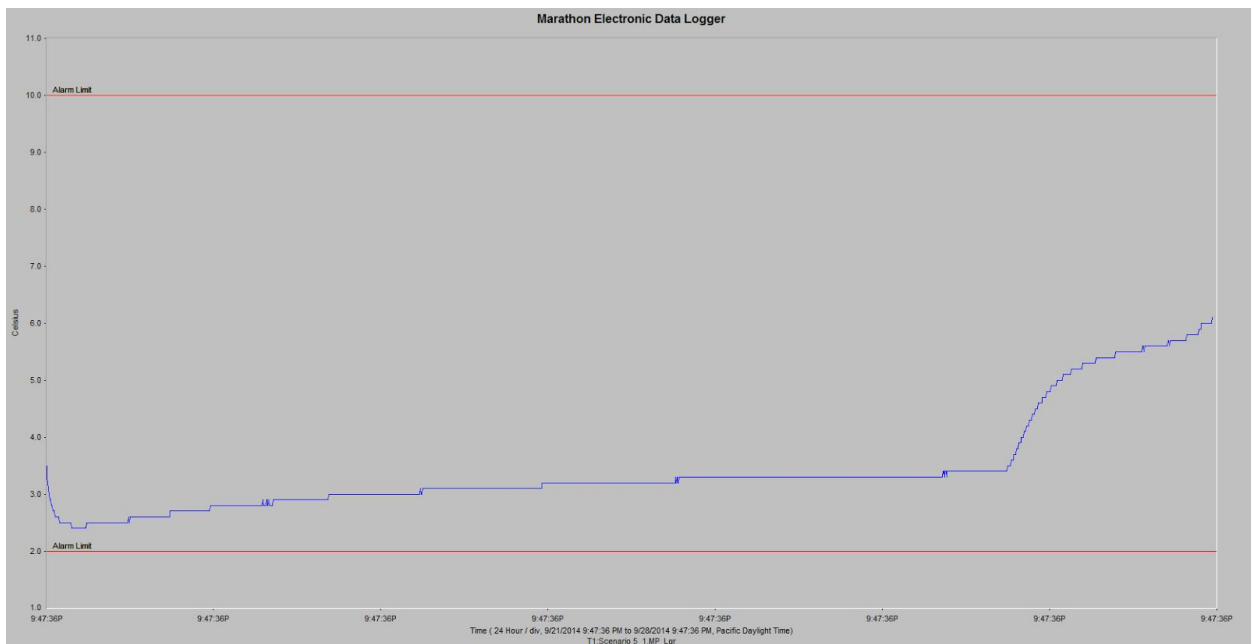


Figure 5 - Results of the performance qualification: scenario four.

The internal temperature reached 6°C at the end of the 24 hour period in a 37°C incubator but otherwise remained at appropriate temperatures for the duration of the scenario.

Performance Qualification - Scenario Five

The final scenario involved stress testing the cooler. The cooler was to be left at a high temperature for an extended period of time to determine how long an appropriate blood storage temperature could be maintained at extreme temperatures.

On day zero, the cooler was packed appropriately and placed in an incubator set at 37°C for seven days. At the end of this period, the cooler was unpacked the data were retrieved and analyzed. Figure 6 shows the results of scenario five.

Scenario five showed that the Credo Cooler was capable of maintaining a temperature $\leq 10^{\circ}\text{C}$ for up to 48 hours at extreme temperatures, which is in line with the product specifications provided by the manufacturer. This scenario reinforced an upper limit for how long coolers should be allowed out of a refrigerator when constructing procedures for appropriate cooler use.

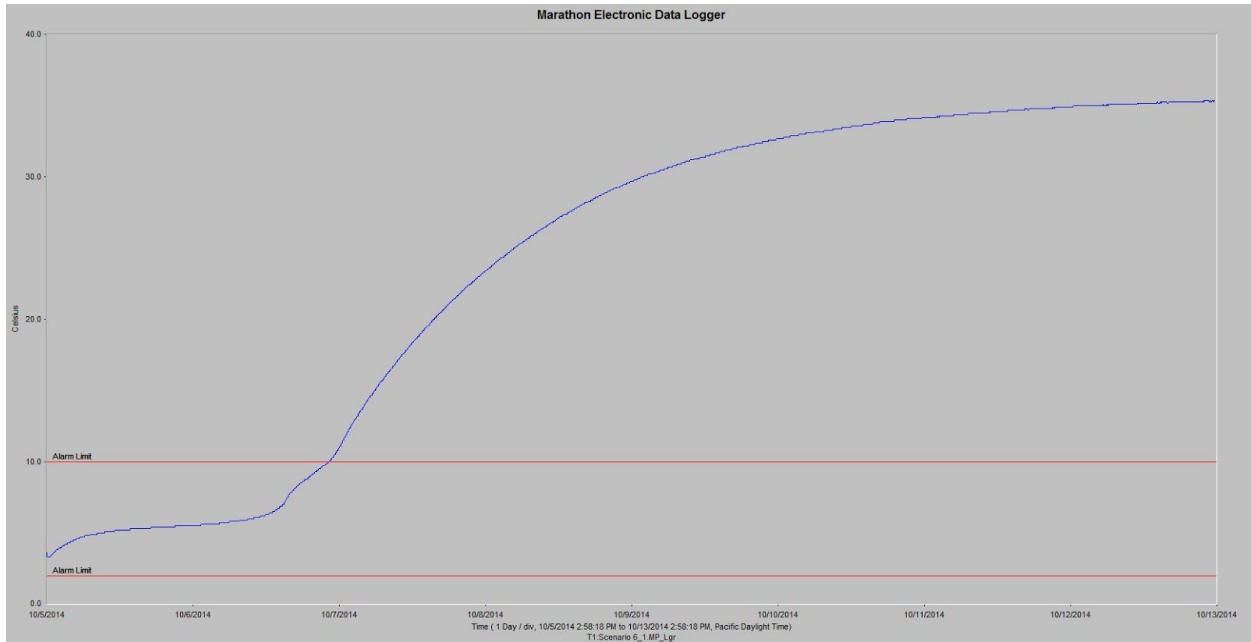


Figure 6 - results of the Performance Qualification Scenario Five.

The internal temperature exceeded 6°C at around the 36 hour mark and 10°C around 48 hours. By the end of the week the cooler’s internal temperature had reached equilibrium with the incubator.

4.3.6 Validation Results

Following installation qualification, operational qualification, and performance qualification, the Credo Coolers were approved for use at the ALNW bases for up to one week. The coolers were able to maintain an appropriate internal temperature between 1-6°C for multiple mock runs as long as the cooler was returned to a refrigerator after each run. Potential problems were noted for runs that exceeded 24 hours, as it was at this point that the internal temperature could exceed 6°C. It was determined that if a cooler was removed from the refrigerator for ≥ 24 hours, it would have to be returned to HMC TSL for replacement. This was done to both preserve the blood products for continued use and prevent potentially unsafe blood products from being transfused. The cooler’s ability to maintain temperature after being opened

was not assessed; instead it was determined that opening the cooler would warrant immediate return to HMC TSL for replacement even if no products were used.

4.4 Pyxis Refrigerator

ALNW uses Pyxis refrigerators to store medications requiring refrigeration as well as the Credo cooler. The refrigerator is locked when not in use and requires a code in order to access the materials stored within. The refrigerator's temperature is monitored at the air base which allows for a prompt response by ALNW staff when there are problems.

4.5 Removable Lock

As a way visually to confirm if a cooler has been opened, a one time use, removable lock is threaded through the zipper of the cooler. In order to open the cooler, the lock must be broken and pulled off. This lock allows for both HMC TSL staff and ALNW to easily check if the cooler has been accessed at any point during the week. The lock was designed though to not interfere with normal use of the cooler but rather to act as a safeguard against accidental opening. The lock been pulled off accidentally with no negative impact on the blood products stored in the cooler.

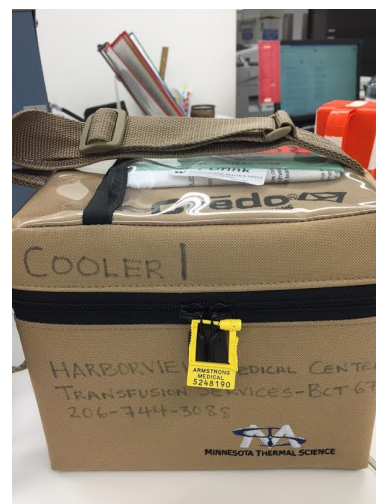


Figure 7 - A lock before use on the left and an in-use lock on the right.

The cooler cannot be opened until the lock has been removed, which can only be accomplished by breaking the lock. This allows ALNW staff easy access to the blood products while also creating a visual check to determine if the cooler has been opened at any point.

4.6 Marathon microDL

Maintaining and documenting maintenance of appropriate storage temperature with transport containers is key to ensuring the quality and safety of blood products. The Marathon microDL mdl4 by Marathon in San Leandro included certification by the National Institute of Standards and Technology (NIST). The microDL was used to ensure the blood products were kept at an appropriate temperature by recording and logging the temperature inside the cooler. Purchase of the microDL also included NIST calibration. The microDL were programmed to record the temperature 30 minutes after activation, to allow for a temperature equilibrium to be reached, and every five minutes after that. After recording the data could be retrieved and saved. These data was then used to determine the viability of the blood products for continued used. The Marathon microDL was chosen due to its small size and reusability. Without the microDL, other methods, such as single-use temperature-sensitive stickers, would have had to be used to ensure appropriate storage temperatures were maintained.

5 Results

After the initial assessment and validation of the materials, development began on providing prehospital transfusion services with ALNW. Based on validation results, procedures were developed at both ALNW and HMC TSL outlining the objectives for prehospital transfusion, the preparation and use of the materials provided for the program, and the methods of reporting program usage as well as deviations with the process. Staff were at ALNW and HMC TSL were trained regarding their designated roles. After prehospital transfusion began, data was collected at HMC TSL regarding blood product usage and wastage. This data was analyzed for patterns, and corrections were made as needed. Problems were noted with product selection for prehospital transfusion, increased product wastage, temperature trends within the cooler, and structural issues with the cooler.

5.1 Established Prehospital Transfusion Process

After validation and training, HMC TSL began providing blood products to ALNW in May 2015. Two O neg pRBCs and two AB or low titer A plasma units were provided in a Credo cooler. Due to the logistical concerns regarding prehospital transfusion and the risk of transfusion reactions, blood products in the cooler would all be from separate donations. If a patient had a transfusion reaction, further transfusions could be provided while minimizing exposure to factors which may have instigated the first reaction. If further testing is required at HMC TSL for post transfusion crossmatch or transfusion reaction investigation, aliquots of the pRBC products are removed and stored. ALNW picked up the cooler at HMC TSL and delivered it to their air base at Boeing Field, approximately six miles away. The cooler was stored in a Pyxis refrigerator when not on a flight. If the cooler was opened, removed from monitored

storage for ≥ 24 consecutive hours, or with ALNW for 7 days, it would be returned to HMC TSL for replacement. If products were transfused, documentation was provided with each unit so transfusion information could be placed in the patient's chart regarding the start time of the transfusion, the transfusionist, and the witness. Paperwork was also completed so HMC TSL could perform post transfusion crossmatches and allow for traceability of blood products.

5.2 Education

After the development of processes at ALNW and HMC TSL to support prehospital transfusion, training needed to be developed for staff members. Both ALNW and HMC TSL are accredited by agencies which require documentation of both initial training on new processes as well as documentation of continued competency. Since each facility had their own processes and accreditation standards, training was performed and documented by each facility for their own staff.

5.2.1 HMC TSL Initial Training

HMC TSL training would need to cover why this process was being initiated, the role staff members would have in the new prehospital transfusion process, and using the validated materials required to support ALNW. To begin training, technical meetings were held with all staff at HMC TSL, where the proposal to support ALNW was outlined. Staff were also provided the opportunity to ask questions and provide feedback. Staff feedback demonstrated was used during the development of written standard operating procedures (SOPs) to ensure instructions were clear.

While the technical meetings were being held, the SOPs were provided to HMC TSL staff members. Staff were given the opportunity to validate these documents and the entire

process could be followed as written. Forms were also developed to allow for documentation of cooler preparation, cooler transfers and returns, as well as blood product transfusion.

Involvement of staff in the process of SOP development strengthened staff connection with the process and allowed for an easier transition. Formal training regarding the process for prehospital transfusion included documentation so HMC TSL would be compliant with their accrediting agencies: AABB and the College of American Pathologists (CAP).

AABB's requires "The blood bank or transfusion service shall have a process for identifying training needs and shall provide training for personnel performing critical tasks," and goes on to define critical tasks as a, "...task that can affect the quality of the facility's products and services."³² Providing blood products for prehospital transfusion would be defined as a "critical task" as it involves products being tested and issued by HMC TSL. Therefore, HMC TSL would be required to provide documentation showing compliance with AABB's standard. CAP has similar requirements, stating, "There are records that all laboratory personnel have satisfactorily completed initial training on all instruments/methods applicable to their designated job."³³

Following the technical meetings and the creation of policies and procedures, staff were then trained individually on the appropriate use of the coolers. This included demonstrating preconditioning the coolers, packing the coolers with the appropriate blood products, activating the data logger, locking the cooler, and all associated documentation of these steps. Staff were also shown the appropriate process to ensure that all blood products were documented as uncrossmatched and that the products were correctly assigned in the LIS. At end of training, staff members took a written test that included problem-solving scenarios, and then underwent a direct

observation of their ability to provide a cooler to ALNW and reconcile paperwork when a cooler was returned. All steps in the training process were documented and filed with the employee's training folder. Any training results which were deemed unacceptable had appropriate retraining and follow-up.

Following the initial training, the process of providing blood products to ALNW was implemented. Deviations in policy, product wastage, and staff concerns were documented and reviewed by project leaders. When necessary, follow-up with staff was conducted to address concerns. Any deviations were compiled and a six month reassessment was created to address recurring problems. Based on the results of the six month assessment, adjustments to workflow were made to ensure all staff were given equal opportunities to work with the coolers.

Previously routine preparation of the cooler was just done by dayshift. Evening shift and night shift only would prepare coolers when ALNW used products and a new cooler was needed as a replacement. Since ALNW was using the cooler once a month on average, evening and night shift staff were not maintaining proficiency in preparing the products and cooler. To address the lack of proficiency, responsibility for preparing the routine replacement cooler was rotated among all shifts. This allowed more staff to get regular experience with the process of preparing a cooler, allowing them to become more comfortable.

5.2.2 ALNW Training

ALNW's education coordinator led the training of ALNW staff. The coordinator also worked with the ALNW medical director to create appropriate policies and procedures to govern prehospital transfusion. These covered on what flights the cooler would be brought and which patients would qualify for transfusion. HMC TSL also provided job aids and training

presentations to assist in staff education. These tools were provided to staff to demonstrate what products would be available and how they would be packaged. Assessments of training were performed by ALNW and retraining was provided as necessary. All documentation for ALNW's training was kept for CAMTS accreditation.

5.3 Initiating Prehospital Transfusions

ALNW began independently carrying blood products in May 2015 and blood products are now on approximately nine flights a week with an average flight being 2-3 hours. Since May 2015 there have been a total of 24 patients transfused, averaging about 1-2 transfused patients a month. All of these patients were originally trauma patients being transported from the scene and were being brought to a medical facility. ALNW has not yet started using their own blood products with patients being transferred from an outside hospital or patients not anticipated to require blood during transport, such as GI bleeds. All 24 patients that have received blood products would originally have to have been supported en route with other treatment options. Further investigation is ongoing regarding the appropriateness of transfusion in these cases with regards to product selection. As of March 2017, transferring facilities are still supplying blood products for patients being transferred to HMC, and these products are still being wasted.

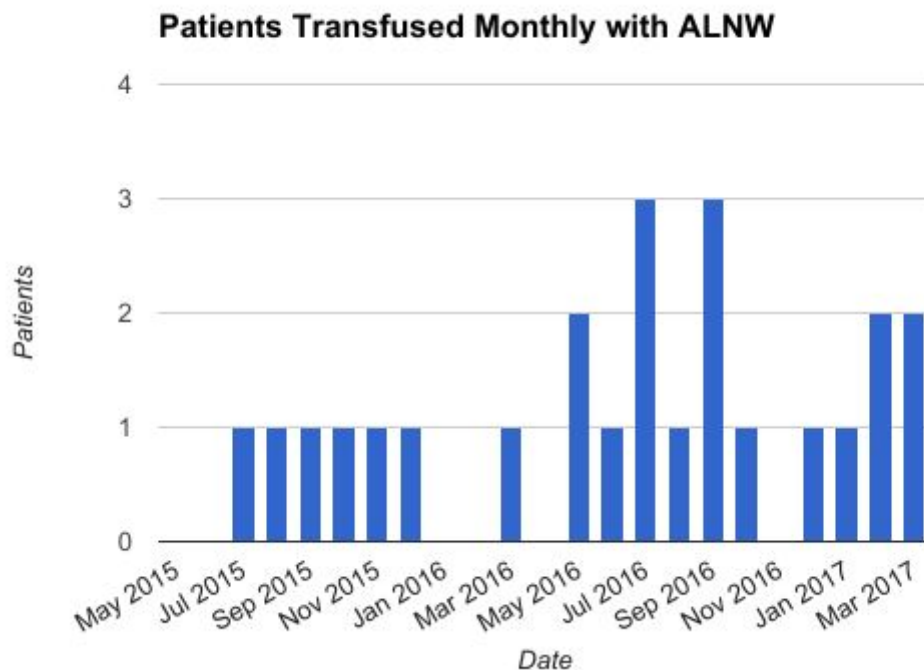


Figure 8 - Patients transfused by ALNW over time.

As of March 2017, Boeing Field and Olympia were the only sites stocked with blood products. The increased usage over time could indicate growing comfort with the use of blood products and their continued availability or it could also reflect an increased number of hemorrhaging traumas during the summer of 2016. Although it is too early yet to determine clear patterns of product use, increased use is anticipated as more ALNW sites are stocked.

ALNW transfused patients, on average, received one transfusion enroute, and typically the product favored by ALNW is pRBCs. The patients who do receive the pRBC transfusion would often tolerate plasma transfusion well, but the plasma is often not initiated until patients arrive at a medical center. This could be a constraint of short flight times from Boeing Field and Olympia to HMC, however as of March 2017, a total of six patients have received multiple transfusions during their flight. Of these six, four patients received two pRBCs, one received two plasma units, and one received one pRBC and one plasma unit. While these are small numbers, and the results could be due to artifacts like small sample size and short flight times, they do

indicate a propensity to favor pRBC transfusion over plasma. Going forward, educational materials may need to be provided with the aim to bring the ratio between RBCs and plasma closer to 1:1. It may also be warranted to discuss initially supporting patients with plasma and if there is time, transfusing the pRBC. ALNW does have separate policies from HMC regarding blood product selection and transfusion. Reviewing and possibly revising these documents may be warranted at a future point. The HMC Emergency Department (ED)'s trauma resuscitation policy stipulates a 1:1 ratio of pRBCs and plasma. As ALNW has begun using blood products, the ED has integrated prehospital transfusion into their response. If a patient receives pRBCs while being transported, the patient is evaluated for potential further blood need, and if it is warranted plasma will be transfused.

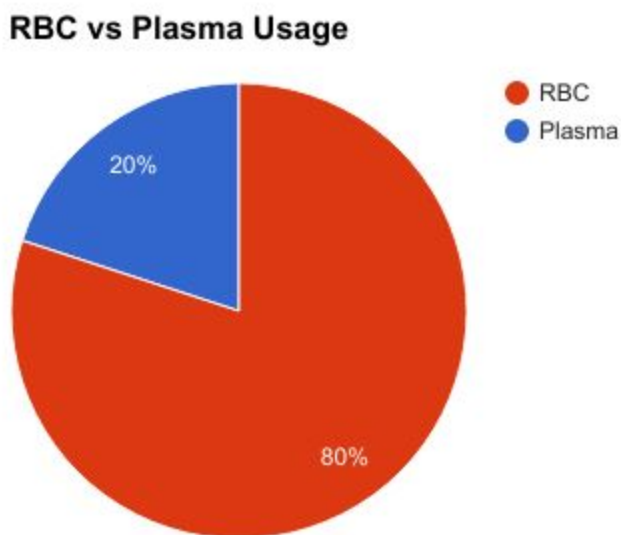


Figure 9 - Relative usage of RBC and plasma products by ALNW.

RBCs are transfused at a ratio of 5:1 while HMC's trauma protocol calls for a ratio of 1:1. ALNW's policies regarding transfusion and blood product selection are separate from HMC's policies.

5.4 Maintenance of blood storage temperature

Over time, more variability has been seen in the temperature recordings including problems with longer time needed for the internal cooler temperature to reach equilibrium and higher equilibrium set points. This variability raises concerns that the blood products are being exposed to excessive temperatures which could impact their purity, potency, or safety. HMC TSL continues to lack a method of monitoring the storage conditions of the blood products in real time. This could lead to blood products being transfused that were stored inappropriately. Even if these blood products were not transfused, upon receipt back at HMC TSL the blood products would be discarded, leading to a financial loss. In addition, regional blood supplies remain limited, and increased wastage of universal products impacts blood inventory levels.

To address this issue of increased temperature variability, a number of corrections have been attempted. Staff competency was assessed with a direct observation by laboratory supervisors to ensure all staff were completing Credo cooler preparation adequately. The procedure was also adjusted so blood product preparation occurred earlier than cooler preparation thus allowing the blood products time to return to a refrigerated temperature before being packed. Previously the blood products were prepared at the same time as the Credo cooler so that blood products were out for ten minutes at room temperature before being packed. Now, blood products are taken directly from the refrigerator and placed in the cooler. It is too early to fully evaluate the effectiveness of this adjustment, but initial assessments show decreased variability.

A higher overall temperature has also been noted when supplying blood products to Olympia. The cooler's internal temperature will settle around 5°C after being packed and when the cooler is returned seven days later, the temperature will be around 5.8°C. The coolers have been examined for physical defects and none have been found. Olympia's ALNW base has checked their Pyxis refrigerator and its temperature has been appropriate. The Olympia ALNW has also supplied their flight logs, documenting how often the cooler is brought for patient care and how long each flight lasts. When examined, these logs show no marked differences between the flight logs from Boeing Field, indicating ALNW usage of the cooler is not resulting in the temperature differences. The current hypothesis for the differences between the temperature recordings of Boeing Field and Olympia are related to the increased transportation time between HMC and Olympia. To prevent the cooler from warming during the transportation to Olympia, and to hopefully achieve a lower temperature setpoint within the cooler, coolers will now be transported packed in ice. This will minimize the time the cooler is exposed to ambient temperatures and hopefully allow it to remain cooler for longer periods. This process has just begun and there have been no evaluations yet on its effectiveness.

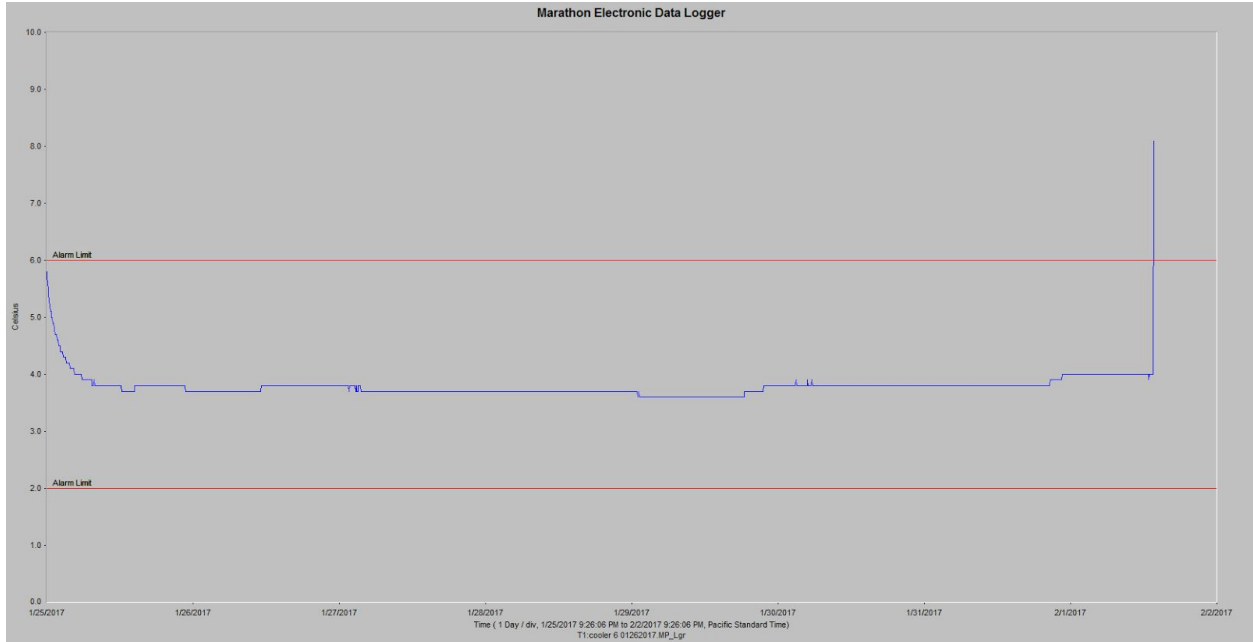


Figure 10 - An acceptable temperature recording taken over seven days.

The blood products were maintained at appropriate temperatures during the entire time with ALNW and were brought back into general inventory at HMC TSL. The temperature shows little deviation over the course of a week once the internal temperature stabilizes around 4.0°C. The sharp rise in temperature at the very end is an artifact from unpacking the cooler and stopping the temperature recorder.

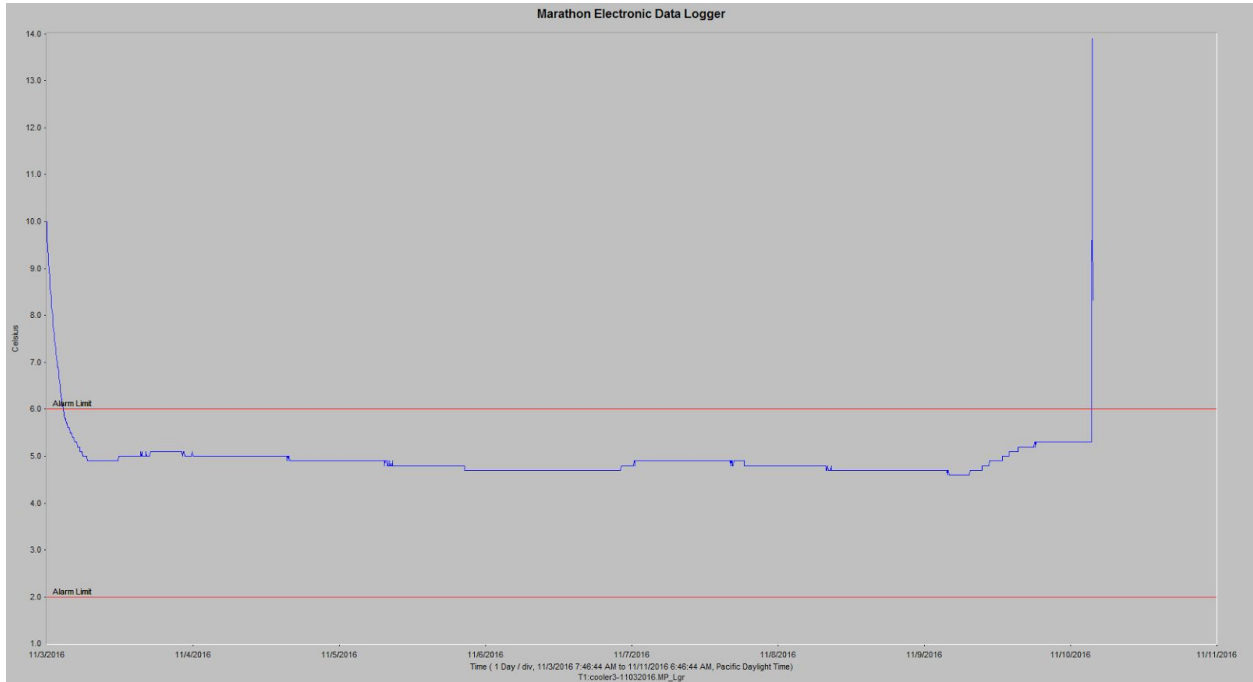


Figure 11 - A temperature recording with a larger tail at the beginning.

The internal temperature reached 6°C 2.5 hours after being packed. The internal temperature then stabilized around 5°C. These blood products were deemed acceptable for acceptance back into HMC TSL. The longer tail was hypothesized to be an artifact of cooler packing possibly related to too much handling of the temperature recorder or the blood products warming while being prepared for packing.

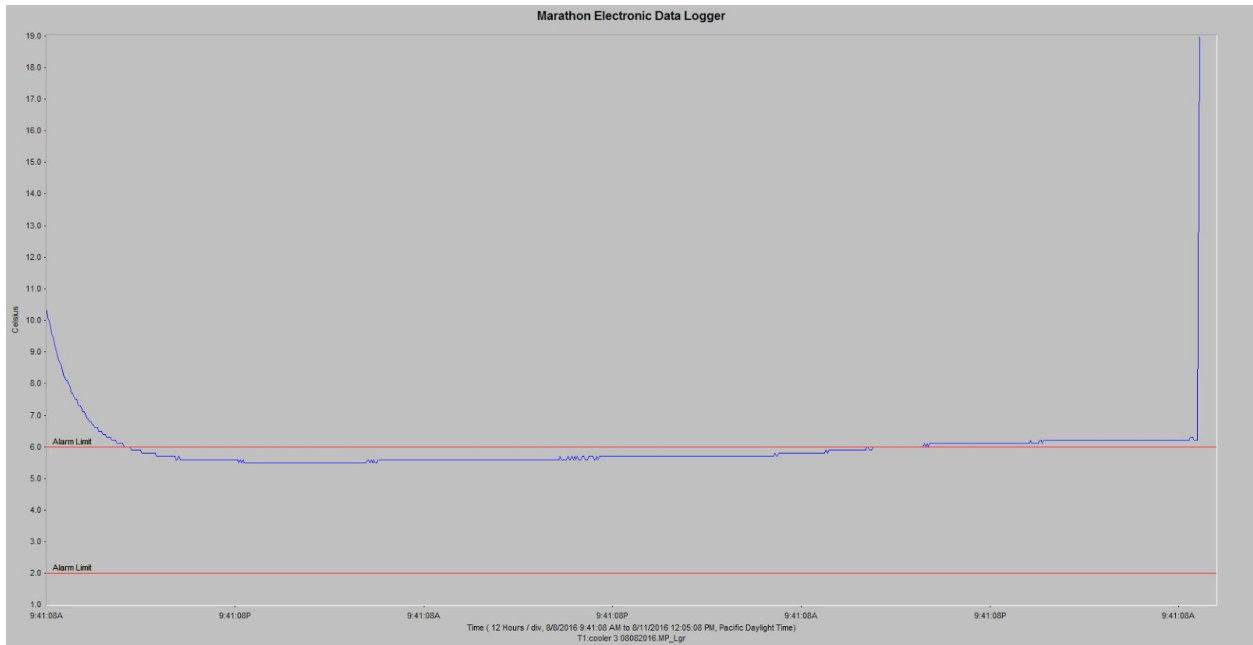


Figure 12 - An unacceptable temperature recording.

The temperature exceeded 6°C and the blood products when returned to HMC TSL were discarded.

5.5 Data logger usage

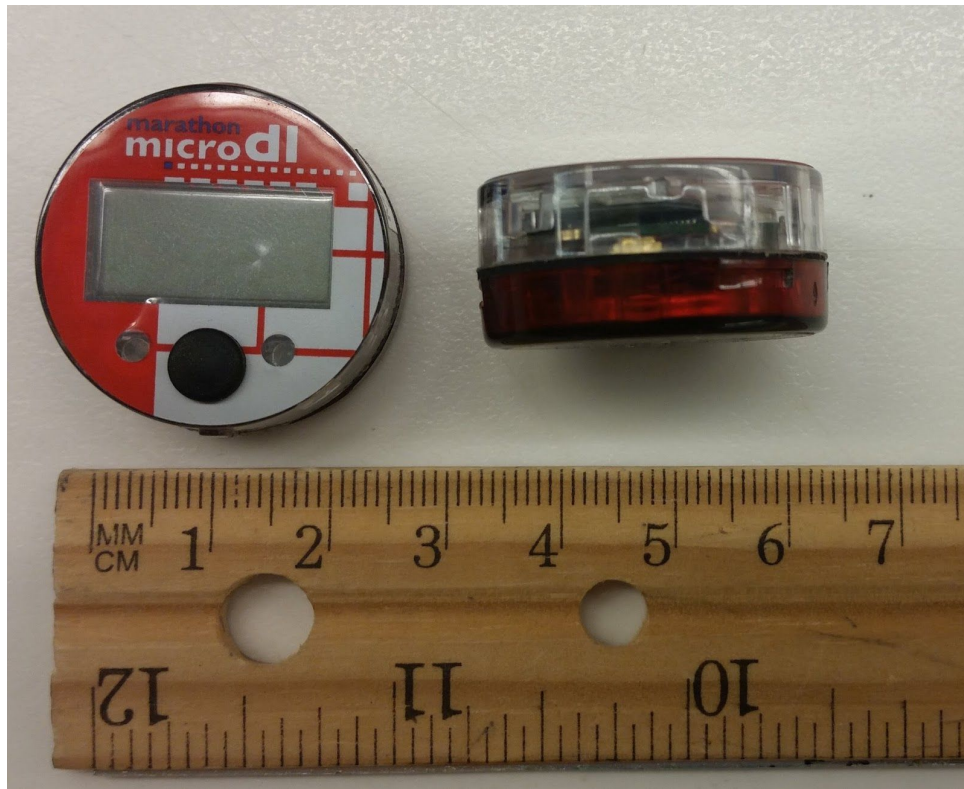


Figure 13 - A data logger both from the front and on its side.

Staff can activate the data logger by holding the single button until the logger flashes “REC”. Once activated the logger will not stop recording until synced with a computer; this prevents inadvertent deactivation due to mishandling.

Both HMC and ALNW staff have encountered problems with the data loggers. When ALNW staff have opened the cooler to retrieve blood products, the data logger has fallen to the floor of the rotary-wing aircraft and not been found again until after the patient has been taken to the medical center. So far the data logger has always been found eventually and the remaining blood products successfully evaluated, but if the logger were to be permanently lost, the products would need to be discarded. On the HMC TSL side, staff have omitted activation of the data logger while packing the cooler, leading to a loss of all blood products. Packing the cooler

requires a second staff member to review all steps, but activation of the data logger has still sometimes been missed. Efforts continue to find technical and user-training solutions to this important problem.

5.6 Fresh thawed plasma

Packing the Credo cooler and providing blood products to ALNW occurs in two different situations: regularly scheduled intervals and unscheduled cooler replacements that take place after prehospital transfusion of a patient. For routine deliveries, long-dated products, that is, products with the greatest shelf-life remaining are ordered and set aside ahead of time. Liquid plasma with adequate shelf life is not always available though for unscheduled cooler replacements and thawed plasma may be substituted. This thawed plasma may be freshly thawed as well if there was no thawed plasma available in the refrigerator. When plasma is first thawed, its temperature is typically between 20-36°C and using this freshly thawed plasma leads to a delay in the cooler reaching its set point and a higher overall set point. Since these issues can lead to a cooler which is less resilient to temperature changes, freshly thawed plasma is no longer used for packing coolers. If no plasma is available at the time ALNW is returning the previously used cooler, than HMC TSL will provide a cooler at a later point, when optimum products are available.

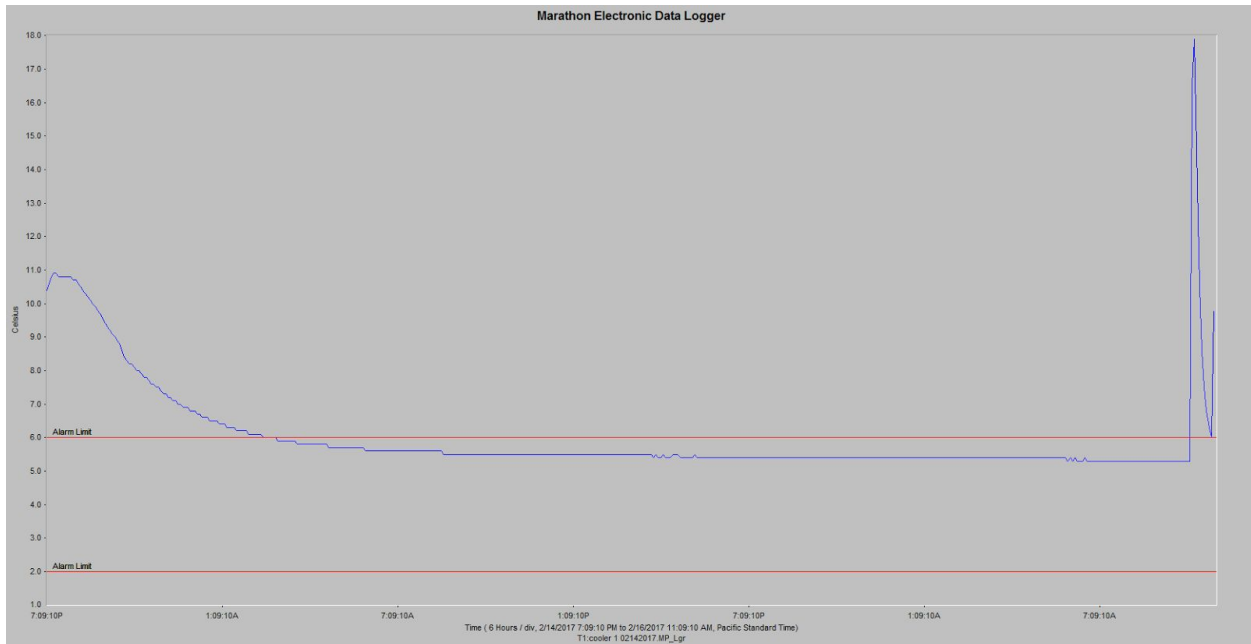


Figure 14 - Impact freshly thawed plasma has on the internal temperature of the Credo cooler.

The internal temperature continues to rise after packing and then tapers down to just inside the acceptable range.

5.7 Inappropriate use of liquid plasma

Liquid plasma was chosen to be provided to ALNW over thawed plasma, in order to provide a long dated product. Liquid plasma has an expiration date up to 26 days after collection and could be packed into a Credo cooler for a week without outdating. Liquid plasma has the same indications as thawed plasma with one exception; liquid plasma is not considered acellular. The freezing and thawing of thawed plasma leads to the destruction of viable lymphocytes while liquid plasma never undergoes this process. After collection, liquid plasma is separated from its cellular components via centrifugation which can leave small amounts of red and white blood cells. Liquid plasma therefore should not be provided to patients who require leukoreduced or

irradiated products outside of emergency situations as it could potentially lead to transfusion associated graft versus host disease (TAGVHD).

Development of TAGVHD occurs when viable donor lymphocytes engraft in the transfusion recipient and begin mounting an immune response against the host. Mortality associated with TAGVHD can approach 90%.³⁴ TAGVHD is typically seen in immunocompromised patients, either congenital or therapeutic, or patients receiving blood products from matched or related donors. Irradiation of blood products can prevent TAGVHD by destroying lymphocytes, and is typically requested for transfusion in cancer patients who have been immunocompromised by treatment.

The differences between liquid plasma and thawed plasma were taken into account when designing the LIS; computer generated warnings would appear when liquid plasma was being given to a patient requiring leukoreduction or irradiation. These warnings are allowed to be overridden to make allowance for emergencies. Patients requiring irradiation may receive products as part of a trauma resuscitation and due to time constraints liquid plasma may be accepted by the trauma physicians. Confusion though among staff has led to patients receiving liquid plasma inappropriately, outside of trauma situations, putting the patients unnecessarily at risk for developing TAGVHD. These mistakes were always discovered within 24 hours when routine review of overrides was performed and appropriate follow up was initiated. Involved staff were educated regarding the different types of plasma products stocked at HMC TSL and the problem stopped occurring. This was most likely due to staff's unfamiliarity with a new product as well as misunderstandings regarding the LIS's warning system.



Figure 15 - Liquid plasma on the left and a thawed plasma on the right.

The only difference between the labels is in the bottom left quadrant's barcode and description. This small difference has led to staff inappropriately allocating and issuing liquid plasma. Due to accurate barcoding performed by the regional blood supplier, no problems have been documented with the LIS recognizing liquid plasma.



Figure 16 - Example of LIS warning

When a blood product is allocated for a patient, the LIS at HMC TSL compares the defined unit attributes with the attributes in the patient’s electronic blood bank record. When the LIS detects a blood product does not have the required attributes, it will create a warning for the staff member performing the allocation. Staff can either stop the allocation and use another product, or they can continue with the allocation and perform an override. When overrides are performed, HMC TSL management reviews the rationale and follows up when appropriate.

5.8 Wear and tear of credo coolers

The Credo coolers have developed tears in their VIP with prolonged use. These tears lead to a loss in the vacuum packing of the VIP which then leads to poorer resistance to temperature changes. Over the course of a year, four VIPs have been torn by normal use requiring complete replacement of the VIP since HMC TSL staff are unable to repair the damage. This led to increased operating costs for the program and time lost to perform validation studies to ensure the new equipment is functioning appropriately.



Figure 17 - Example of a tear in the Credo cooler’s VIP.

These tears typically occur at stress focal points such as where the lid is cinched and the corners which experience a lot of abrasion. Once a tear develops, the vacuum sealing of the VIP is lost along with the insulative properties. These VIPs need to be replaced and revalidated.

6 Discussion

Offering prehospital transfusion with ALNW has been well received by HMC and ALNW staff. Patients are now able to begin transfusion support before arriving at a medical facility without hindering operations at either facility. There have been some initial problems such as inappropriate use of products and increased product wastage but addressed and minimized since the program began in May 2015. The success of the program has allowed the program to begin expanding to provide services to more patients and also allowed for support of other unplanned programs such as solid organ transplantation.

6.1 Expansion of Program

When the program began, HMC TSL supplied blood products to just one of ALNW's six air bases, Boeing Field. The cooler was picked up by ALNW staff at weekly intervals and delivered to the appropriate monitored refrigerator. The blood was then available whenever the team at ALNW's Boeing Field needed it. This limited launch of the program allowed both teams to evaluate the process and resolve problems on a smaller scale. Now ALNW and HMC TSL are supporting blood use at Olympia and planning to accommodate blood products at the other three air bases in Washington state.

HMC TSL has begun validating more coolers in order to supply multiple air bases at once. This has led to increasing the number of blood products kept at HMC TSL so the coolers could be stocked and replaced at any time if used. Alternate types of coolers have also been investigated including the Credo ProMed Series 4 472. This cooler has been validated by the manufacturer to maintain temperature for longer than the cooler currently used by HMC TSL. The ProMed series is originally designed to maintain a temperature between 2-8°C for up to 73

hours compared to the EMT series currently in use which maintains temperature for 48 hours.³⁵ The ProMed cooler though is approximately two kilograms heavier than the Credo Series 4 EMT. Talks are currently underway whether this weight increase would be acceptable with ALNW.

HMC TSL is also investigating methods that would allow for real time monitoring of the temperature within the coolers. The current process records temperatures within the cooler but the data can only be accessed once the cooler has been returned. Real-time monitoring would allow for the coolers to be monitored and recalled if the temperature exceeds the blood storage guidelines. While this technology does exist, size and weight restrictions limit its usefulness.

Whole blood was also considered as a potential blood product that would be provided to ALNW. Two whole blood units would be substituted for two pRBC and two plasma units. These units would allow for the patients to receive the 1:1 ratio of pRBCs to plasma while also minimizing the donor exposure patients experienced. There are no current plans to switch use to this product due to the burden of finding appropriate patients to receive the product at HMC if the product was unused by ALNW.

ALNW has continued to expand with support now extending to the Olympia and Arlington air bases, with plans to soon support the Yakima and Bellingham bases. The Yakima and Bellingham air bases pose a logistical challenge due to their distance from HMC TSL and the challenges of maintaining a temperature within the cooler between 2-6°C for the week when shipment is protracted. To accommodate the longer shipment time, the coolers may be packed in an external carrier with ice, to minimize any temperature gains that may occur during shipment to these further air bases. ALNW also has an air base in Juneau, Alaska. There are no

plans to currently supply blood to that air base due to the extreme distance from HMC TSL. This may be addressed at a later time.

6.2 Transplant support

Prehospital transfusion has also interested the solid organ transplant team at the University of Washington. The TransMedics Organ Care System (OCS) is a portable, warm blood perfusion system used for organ retrieval.³⁶ The system allows for the organs to be transported in an environment similar to the human body and therefore minimize any tissue damage that may result from transport. The OCS has been used successfully with heart and lung transplants, and clinical trials are currently underway to evaluate its use with liver retrievals.^{37 38}
³⁹ Since organ retrieval can take place at remote sites, being able to bring a reliable source of blood products would allow for physicians to transport the organs they are retrieving without draining the potentially scarce blood products at the remote sites. This type of potential use would not require blood being off site from a transfusion service for as long as week, but due to the demands of organ retrieval, blood would need to be available for use at all times. Currently only pRBCs are being evaluated for use during transplant support due to their ability to maintain oxygen delivery. A similar process of signing out the cooler when it is needed and evaluating the blood products when returned would be used.

7 Conclusion

An adult man was involved in a high speed motor vehicle accident and was transported by ALNW to HMC. In route the patient received two pRBC units and two plasma units were available if needed to provide support. When he arrived, his arterial pH was 6.8, his hemoglobin was 12.7, and his INR was 2.9 demonstrating the patient was acutely exsanguinating and prehospital transfusion was warranted. During his initial resuscitation at HMC, he went on to receive 12 pRBCs, 15 plasma units, 2 units of platelets, and 2 pools of cryoprecipitate. ALNW was able to provide this patient products to both restore his oxygen carrying capacity and maintain his blood volume while in transit which would have been impossible previously. The unused plasma products, meanwhile, were returned to HMC TSL and after evaluation placed back into inventory. These universal plasma products were later used to support other patients requiring transfusion at HMC.

Developing a process for ALNW to provide prehospital transfusion has allowed for 24 patients to receive blood products who otherwise would have been supported with other means aimed at preserving blood volume while neglecting oxygen carrying capacity and coagulation. This process has encompassed many areas of HMC TSL's services including equipment validations, blood product evaluation, training, and trauma support. All of these tasks were completed to the standards set forth by HMC TSL's accreditation agencies, CAP and AABB. Due to the scope of this effort, there have been a number of problems that required resolution, and while not all problems have been completely addressed, HMC TSL and ALNW have begun expanding the program across Washington state. There are plans to begin supporting Arlington, WA, and Bellingham, WA, by July of 2017 and later extending support to Yakima, WA. Going

forward, a more robust system allowing for prehospital transfusion will benefit patients across Washington, Alaska, Montana, and Idaho by giving more options for trauma resuscitation in the field. Previously blood products could only be provided once a patient arrived at the hospital but this could be too late; now patients can begin receiving the right blood product at the right time.

7 Bibliography

1. Giangrande PLF. The history of blood transfusion. *Br J Haematol.* 2000 Sep;110(4):758–67.
2. Learoyd P. The history of blood transfusion prior to the 20th century-part 1. *Transfus Med.* 2012 Oct;22(5):308–14.
3. Greenwalt, T. (1997). A short history of transfusion medicine. *Transfusion*, 37(5), 550–563.
4. Learoyd, P. (2012). The history of blood transfusion prior to the 20th century-part 2. *Transfusion Medicine*, 22(6), 372–376.
5. Schwarz HP. Historical review: Karl Landsteiner and his his major contributions to haematology. *Br J Haematol.* 2003 May;121(4):556–65.
6. Boulton F, Roberts DJ. Blood transfusion at the time of the First World War - Practice and promise at the birth of transfusion medicine. Vol. 24, *Transfusion Medicine*. Blackwell Publishing Ltd; 2014. p. 325–34.
7. Hess JR, Schmidt PJ. The first blood banker: Oswald Hope Robertson. *Transfusion.* 2000 Jan;40(1):110–3.
8. Lam DM. To pop a balloon: Aeromedical evacuation in the 1870 siege of Paris. *Aviat Sp Environ Med.* 1988;59(10):988–91.
9. Lam DM. Wings of Life and Hope: A History of Aeromedical Evacuation. *Probl Crit Care.* 2006;4(4):927.
10. The History of the UM R Adams Cowley Shock Trauma Center | University of Maryland Medical Center [Internet]. [cited 2017 Apr 28]. Available from:

<http://www.umm.edu/programs/shock-trauma/about/history>

11. Association of Air Medical Services. Atlas & Database of Air Medical Services: A National Database Showing Base Locations for Rotor and Fixed Wing Air Medical Services. 2015.
12. Karl A, Pham T, Yanosky JD, Lubin J. Variability of Uncrossmatched Blood Use by Helicopter EMS Programs in the United States. *Prehospital Emerg care Off J Natl Assoc EMS Physicians Natl Assoc State EMS Dir.* 2016;20(6):688–94.
13. Kauvar DS, Lefering R, Wade CE. Impact of hemorrhage on trauma outcome: an overview of epidemiology, clinical presentations, and therapeutic considerations. *J Trauma.* 2006;60(6 Suppl):S3-11.
14. Lyon RM, de Sausmarez E, McWhirter E, Wareham G, Nelson M, Matthies A, et al. Pre-hospital transfusion of packed red blood cells in 147 patients from a UK helicopter emergency medical service. *Scand J Trauma Resusc Emerg Med.* 2017 Dec;25(1):12.
15. Holcomb JB, Donathan DP, Cotton BA, Del Junco DJ, Brown G, Wenckstern T von, et al. Prehospital Transfusion of Plasma and Red Blood Cells in Trauma Patients. Vol. 19, *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors.* 2015. p. 1–9.
16. Holcomb JB, Pati S. Optimal trauma resuscitation with plasma as the primary resuscitative fluid: the surgeon’s perspective. *Am Soc Hematol Educ Progr.* 2013;2013(1):656–9.
17. Duchesne JC, Hunt JP, Wahl G, Marr AB, Wang Y-Z, Weintraub SE, et al. Review of current blood transfusions strategies in a mature level I trauma center: were we wrong for

- the last 60 years? *J Trauma*. 2008 Aug;65(2):272-276-278.
18. Hervig T, Doughty H, Ness P, Badloe JF, Berseus O, Glassberg E, et al. Prehospital use of plasma: the blood bankers' perspective. *Shock*. 2014 May;41 Suppl 1(11):39–43.
 19. Berséus O, Boman K, Nessen SC, Westerberg L a. Risks of hemolysis due to anti-A and anti-B caused by the transfusion of blood or blood components containing ABO-incompatible plasma. *Transfusion*. 2013;53(SUPPL. 1).
 20. Sunde GA, Vikenes B, Strandenes G, Flo K-C, Hervig TA, Kristoffersen EK, et al. Freeze dried plasma and fresh red blood cells for civilian prehospital hemorrhagic shock resuscitation. *J Trauma Acute Care Surg*. 2015 Jun;78(6 Suppl 1):S26-30.
 21. Spinella PC, Perkins JG, Grathwohl KW, Beekley AC, Holcomb JB. Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries. *J Trauma*. 2011 Apr;66(4):69–76.
 22. Zielinski MD, Stubbs JR, Berns KS, Glassberg E, Murdock AD, Shinar E, et al. Prehospital blood transfusion programs: Capabilities and lessons learned. *J Trauma Acute Care Surg*. 2017;1.
 23. GO-TEAM - UM Shock Trauma Center | University of Maryland Medical Center [Internet]. 2017 [cited 2017 May 6]. Available from: <http://www.umm.edu/programs/shock-trauma/professionals/ems/go-team>
 24. "About Harborview Medical Center | UW Medicine."
<http://www.uwmedicine.org/harborview/about>. Accessed 4 Mar. 2017.
 25. Unpublished internal data
 26. "Emergency Transportation | UW Medicine."

- <http://www.uwmedicine.org/airlift-nw/services/emergency-transportation>. Accessed 4 Mar. 2017.
27. CAMTS. Accredited Services [Internet]. 2017 [cited 2017 May 7]. Available from: <http://www.camts.org/Accredited-Services.html>
 28. Frazer E. How many state EMS agencies require CAMTS accreditation for air ambulance services? *Air Med J*. 2001 Jan;20(1):8.
 29. American Association of Blood Banks. Circular of Information. Circ Information—for use blood blood components. 2013;
 30. Backholer L, Green L, Huish S, Platton S, Wiltshire M, Doughty H, et al. A paired comparison of thawed and liquid plasma. *Transfusion*. 2016 Apr;0(October):881–9.
 31. Pelican BioThermal. Crēdo™ Medic Pack Series 4 248 EMT [Internet]. 2017 [cited 2017 May 7]. Available from: <http://pelicanbiothermal.com/products/credo-medic-pack-series-4-248-emt>
 32. AABB. Standards for Blood Banks and Transfusion Services. 30th ed. Bethesda, MD; 2016. 3, 96 p.
 33. College of American Pathologists. Laboratory General Checklist. Northfield, IL; 2016. 51-53 p.
 34. Alter HJ, Klein HG. The hazards of blood transfusion in historical perspective. *Blood*. 2008 Oct 1;112(7):2617–26.
 35. Pelican BioThermal. Crēdo ProMed™ Series 4 472 [Internet]. 2017 [cited 2017 May 7]. Available from: <http://pelicanbiothermal.com/products/credo-promed-series-4-472>
 36. Organ Care System [Internet]. TransMedics. 2017 [cited 2017 May 7]. Available from:

http://www.transmedics.com/wt/page/organ_care

37. Dhital KK, Iyer A, Connellan M, Chew HC, Gao L, Doyle A, et al. Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: A case series. *Lancet*. 2015;385(9987):2585–91.
38. Bozso S, Vasanthan V, Luc JGY, Kinaschuk K, Freed D, Nagendran J. Lung transplantation from donors after circulatory death using portable ex vivo lung perfusion. *Can Respir J*. 2015;22(1):47–51.
39. TransMedics. TransMedics (OCS) Liver Trial: Preserving and Assessing Donor Livers for Transplantation [Internet]. 2016 [cited 2017 May 7]. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT02522871>