

BLOOD TRANSPORT CONTAINER VALIDATION TESTING GUIDELINES

1. Purpose

To provide a guideline to facilitate a standard approach to the validation of a container that would be used to transport blood components or blood products between destinations and maintain the contents at the appropriate temperature.

In scope

Validation of a container for the transport of blood components and blood products between blood service distribution points and other health establishments.

Out of scope

Blood at collection centres that will be transported to the blood processing centre. A separate guideline is required due to the complexity of the requirements. Transportation in extreme weather conditions below 4°C and above 42°C.

2. Background

Blood components (red cells, platelets, fresh frozen plasma, cryoprecipitate and cryo-depleted plasma) and blood products (manufactured from and containing human plasma e.g. Hepatitis Immunoglobulin, anti-D immunoglobulin etc) must be stored and transported in a manner which maintains the temperature range they are expected to stay within. Expected temperature ranges are different depending on the component/product and can differ if the product is in storage or in transport. As an example Table 1 shows the temperature range of components as per the "Council of Europe. Guide to the preparation, use and quality assurance of blood components 18th Edition (2015)". These ranges may differ between quality guidelines in different countries. You will need to identify the temperature ranges that apply to your applicable quality system.

Component	Storage temperature	Transport temperature
Red cells	Between +2°C and 6°C Must not go below 1°C	Between 2°C and 10°C with a maximum transit time of 24 hours.
Platelets	Between 20°C to 24°C Under constant agitation	Between 20°C to 24°C maximum transit time of 24 hours Agitation can be interrupted up to 30 hours
Fresh Frozen Plasma, Cryoprecipitate and Cryoprecipitate-depleted plasma	Below -25°C	Below -25°C

Table 1. Storage and temperature requirements for 'fresh' components (Council of Europe Guidelines 2015 ¹)

The blood supply chain includes transport of blood components /products between blood collection centres, processing facilities, distribution centres, transfusion service laboratories, hospitals, medical retrieval services and hospital-in-home services. Maintenance of the correct temperature of blood products and/or components during transport is vital for the maintenance of cell viability, product function and prevention of bacterial contamination. The correct temperature is to be achieved using a combination of transport container (ie. box/shipper), coolant packs and specific packing configurations. Maintaining temperature, records of temperature and transport, records of issue and receipt and maintenance records of storage equipment is necessary and is often referred to as the "Cold Chain".

These Guidelines describes how to perform validation testing on any blood transport container to determine its performance characteristics, suitability and appropriate packing configurations for the transport of blood components or blood products.

Blood transport container validation testing is performed by exposing simulated blood consignments to the geographical temperature variations that may occur during transport. The method uses temperature data loggers to measure the product temperature during the transport time. Transportation may occur in a temperature controlled environment (e.g. hospital) or a non-controlled environment e.g. motor vehicle, airplane, drone, courier in which case seasonal weather variation has to be considered.

Table 2 illustrates the temperature ‘zones’ that will have different temperature ranges needing to be considered in the validation

Transport environment	Example	Seasonal Variation	
		Winter (Minimum expected temperature of this environment)	Summer (Maximum expected temperature of this environment)
Temperature controlled environment	Hospital	20°C to 24°C	20°C to 24°C
Non temperature controlled environment	motor vehicle, airplane, drone, courier	4°C	42°C

Table 2. Transport temperatures as per the Council of Europe Guidelines, 2015 ¹

These Guidelines do not cover extreme weather environments below 4°C or above 42°, such conditions require blood providers to develop specialized validation protocols.

Cyclic exposures between the extreme temperatures for periods between 4 to 8 hours may also be performed. This attempts to replicate real world extremes of temperature exposure.

The maximum transport time allowable is determined from the period the blood product remains within the expected accepted temperature range for the particular blood product being assessed. A safety margin of time can be incorporated into the maximum transport time e.g. reduce the maximum time as a safety margin. It is good blood supply chain practice that the maximum time for transport of blood products should not exceed 24 hours ^{2b}.

Your blood product supplier should have a specification for the acceptable transport temperature range for red cells, platelets and frozen plasma components, which is generally between 2°-10°C for red cells, 20°-24°C for platelets and <-25°C for frozen plasma components.

For general information regarding blood and blood product cold chain management which includes transportation refer to these WHO documents (http://www.who.int/bloodsafety/processing/cold_chain/en/) ²

- Aide-memoire: Blood cold chain ^{2a}
- The blood cold chain: guide to the selection and procurement of equipment and accessories ^{2b}
- Manual on management, maintenance and use of blood cold chain equipment ^{2c}

For an article describing blood cold chain in general, suggest referring to the “Blood cold chain” by J. C. Faber ³

3. Pre-Validation Testing Variables for Consideration

3.1 Estimate the geographic temperature range the transport container will be exposed to during transport

- In a controlled environment, perform validation testing between 20°C and 24°C.
- In an uncontrolled environment, perform validation testing at 4°C, 22°C & 42°C or use local summer maximum and winter minimum temperature.
- Perform set-point and cyclic exposure testing. Cyclic periods of 4 to 8 hour at extreme temperature followed by 22°C mimics real world courier cartage. 'Set-point' refers to a constant temperature. To assist in determining validation cyclic extreme temperature exposures, assess the typical blood transport routes and record the temperature on these routes over the different weather seasons.

3.2 Considerations for selecting a suitable transport container

- Usability
- Weight (below maximum allowed by local health and safety requirements)
- Storage and stacking both inside facilities and in transport vehicle
- Security – can the lid/opening be secured from tampering
- Re-usable or single use. Consider costs including return of container for re-use
- Disposal of end of life containers – environmental considerations
- Shedding off of container material particles if it is potentially to be used in a clean areas e.g. operating theatres

3.3 Consider the blood product or component to be transported?

- The type of blood component or product will determine the temperature to be maintained during transport. For validation testing, the most appropriate blood products to use are expired or discarded products, but simulated blood products can be used, if necessary – e.g. water-filled blood packs can be used to simulate red cells.

3.3 The maximum and minimum number of blood components/products to be packed in the transport container.

- Depending on the blood component you will need to try packing the container with packs until you identify the maximum number of units that can safely be packed into the container. Do not put the units under any physical pressure and do not exceeding the maximum safe carrying weight.
- Test the container with a single unit and then the maximum number of units and record the time and temperature range. If the temperature for a single unit goes out of range then add one coolant pack conditioned to the same temperature and repeat the monitoring. Do this repeatedly adding more coolant if required to obtain the desired time and temperature.
- Repeat the above using two units and coolant packs. It may be necessary to create a table showing the rate of coolant packs to units to maintain the required temperature and time.
- Depending on ambient temperature, quantity and type of component /product being transported, the use of both frozen and chilled coolant packs may be required. This will be part of the iterative testing required.

3.4 Consider the type and number of coolant packs to be used

- For transport of components only use sealed wet-ice coolant packs preferably water-based or food grade materials e.g. non-toxic sodium polyacrylate gel. Use of phase-change materials with melting points below 0°C may cause red cell freezing leading to haemolysis should not be used.
- Coolant packs should only be frozen at temperatures of approx. -20°C. Do not freeze coolant packs below this temperature e.g. ultra-cold temperature.

3.5 Consider the starting temperature of all transport container materials to be used

- Ensure all transport containers, coolant packs and packing material have stabilised at required temperature for at least 24 hours prior to validation experiment.

3.5 The packing configuration or how the blood product is packed in the container

- Components should be packaged in a plastic bag closed to prevent escape of fluid in case of component leakage.
- If it is not possible to provide tamper evidence on the outside of the container consider using tamper proof tape to show if the plastic bag has been opened i.e. when folding the bag closed tape it down.

- Use a divider made of cardboard or similar to prevent direct contact with coolant pack, especially if they are frozen packs.
- The outer walls of the inside of the box are the most likely to be compromised from external heat / cold sources therefore in designing the packing configuration place components in the centre of the container with coolant packs surrounding them.
- When a suitable configuration of components, coolants, dividers etc has been tested, ensure very clear preparation and packing instructions are provided. The use of codes to identify the component and packing configuration may be useful for staff in adhering to the relevant procedure e.g. RC-A for red cells configuration A, P1 for a platelet configuration 1.

3.6 Identify the maximum transport time required for the particular configuration

- Estimate the maximum journey time to reach the furthest destination required. This time will determine the maximum required validation testing time.
- When conducting the validation continue the time of the testing to 150% or 200% of the maximum required time. If the temperature is still in range this provides a safety buffer in case of transport failure.
- If required, the validation time could be extended to find the time that the temperature departs from the desired range.
- Repeat the experiment challenging the container with temperatures at the three selected levels (winter, summer, room temperature)

3.7 Identify the coldest and warmest areas inside the container

- Logger or sensor probes should be placed on the surface of the components/products under test.
- Place these units in the expected warm and also cool positions inside the transport container. Typically these positions would be the top, centre and bottom of the container.
- Utilise these data to map out the thermal profile of the container.
- If the mapping data is acceptable then future tests only require a single point of temperature recording using the position where the temperature is expected to fail first.

4. Procedure

4.1 Equipment & Consumables

- 4.1.1 Temperature logging device(s) that have been calibrated by a certified testing service. Multiple individual loggers or multi-probe loggers may be used.
- 4.1.2 Blood products used for validation may be recently expired units or alternatively simulated products can be used for testing. Ensure any expired products for validation testing are segregated from normal blood stocks and positively labelled as quarantined. For correct transport container thermal loading, these test products must have been stored at the required temperature for at least 24 hours to stabilise. The use of existing temperature monitored blood storage facilities suffices for this purpose.
- 4.1.3 Transport containers and packaging materials are to be stored at controlled ambient temperature for at least 24 hours. Do not use transport containers that have been recently used as these may be cold or warm.
- 4.1.4 Precondition the selected coolant packs at the required temperature for at least 24 hours prior to commencing validation experiments. This ensures sufficient thermal equilibration. For storage of red cells and thawed plasma, only use wet ice coolant packs preferably water-based. Use of phase-change materials (PCM) with melting points well below 0°C may cause red cell freezing which leads to haemolysis, these should not be used. Use of PCM should only be considered in exceptional situations. Wet ice packs should only be frozen at regular freezer temperatures of -20°C, do not freeze wet ice packs below this temperature e.g. ultra-cold freezing. NOTE: frozen coolant packs must not come in direct contact with red cell packs as cell freezing and haemolysis will occur. 4°C buffer packs may be used in-between the red cell packs and the frozen packs (if used).
- 4.1.5 To provide an artificial ambient temperature challenge to the container, use an incubator for the 'summer' ambient test and a cool room for the 'winter' ambient test. Both incubator and cool room must have had their temperature checked using a calibrated thermometer. The 'summer' temperature should be set at 42°C or your expected maximum temperature for summer. The cool room should be set to (2-6°C) and be used for 'winter' temperature testing. For room temperature validation ensure the room temperature is monitored constantly and is within the ambient temperature range using a calibrated thermometer.

5. Method

- 5.1 From the information determined above, the validation experiments can be designed, tested and the data recorded.
- 5.2 Organise the container and other packaging materials ready for use. Do not remove the blood products or coolant packs from their storage devices/locations until immediately before packing.
- 5.3 Remove the blood products from their storage device/location & pack the container according to the pre-determined packing configuration.
- 5.4 Loggers should be programmed to record at least every 2 min for longer validation periods.
- 5.5 Place temperature loggers/probes onto surface of test products. If multiple packs/bottles are to be in the packing configuration then affix a logger to top, middle and bottom of packs/bottles.
- 5.6 Affix the 'ambient temperature' probe to the outside of the container, but allow the free end of the probe to protrude into ambient air space to ensure accurate measurement of ambient temperature. If using a button logger, then it can be affixed to the outside of the container. The variation between ambient 'air' temperature and container outer surface temperature is minimal so the addition of an insulating spacer between the shipper and logger is optional.
- 5.7 Once the container has been setup, leave it at 22°C for 1 hour to mimic the waiting time prior to collection by a courier. Shorter wait times may be used if necessary e.g. emergency use container, massive transfusion pack etc.
- 5.8 After the waiting period place the shipper at the required ambient temperature (incubator set at 42°C, air-conditioned room (20°C – 24°C), or cool room (4°C). Use a foam insert in either incubator or cool room, to prevent direct metal to container contact thermal transfer. Ensure container is removed at set time when cyclic extreme temperature exposures are being performed.
- 5.9 Perform repeat experiments for each packing configuration. Analysis of initial validation experiments will indicate if the configuration requires changing and if repeat testing is required. If the data exhibits precision and the values obtained are what are required then consider this as the suitable configuration.
- 5.10 From the temperature data analysis determine an acceptable safe maximum transport time that maintains acceptable temperature of component for the particular packing configuration.
- 5.11 Once all validation testing has been performed and confirms the required transport container time period, prepare a validation report (see example template Appendix).

6. Appendix Example Validation Report Template

Validation Report	Contents
Title	Brief title of validation process
Site	Validation location
Validation Start/Finish Dates	Operator
Performed By	
Validation Description	paragraph briefly detailing purpose, method and acceptance criteria for the shipper system being validated
Equipment details	List all items used in the validation, stating all certifications
Test Method details	Describe the exact method of transport container validation explaining any relevant issues
Validation Results	In table format, present appropriate data relating to validation experiments. Briefly overview the results
Validation Summary	Overview of the validation. Briefly state what was done and provide final results. Include any qualifications and or provisos
Recommendation	List all recommendations for the transport container system validated. State any conditions and/ or limitations
Authorisation	List names, signatures, position title, dates of testing staff member, quality delegate and manager
Appendices	<ul style="list-style-type: none"> • Raw test results • Figures • Detailed description of the approved packing configuration • Table of component/ product quantities and associated coolant packs required

7. References

1. Council of Europe. Guide to the preparation, use and quality assurance of blood components. 18th edition (2015)
2. WHO documents (http://www.who.int/bloodsafety/processing/cold_chain/en/)
 - a. Aide-memoire: Blood cold chain
 - b. The blood cold chain: guide to the selection and procurement of equipment and accessories
 - c. Manual on management, maintenance and use of blood cold chain equipment
3. Blood cold chain J. C. Faber, ISBT Science Series (2007) 2, 1–6

8. Authors

Prepared for the ISBT Blood Supply Management Working Party by Rick Tocchetti (Department of Health, Government of South Australia) and David Jones (Australian Red Cross Blood Service)