Guidelines for the Blood Transfusion Services

Annexe 3: Provisional Components

http://aws-lon-jpac.targetservers.uk/red-book/annexe-3

Annexe 3:

Provisional Components

This section contains information regarding provisional components.

Provisional Component

A3.1: Platelets in Additive Solution and Plasma, Leucocyte Depleted, Pathogen Reduced

A platelet concentrate, derived from buffy coats or apheresis, which contains less than 1×10^6 leucocytes and where the suspending medium comprises approximately 30-50% plasma and 50-70% additive solution. Subsequently the component is subjected to treatment using a licensed pathogen inactivation system prior to storage.

A3.1.1: Technical Information

- The primary platelet component prior to pathogen-reduction must meet the specifications set by the manufacturer of the pathogen-reduction system.
- Provided the pathogen reduction system used has been validated to inactivate lymphocytes, irradiation of the component to prevent transfusion-associated graft versus host disease is not required.
- The level of removal of the photo-sensitising agent prior to final storage should be validated, if such a step is included in the pathogen-reduction system.
- Provided the pathogen reduction system used has been validated to inactivate CMV, CMV testing of the component to prevent transfusion-associated CMV infection is not required.
- The component is manufactured as a primary component and not as a remanufactured secondary component.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for platelet production.

- Where prepared from buffy coats, the buffy coats must be prepared at ambient temperature before the whole blood is cooled to below 20°C.

- Where prepared from buffy coats, initial separation of buffy coat must occur within 24 hours of venepuncture (unless supported by additional validation), with a minimum buffy coat rest period of 2 hours before secondary pooling and processing of buffy coats to produce the final component, which is generally completed before the end of Day 1.

- Screening of female apheresis donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy.

- The volume of suspension medium must be sufficient to maintain the pH at >=6.4 at the end of the shelf life of the component.

- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the audit trail and the correct identification number is put on the final component pack.

- Platelets in Additive Solution and Plasma, Leucocyte Depleted, Pathogen Reduced should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.1.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, (pooled or apheresis) in Additive Solution and Plasma, Leucocyte Depleted, Pathogen-Reduced (name of PR method)* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing platelet units*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant and platelet additive solution
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.1.3: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the pathogen inactivation system, additive solution and storage container.

- Systems currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 7 days in a closed system.

- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.

A3.1.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 and leucocyte counting (see section 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown at Table A3.1 shall meet the specified values.

Table A3.1 Platelets in Additive Solution and Plasma, Leucocyte Depleted, Pathogen Reduced – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count [1]		>=240 × 10^9/pool
pH at end of shelf life	If less than 10 per month, every available component	>=6.4
Leucocyte count [2]	As per sections 6.3 and 7.1.1	<1 × 10^6/pool
[1] Units measured and found to have <160 × 10^9/pool should not be issued for transfusion		
[2] Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

A3.1.5: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.

- Plastic overwraps should be removed prior to storage.

Provisional Component

A3.2: Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced

A red cell component containing less than 1×10^6 leucocytes and suspended in an approved additive solution. Subsequently the component is subjected to treatment using a pathogen inactivation system prior to storage.

A3.2.1: Technical information

- The primary red cell component prior to pathogen-reduction must meet the specifications set by the manufacturer of the pathogen-reduction system.
- Provided the pathogen reduction system CE/UKCA/UKNI mark states that it may be used as an alternative to irradiation to prevent transfusion-associated graft versus host disease, irradiation of the component is not required.
- Provided the pathogen reduction system CE/UKCA/UKNI mark states that it may be used as an alternative to serological testing for the prevention of transfusion-associated CMV infection, CMV testing of the component is not required.
- The component is manufactured as a secondary component from red cells in additive solution, leucocyte depleted. The primary component (red cells in additive solution) must not have been previously remanufactured from red cells for exchange transfusion.
- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the audit trail and the correct identification number is put on the final component pack.
- Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.2.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced* and volume
- the blood component producer’s name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the additive solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.2.3: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
  - the component has been exposed to such a temperature change on one occasion only
  - the duration of the temperature excursion has not exceeded 5 hours
  - a documented system is available in each Blood Centre to cover such eventualities
  - adequate records of the incident are compiled and retained.

A3.2.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown in Table A3.2 shall meet the specified values.

Table A3.2 Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	190 – 330 mL
Haemoglobin content [1]		>=40 g/unit
Haemolysis	As per section 7.1.3	<0.8% of red cell mass
Leucocyte count [2]	As per sections 6.3 and 7.1.1	$<1 \times 10^6$/unit
[1] Units measured and found to have <30 g/unit should not be issued for transfusion		
[2] Methods validated for counting low numbers of leucocytes must be used		

A3.2.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components

- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

Provisional Component

A3.3: Liquid Plasma, Leucocyte Depleted

Plasma that has been obtained from whole blood from a previously tested donor (as defined in section 7.1.4). The plasma contains less than 1×10^6 leucocytes per component.

A3.3.1: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Plasma should be selected from male donors only.
- The plasma should be separated before the red cell component is cooled to its storage temperature.
- The method of preparation should ensure minimum cellular contamination. The plasma should be placed at 2-6°C as soon as possible after separation from the red cell component. The production process should be validated to ensure that components meet the specified limits for FVIII concentration at the end of expiry.
- Liquid Plasma, Leucocyte Depleted should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.3.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Liquid Plasma, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection

- the expiry date of the component*
- the temperature of storage
- the blood pack lot number*
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.3.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 4 ±2°C for a maximum of 7 days
- The component must not be frozen and should be transfused as soon as possible. It should be borne in mind that the content of labile coagulation factors declines with the duration of storage.

A3.3.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown in Table A3.3 shall meet the specified values.

Table A3.3 Liquid Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	Stated volume ±10%
Platelet count [2]		<30 × 10^9/L
Red cell count [2]		<0.2 × 10^9/L
FVIII [3]		[>=X IU/mL]
Leucocyte count [2,4]	As per sections 6.3 and 7.1.1	<1 × 10^6/unit
[1] Units measured and found to be outside of the range 200 to 360 mL should not be issued for transfusion		
[2] Pre-freeze in starting component		
[3] Units measured and found to have <0.3 IU/mL should not be issued for transfusion		
[4] Methods validated for counting low numbers of leucocytes must be used		
[To be defined following operation validations]		

A3.3.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be used straight away it should be transferred immediately to storage at the recommended temperature.

For liquid plasma components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

Provisional Component

A3.4: Red Cells, Rejuvenated and Washed, Leucocyte Depleted

A red cell component, containing less than 1×10^6 leucocytes, which has been rejuvenated, washed, and resuspended in a validated additive solution (SAGM). The component is intended to be used as part of the REDJUVENATE clinical study only, with a maximum of 6 units to be transfused in any 24 hours.

A3.4.1: Technical information

- The starting material is Red Cells in Additive Solution, Leucocyte Depleted, on or after Day 7 and no later than Day 32.
- To reduce the risk of bacterial growth, periods where Red Cells in Additive Solution, Leucocyte Depleted for the trial are removed from controlled storage must not exceed 30 min on each occasion prior to receipt in NHSBT.
- Rejuvenation of red cells occurs via the addition of 50 mL rejuvesol® Red Blood Cell Processing Solution (rejuvesol Solution) and incubation at 37 ±2°C for 60 mins ±5 mins.
- The time that red cells are removed from controlled temperature storage for rejuvenation prior to placement in transport containers and cooling towards 10°C must be kept to a minimum and should not exceed 4 hours.
- Each 50 mL of rejuvesol Solution contains sodium pyruvate 0.550 g, inosine 1.34 g, adenine 0.034 g, dibasic sodium phosphate (heptahydrate) 0.730 g, and monobasic sodium phosphate (monohydrate) 0.311 g, in water for injection, pH 6.7-7.4.

- A validated closed manual washing procedure should be used following rejuvenation. The washing protocol used must be validated to ensure effective removal of the rejuvenating solution.
- Monitoring of component volumes and temperatures must be used to assure that the washing process has taken place on every unit rejuvenated.
- If the washing process results in the transfer of the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation identification number is put on the component pack of Red Cells, Rejuvenated and Washed, Leucocyte Depleted.
- Red Cells, Rejuvenated, Washed, Leucocyte Depleted should be administered through a CE/UKCA /UKNI marked transfusion set.

A3.4.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- REDJUVENATE trial Red Cells, Leucocyte Depleted* and volume (note the trial is blinded and therefore control and treatment arms are labelled the same but that they can be differentiated through PULSE).
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the suspending solution
- the date and time of preparation
- the expiry date and time*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.4.3: Storage

The component should be used as soon as possible. Where the component has been produced in a closed system and storage is required the component should be stored at a core temperature of 4 ±2°C and used within 72 hours of rejuvenation if suspended in SAGM.

A3.4.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 of the Red Book, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown in Table A3.4 shall meet the specified values. Provided the component is

prepared from a process that is validated for leucocyte removal, testing of washed red cells for residual leucocytes is not required.

Table A3.4 Red Cells, Rejuvenated and Washed, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	100% (all tests are on the day after manufacture and are retrospective quality monitoring, not pre-release criteria)	Within locally specified volume range
Haemoglobin content		>=40 g/unit
Haematocrit		0.50 – 0.70
Haemolysis [1]		<0.3%
ATP and/or 2,3-DPG		ATP: >6 mol/g Hb 2,3-DPG: >9 mol/g Hb
Supernatant potassium (as a marker of washing efficiency)		<3.5 mmol/L
Leucocyte count [2] (pre-wash)	As per sections 6.3 and 7.1.1	<1 × 10^6/unit
[1] Note: this measurement is not at end of shelf-life as for standard red cell components		
[2] Methods validated for counting low numbers of leucocytes must be used. Since the starting material Red Cells in Additive Solution are monitored and controlled for LD performance, the final component does not require a leucocyte count.		

A3.4.5: Transportation

For general guidelines, see section 6.11.

- For red cell components, transit containers, packing materials and procedures must have been validated to ensure the component core temperature can be maintained between 2°C and 6°C during transportation between trial sites, and NHSBT prior to rejuvenation.
- Following rejuvenation and washing, red cells must be placed in transport containers with packing materials and procedures that are validated to reduce the core temperature of red cells to below 10° C within 3 hours and maintain a temperature below 10°C for at least 10 hours. Red Cells, Rejuvenated and Washed, Leucocyte Depleted should be returned to controlled storage at 2-6°C as soon as possible thereafter, and no later than 10 hours from being placed in the transport container to ensure that the core temperature does not exceed 10°C.

A3.4.6: Removal from and return to 2-6°C controlled storage within hospitals

For occasions when Red Cells, Rejuvenated and Washed, Leucocyte Depleted are removed from 2-6 °C controlled storage (e.g., when issued to a clinical area immediately prior to transfusion) then:

- The unit should not be returned to the issue location refrigerator for re-issue.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

A3.5: Red Cells for Neonates and Infants, Leucocyte Depleted, Washed

A red cell component (>=250 mL) suitable for neonates and infants under 1 year that contains less than 1×10^6 leucocytes (per starting component), which has been washed with a validated solution. The Red Cells for Neonates and Infants, Leucocyte Depleted (LD), Washed will be divided into approximately equal volumes using a closed system.

A3.5.1: Technical information

- The amount of residual protein will depend on the washing protocol. Washing can be performed by interrupted or continuous flow centrifugation.
- The use of validated closed system washing procedures that incorporate chilled validated solution for suspension is recommended. This will minimise the risk of bacterial growth and help to produce a component that meets the transit temperature requirements.
- If the washing process results in the transfer of the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation identification number is put on the component pack of Red Cells, Washed, LD.
- Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- Red Cells for Neonates and Infants, LD, Washed should be administered through a CE/UKCA/UKNI marked transfusion set.
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.

A3.5.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells for Neonates and Infants, Leucocyte Depleted, Washed* and volume
- the blood component producer’s name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection

- the expiry date*
- the temperature of storage
- the blood pack lot number*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection

A3.5.3: Storage

For general guidelines, see section 6.7.

For top-up transfusions of neonates and infants under 1 year, where the component has been produced in a closed system and storage is required the component should be stored at a core temperature of 4 ±2°C and used up to 14 days if stored in SAGM. Where alternative additive solutions are used, storage will be defined through validation.

A3.5.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV.

Furthermore, a minimum of 75% of those components tested for the parameters shown in Table A3.5 shall meet the specified values. Provided the component is prepared from a process that is validated for leucocyte removal, testing of washed red cells for residual leucocytes is not required.

Table A3.5 Red Cells for Neonates and Infants, LD, Washed – additional tests

Parameter	Frequency of test	Specification
Volume	100% unless the process capability by SPC demonstrates otherwise	Within locally specified volume range
Haemoglobin content		Locally defined
Haematocrit [1]		0.50–0.70
Haemolysis at end of storage		0.8% of red cell mass
Residual protein [2]		<0.5 g/starting component
Leucocyte count (pre-wash)[3,4]	As per sections 6.3 and 7.1.1	$<1 \times 10^6$/starting component
[1] Units tested and found to have haematocrit <0.40 or >0.70 should not be issued for transfusion		
[2] Tested in the starting component (Red Cells, Washed, LD)		
[3] Tested in the pre-wash component		
[4] Methods validated for counting low numbers of leucocytes must be used		

A3.5.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

Provisional Component

A3.6: Whole Blood, Leucocyte Depleted, for Clinical Studies

A unit of blood collected into CPD anticoagulant, containing red cells, plasma and platelets as well as less than 1×10^6 leucocytes.

A3.6.1: Technical information

- Whole Blood, Leucocyte Depleted (LD), for Clinical Studies is intended for the treatment of major haemorrhage only, and currently only as part of clinical studies, initially in the pre-hospital situation, with transfusion of a maximum of 4 units (or weight-related equivalent for children) prior to switching to standard component therapy.
- A unit of whole blood collected in the UK currently consists of 470 mL ±10% of blood from a suitable donor (see Chapter 3), plus 63 mL of CPD anticoagulant, which is then LD, and stored in an approved container. The Eurobloodpack contains 66.5 mL of anticoagulant and is suitable for the collection of 475 mL ±10%, although in the UK a volume of 495 mL will not be exceeded.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for direct clinical use.
- Donations should be selected from male donors as a TRALI risk reduction measure.
- The component should be produced from group O RhD negative, Kell negative donations

- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B

- Whole Blood, Leucocyte Depleted, for Clinical Studies should be administered through a CE/UKCA /UKNI marked transfusion set.

A3.6.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Whole Blood, Leucocyte Depleted, for Clinical Studies* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.6.3: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 21 days at a core temperature of 4 ±2°C.

- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre to cover such eventualities
    - adequate records of the incident are compiled and retained.

A3.6.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the

parameters shown in Table A3.6 shall meet the specified values. Table A3.6 does not include plasma quality monitoring parameters as the component will not be within the Blood Service at the end of shelf-life. This should be revalidated annually.

Table A3.6 Whole Blood, Leucocyte Depleted, for Clinical Studies – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	Within locally defined nominal range
Platelet count		
Haemoglobin content		>=40 g/unit
Haemolysis	As per section 7.1.3	<0.8% of red cell mass
Leucocyte count [2]	As per sections 6.3 and 7.1.1	$<1 \times 10^6$/unit
[1] After volume losses resulting from leucodepletion		
[2] Methods validated for counting low numbers of leucocytes must be used. 100% of units must be monitored for residual leucocytes and any units measured and found to be $>5 \times 10^6$/Unit must not be issued for clinical use.		

A3.6.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

A3.6.6: Removal from and return to 2-6°C controlled storage within hospitals / pre-hospital clinical environment

For occasions when units of Whole Blood, Leucocyte Depleted, for Clinical Studies are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- the time out of a controlled temperature environment should be restricted to under 30 minutes and on one occasion only.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

Provisional component

A3.9: Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw

The pooled component represents a source of concentrated FVIII, von Willebrand factor, fibrinogen, FXIII and fibronectin from primary cryoprecipitate components derived from units of fresh frozen plasma. The plasma from which the cryoprecipitate was produced contains less than 1×10^6 leucocytes per primary component.

A3.9.1: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw is the cryoglobulin fraction of plasma obtained by thawing and pooling five single cryoprecipitate components or pooling five single cryoprecipitate components immediately after production from thawed fresh frozen plasma.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- For storage, Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Initial process validation must ensure that for a minimum of 20 tested Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw components a minimum of 75% of those components tested for the parameters shown in Table A3.9 shall meet the specified values.
- Annual process validation is acceptable for quality monitoring purposes, provided that the primary components, Fresh Frozen Plasma, Leucocyte Depleted and/or Cryoprecipitate, Leucocyte Depleted, Extended Shelf-life Postthaw are separately monitored as part of monthly testing. If this is not the case, test monthly 1% or as determined by statistical process control (if <=10 components produced per month then test every available component), of Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw components. A minimum of 75% of those components tested for the parameters shown in Table A3.9 shall meet the specified values.
- A secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.

- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw should be transfused through a CE/UKCA/UKNI marked transfusion set.

A3.9.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing units*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing if maintained at 22 ±2°C, or up to a maximum of 120 hours of thawing if stored at 4 ±2°C
- the name, composition and volume of anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.9.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.

- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuumsealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.

- Protocols must be in place to ensure that the equipment is regularly cleaned and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble precipitate is visible and that the container is intact.

- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component should either be used or returned to 4 ±2°C within a maximum of 4 hours if maintained below 24°C. Extended Shelf-life Post-thaw cryoprecipitate may be stored up

to 120 hours at 4 ±2°C following thawing. Following storage at 4 ±2°C, Extended Shelf-life Post-thaw cryoprecipitate must be briefly warmed using a plasma thawing device at 33-37°C until any precipitate has gone back into solution (through visual inspection). This should occur in the majority of units within 5 minutes, and should not exceed 20 minutes. Once re-warmed, Extended Shelf-life Post-thaw cryoprecipitate should not be placed back in the refrigerator.

- Transfusion of Extended Shelf-life Post-thaw cryoprecipitate should be completed within 4 hours of issue out of a controlled temperature environment unless it fulfils the criteria to be returned to storage at 4 ±2°C and if this occurs on one occasion only.

A3.9.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown at Table A3.9 shall meet the specified values.

Table A3.9 Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-Life Post-Thaw – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	100 – 250 mL
Fibrinogen	Refer to Technical information (section A3.9.1) above	>=700 mg/unit
FVIII		>=350 IU/unit
Leucocyte count [1]	As per sections 6.3 and 7.1.1	$<1 \times 10^6$/unit in the starting component
[1] Pre-freeze methods validated for counting low numbers of leucocytes must be used		

A3.9.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

Provisional component

A3.10: Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted

Plasma that has been obtained by apheresis from vaccinated donors who have very high titre antibodies (Roche Elisa of at least 20,000 units/ml or equivalent), for the treatment of patients with COVID-19. The plasma contains less than 1×10^6 leucocytes per component and has been rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

A3.10.1: Technical information

- Plasma can be selected from male or female donors. Female donors must be screened and negative for HLA/HNA antibodies, as a TRALI risk reduction measure. Plasma should only be selected as CP for treatment of patients with COVID-19 if it is validated to contain a minimum concentration of SARS-CoV-2 antibody levels according to national clinical guidelines.

- Greater FVIII yields will be obtained when the plasma is rapidly frozen to –25°C or below.

- The method of preparation should be validated to ensure there is no evidence of significant activation at 24 hours shelf life, with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII concentration. If plasma collected for CP were to be re-manufactured for any other purpose these procedures must be fully validated and in accordance with the specification of the alternative component.

- Component samples collected for the quality monitoring assessment of FVIII should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.

- Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted should be administered through a CE /UKCA/UKNI marked transfusion set.

A3.10.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted* and volume
- the blood component producer’s name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within four hours of thawing if maintained at 22 ±2°C, or up to a maximum of 24 hours of thawing if stored at 4 ±2°C.
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity

Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.10.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a water bath or other equipment designed for the purpose, within a vacuumsealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is regularly cleaned and maintained to minimise the risk of bacterial contamination. After thawing, and at the time of administration, the content should be inspected to ensure that no insoluble precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C or up to a maximum of 24 hours if stored at 4 ±2°C.
- Transfusion of Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted should be completed within 4 hours of issue out of a controlled temperature environment.

A3.10.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1 and Table A3.10), a minimum of 75% of those components tested for the parameters shown in Table A3.10 shall meet the specified values with the exception of FVIII.

Table A3.10 Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	Stated volume ±10%
Total protein		>=50 g/L
Platelet count [1,2]		<30 × 10^9/L
Red cell count [1]		<6 × 10^9/L
FVIII [3,4]		Mean >= 0.70 IU /mL
Leucocyte count [1,5,6]	As per sections 6.3 and 7.1.1	<1 × 10^6/unit

[1] Pre-freeze in starting component
[2] Units measured and found to have a platelet count >100 × 10^9/L should not be issued for transfusion
[3] Units measured and found to have <0.3 IU/mL should not be issued for transfusion
[4] A minimum of 90% of those components tested should have >=0.50 IU/mL
[5] Methods validated for counting low numbers of leucocytes must be used
[6] 90% units should have less than 1 × 10^6 leucocytes and more than 99% of units should contain less than 5 × 10^6 leucocytes, both with 95% confidence

A3.10.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

A3.11: Dried Plasma, Leucocyte Depleted

Plasma that has been obtained from whole blood or by apheresis (as defined in section 7.3). The starting plasma must be suitable for the production of FFP. The plasma contains less than 1 × 10^6 leucocytes per component and has been dried using a validated system demonstrated to maintain the activity of labile coagulation factors.

A3.11.1: Technical information

- Dried Plasma, Leucocyte Depleted is intended for the treatment of major haemorrhage currently only as part of clinical studies.
- Dried Plasma, Leucocyte Depleted should be manufactured from group A donations that are negative for high-titre anti-B antibodies.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable to produce plasma components for direct clinical use.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII:C yields will be obtained when the plasma is separated as soon as possible after venepuncture and rapidly frozen to –25°C or below.
- The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII:C concentration.

- Component samples collected for the quality monitoring assessment of FVIII:C should be representative of the distribution of ABO groups issued for clinical use.

- Dried Plasma, Leucocyte Depleted should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.11.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Dried Plasma, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the dried component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 6 hours of rehydration if maintained at ambient temperature
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.11.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 2–25°C for a maximum of 6 months.

- The component should be rehydrated with 200 mL sterile water for injection (SWFI) according to a validated procedure.

- After reconstitution, and at the time of administration, the content should be inspected to ensure that no insoluble plasma is visible and that the container is intact.

- Once rehydrated, the component must not be frozen and should be transfused as soon as possible. If delay is unavoidable, the component should be transfused within 6 hours.

A3.11.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown in Table A3.11 shall meet the specified values with the exception of FVIII:C.

Table A3.11 Dried Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume [1]	10 units per month of production	Within locally defined nominal range
Total protein		>=50 g/L
Platelet count [2,3]		<30 × 10^9/L
Red cell count [2,3]		<6 × 10^9/L
FVIII:C [4]		Mean >=0.60 IU/mL
vWF:RiCof		Mean >=0.40 IU/mL
Fibrinogen		Mean >=2 g/L
Bacterial screening		Negative
Leucocyte count [2,3,5]	As per sections 6.3 and 7.1.1	<1 × 10^6/unit
[1] Units of starting plasma should meet the manufacturers specification of 265-285 mL		
[2] Residual cellular content need not be assessed if the starting material is already monitored		
[3] Pre-freeze in starting component		
[4] A minimum of 90% of those components tested should have >=0.50 IU/mL		
[5] Methods validated for counting low numbers of leucocytes must be used		

A3.11.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature of <=25°C during transportation.

A3.12: Platelets, Apheresis, in Additive Solution and Plasma, Leucocyte Depleted

A single-donor platelet component containing less than 1 × 10^6 leucocytes where the suspending medium comprises 30-50% plasma and 50-70% additive solution and anticoagulant.

A3.12.1: Technical information

- Platelets, Apheresis, in Additive Solution and Plasma, Leucocyte Depleted may be collected by a variety of apheresis systems using different protocols. Since platelet yields may vary, each procedural protocol must be fully validated, documented and specifications set accordingly.

- If a double or triple dose is collected, the platelet concentrate must be temporarily split, as a continuous part of the collection process, into the storage packs integral to the collection set so that the capacity of an individual pack is not exceeded.

- If filtration is used, the recommended capacity of the filter should not be exceeded.

- If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.

- The proportion of plasma carried over into the final component should be determined by validation and will depend upon the type of additive solution and platelet storage pack. Re-validation of the proportion of plasma carried over must be performed at least annually on a minimum of 25 units and after any changes to collection method.

- The volume of suspension medium must be sufficient to maintain the pH at >=6.4 at the end of the shelf life of the component.

- The plasma from group O donors should be tested for high-titre anti-A and anti-B, and ‘high-titre negative’ units labelled. The testing method and acceptable limits should be defined (see also Chapter 9). Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy.

- Platelets, Apheresis, in Additive Solution and Plasma, Leucocyte Depleted should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.12.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, Apheresis in Additive Solution and Plasma, Leucocyte Depleted* and volume
- the blood component producer’s name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.12.3: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.
- Packs currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 5 days in a closed system. Appropriate pack and platelet concentration combinations may allow storage up to 7 days, but due to concerns over bacterial contamination would require either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen reduction procedure.
- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.
- Platelets should be gently agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided that no single interruption lasts for more than eight hours, and the total length of all interruptions is no longer than 24 hours.

A3.12.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 and leucocyte counting (see section 6.3 and 7.1.1), a minimum of 75% of those components tested for the parameters shown at Table A3.12 shall meet the specified values.

Table A3.12 Platelets, Apheresis, in Additive Solution and Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if <=10 components produced per month then test every available component)	Within locally defined nominal range
Platelet count [2]		>=240 × 10^9/unit
pH at end of shelf life [3]	If less than 10 per month, every available component	>=6.4
Leucocyte count [4]	As per sections 6.3 and 7.1.1	<1 × 10^6/unit
[1] Units measured and found to be <150 mL or >380 mL should only be issued for transfusion under concessionary release		
[2] Units tested and found to have <160 × 10^9/unit, or more than the maximum recommended by the manufacturer of the storage pack where stated, should only be issued for transfusion under concessionary release		
[3] A minimum of 95% of components tested shall meet the specified values		
[4] Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

A3.12.5: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.

- Plastic overwraps should be removed prior to storage.