

## Guidelines for the Blood Transfusion Services

### Annexe 3: Provisional Components

<http://www.transfusionguidelines.org/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  $1 \times 10^6$  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  $\geq 6.4$  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

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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

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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  $22 \pm 2^{\circ}\text{C}$  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  $22 \pm 2^{\circ}\text{C}$  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 $\leq 10$ components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count <sup>1</sup>		$\geq 240 \times 10^9/\text{pool}$
pH at end of shelf life	If less than 10 per month, every available component	$\geq 6.4$
Leucocyte count <sup>2</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6/\text{pool}$
<sup>1</sup> Units measured and found to have $< 160 \times 10^9/\text{pool}$ should not be issued for transfusion		
<sup>2</sup> 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  $22 \pm 2^{\circ}\text{C}$  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  $1 \times 10^6$  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

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- 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

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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  $4 \pm 2^{\circ}\text{C}$ .
- Variation from the core temperature of  $4 \pm 2^{\circ}\text{C}$  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  $10^{\circ}\text{C}$  and not less than  $1^{\circ}\text{C}$  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	190 – 330 mL
Haemoglobin content <sup>1</sup>	(if $\leq 10$ components produced per month then test every available component)	$\geq 40$ g/unit
Haemolysis	As per section 7.1.3	$< 0.8\%$ of red cell mass
Leucocyte count <sup>2</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6$ /unit
<sup>1</sup> Units measured and found to have $< 30$ g/unit should not be issued for transfusion		
<sup>2</sup> 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  $2^{\circ}\text{C}$  and  $10^{\circ}\text{C}$  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  $1 \times 10^6$  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  $4 \pm 2^\circ\text{C}$  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 <sup>1</sup>	1% or as determined by statistical process control (if $\leq 10$ components produced per month then test every available component)	Stated volume $\pm 10\%$
Haematocrit <sup>2</sup>		$< 30 \times 10^9/\text{L}$
Haemoglobin content <sup>3</sup>		$< 0.2 \times 10^9/\text{L}$
FVIII <sup>3</sup>		[ $\geq X$ IU/mL ]
Leucocyte count <sup>4</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6/\text{unit}$
<sup>1</sup> Units measured and found to be outside of the range 200 to 360 mL should not be issued for transfusion		
<sup>2</sup> Pre-freeze in starting component		
<sup>3</sup> Units measured and found to have $< 0.3$ IU/mL should not be issued for transfusion		
<sup>4</sup> 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  $1 \times 10^6$  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<sup>®</sup> Red Blood Cell Processing Solution (rejuvesol Solution) and incubation at  $37 \pm 2^\circ\text{C}$  for 60 mins  $\pm 5$  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**

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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**

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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  $4 \pm 2^{\circ}\text{C}$  and used within 72 hours of rejuvenation if suspended in SAGM.

#### **A3.4.4: Testing**

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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		$\geq 40$ g/unit
Haematocrit		0.50 – 0.70
Haemolysis <sup>1</sup>		<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 <sup>2</sup> (pre-wash)	As per sections 6.3 and 7.1.1	$<1 \times 10^6$ /unit
<sup>1</sup> Note: this measurement is not at end of shelf-life as for standard red cell components		
<sup>2</sup> 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.

## Provisional Component

### A3.5: Red Cells and Plasma, Leucocyte Depleted

A unit of blood collected into CPD anticoagulant, containing less than  $1 \times 10^6$  leucocytes.

#### A3.5.1: Technical information

- Red Cells and Plasma, Leucocyte Depleted (LD) is intended for the treatment of major traumatic haemorrhage 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  $\pm$ 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  $\pm$ 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 made 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
- Red Cells and Plasma, LD, should be administered through a CE/UKCA/UKNI marked transfusion set.

#### 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 and Plasma, Leucocyte Depleted\* 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*

### **A3.5.3: Storage**

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 14 days at a core temperature of  $4 \pm 2^{\circ}\text{C}$ .
- Variation from the core temperature of  $4 \pm 2^{\circ}\text{C}$  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  $10^{\circ}\text{C}$  and not less than  $1^{\circ}\text{C}$  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.

### **A3.5.4: 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), a minimum of 75% of those components tested for the parameters shown in Table A3.5 shall meet the specified values. Table A3.5 does not include plasma quality monitoring parameters as the Red Cells and Plasma, Leucocyte Depleted component will not be within the Blood Service at the end of shelf-life and as plasma quality at the point of production is already monitored as part of the process of manufacturing Fresh Frozen Plasma, Leucocyte Depleted from whole blood, using the same filtration process.

**Table A3.5 Red Cells and Plasma, Leucocyte Depleted – additional tests**

Parameter	Frequency of test	Specification
Volume <sup>1</sup>	1% or as determined by statistical process control	470 $\pm$ 50 mL
Haemoglobin content	(if $\leq 10$ components produced per month then test every available component)	$\geq 40$ g/unit
Haemolysis	As per section 7.1.3	$< 0.8\%$ of red cell mass
Leucocyte count <sup>2</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6$ /unit
<sup>1</sup> After volume losses resulting from leucodepletion		
<sup>2</sup> Methods validated for counting low numbers of leucocytes must be used		

### A3.5.5: Transportation

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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.

### A3.5.6: Removal from and return to 2-6°C controlled storage within hospitals / pre-hospital clinical environment

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For occasions when Red Cells and Plasma, Leucocyte Depleted 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

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

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

#### A3.6.1: Technical information

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- 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  $\pm$ 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  $\pm$ 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

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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

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For general guidelines, see section 6.7.

- The component may be stored for a maximum of 21 days at a core temperature of  $4 \pm 2^\circ\text{C}$ .
- Variation from the core temperature of  $4 \pm 2^\circ\text{C}$  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 <sup>1</sup>	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 <sup>2</sup>	As per sections 6.3 and 7.1.1	<1 × 10 <sup>6</sup> /unit
<sup>1</sup> After volume losses resulting from leucodepletion		
<sup>2</sup> 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 × 10 <sup>6</sup> /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.

#### **A3.7 Convalescent Plasma (COVID-19), FFP, Leucocyte Depleted**

This specification is now redundant and has been moved to Annex 4: Redundant Components.

#### **A4.2 Convalescent Plasma (COVID-19), FFP, Leucocyte Depleted**

#### **A3.8 Convalescent Plasma (COVID-19), FFP, for Neonates and Infants, Leucocyte Depleted**

This specification is now redundant and has been moved to Annex 4: Redundant Components.

#### **A4.3 Convalescent Plasma (COVID-19), FFP, for Neonates and Infants, Leucocyte Depleted**

### **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  $1 \times 10^6$  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  $-25^{\circ}\text{C}$  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  $\leq 10$  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  $22 \pm 2^{\circ}\text{C}$ , or up to a maximum of 120 hours of thawing if stored at  $4 \pm 2^{\circ}\text{C}$
- 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**

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For general guidelines, see section 6.7.

- The component should be stored at a core temperature of  $-25^{\circ}\text{C}$  or below for a maximum of 36 months.
- Although a storage temperature below  $-25^{\circ}\text{C}$  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  $37^{\circ}\text{C}$ ; temperatures between  $33^{\circ}\text{C}$  and  $37^{\circ}\text{C}$  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  $4 \pm 2^{\circ}\text{C}$  within a maximum of 4 hours if maintained below  $24^{\circ}\text{C}$ . Extended Shelf-life Post-thaw cryoprecipitate may be stored up to 120 hours at  $4 \pm 2^{\circ}\text{C}$  following thawing. Following storage at  $4 \pm 2^{\circ}\text{C}$ , Extended Shelf-life Post-thaw cryoprecipitate must be briefly warmed using a plasma thawing device at  $33-37^{\circ}\text{C}$  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  $4 \pm 2^{\circ}\text{C}$  and if this occurs on one occasion only.

### **A3.9.4: Testing**

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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 <sup>1</sup>	As per sections 6.3 and 7.1.1	<1 × 10 <sup>6</sup> /unit in the starting component
<sup>1</sup> 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<sup>6</sup> 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

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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  $22 \pm 2^{\circ}\text{C}$ , or up to a maximum of 24 hours of thawing if stored at  $4 \pm 2^{\circ}\text{C}$ .
- 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

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For general guidelines, see section 6.7.

- The component should be stored at a core temperature of  $-25^{\circ}\text{C}$  or below for a maximum of 36 months.
- Although a storage temperature below  $-25^{\circ}\text{C}$  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  $37^{\circ}\text{C}$ ; temperatures between  $33^{\circ}\text{C}$  and  $37^{\circ}\text{C}$  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  $22 \pm 2^{\circ}\text{C}$  or up to a maximum of 24 hours if stored at  $4 \pm 2^{\circ}\text{C}$ .
- 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 $\leq 10$ components produced per month then test every available component)	Stated volume $\pm 10\%$
Total protein		$\geq 50$ g/L
Platelet count <sup>1,2</sup>		$< 30 \times 10^9/\text{L}$
Red cell count <sup>1</sup>		$< 6 \times 10^9/\text{L}$
FVIII <sup>3,4</sup>		Mean $\geq 0.70$ IU/mL
Leucocyte count <sup>1,5,6</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6/\text{unit}$
<sup>1</sup> Pre-freeze in starting component		
<sup>2</sup> Units measured and found to have a platelet count $> 100 \times 10^9/\text{L}$ should not be issued for transfusion		
<sup>3</sup> Units measured and found to have $< 0.3$ IU/mL should not be issued for transfusion		
<sup>4</sup> A minimum of 90% of those components tested should have $\geq 0.50$ IU/mL		
<sup>5</sup> Methods validated for counting low numbers of leucocytes must be used		
<sup>6</sup> 90% units should have less than $1 \times 10^6$ leucocytes and more than 99% of units should contain less than $5 \times 10^6$ 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.