

## Guidelines for the Blood Transfusion Services

### 7.5: Plasma Components

<http://www.transfusionguidelines.org/red-book/chapter-7/7-5>

## 7.5: Plasma Components

Plasma components are manufactured from whole blood or apheresis collections. These components are rapidly frozen to retain labile clotting factors. All plasma components are leucocyte depleted. Some components undergo additional processing steps described.

### Specifications

#### 7.5.1: Fresh Frozen Plasma, Leucocyte Depleted

Plasma that has been obtained from whole blood or by apheresis. The plasma contains less than  $1 \times 10^6$  leucocytes per component and has been rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

##### 7.5.1.1: 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 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 yields will be obtained when the plasma is separated as soon as possible after venepuncture and rapidly frozen to  $-25^{\circ}\text{C}$  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 concentration.
- 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.
- Fresh Frozen Plasma, Leucocyte Depleted should be administered through a CE/UKCA/UKNI marked transfusion set.

##### 7.5.1.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

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

- Fresh Frozen 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 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  $4 \pm 2^{\circ}\text{C}$ , depending on indication
- 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*

### **7.5.1.3: 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 vacuum-sealed 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. If to be stored thawed for an extended period ( $>24$  hours from thawing), thawing methods that do not directly expose units to water must be used to minimise bacterial contamination.
- 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 120 hours if stored at  $4 \pm 2^{\circ}\text{C}$ , but it should be borne in mind that extended post-thaw storage will result in a decline in the content of labile coagulation factors.
- Pre-thawed FFP that is out of a controlled temperature environment ( $4 \pm 2^{\circ}\text{C}$ ), can be accepted back into temperature controlled storage if this occurs on one occasion only of less than 30 minutes. Transfusion of FFP should be completed within 4 hours of issue out of a controlled temperature

environment.

- For indications other than unexpected major haemorrhage, the component should be used within 24 hours of thawing.

#### 7.5.1.4: 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 7.5.1 shall meet the specified values.

**Table 7.5.1 Fresh Frozen 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 $\pm 10\%$
Total protein		$\geq 50$ g/L
Platelet count <sup>2,3</sup>		$< 30 \times 10^9$ /L
Red cell count <sup>3</sup>		$< 6 \times 10^9$ /L
FVIII <sup>4,5</sup>		Mean $\geq 0.70$ IU/mL
Leucocyte count <sup>3,6</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6$ /unit
<sup>1</sup> Units measured and found to be $< 200$ mL or $> 340$ mL should only be issued for transfusion under concessionary release		
<sup>2</sup> Units with residual platelet count $> 100 \times 10^9$ /L should only be issued for transfusion under concessionary release		
<sup>3</sup> Pre-freeze in starting component		
<sup>4</sup> Units measured and found to have $< 0.30$ IU/mL should only be issued for transfusion under concessionary release		
<sup>5</sup> A minimum of 90% of those components tested should have $\geq 0.50$ IU/mL		
<sup>6</sup> Methods validated for counting low numbers of leucocytes must be used		

#### 7.5.1.5: 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.

#### 7.5.2: Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted

Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted, is plasma that has been obtained from whole blood or by apheresis, contains less than  $1 \times 10^6$  leucocytes and has been treated with a pathogen inactivation (PI) system. The PI system must be approved (CE/UKCA/UKNI marked) for this use, and must have been validated by the Blood Service.

Following PI treatment, the plasma is rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

### 7.5.2.1: Technical information

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- 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 or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted may be prepared from small pools of up to 12 individual donations if validated by the blood service and if in accordance with the specifications of the manufacturer of the PI system.
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII yields will be obtained when the plasma is separated as soon as possible after venepuncture, pathogen reduced and rapidly frozen to  $-25^{\circ}\text{C}$  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 concentration.
- It contains, on average, greater than 60% of the labile coagulation factors and naturally occurring inhibitors present in standard fresh frozen plasma.
- The PI system typically reduces the risk of infection from enveloped viruses (e.g. HBV, HCV, HIV) by at least one thousand-fold.
- 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.
- The level of removal of the activating agent prior to final storage should be validated, if such a step is included in the PI system.
- Intact white blood cells in the plasma should be reduced to less than  $1 \times 10^6$  per unit prior to exposure to the PI process.
- Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted should be administered through a CE /UKCA/UKNI marked transfusion set.

### 7.5.2.2: 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)

- Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted\* and the volume
- the name of the PI system used
- the blood component producer's name\*
- the donation 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 should be used within 4 hours of thawing if maintained at  $22 \pm 2^{\circ}\text{C}$  and 24 hours if maintained 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 allergy*

*to the compounds used for, or derived from, PI treatment*

### **7.5.2.3: 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 vacuum-sealed 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 may be stored and should be used within 4 hours if maintained at  $22 \pm 2^{\circ}\text{C}$  or 24 hours if stored at  $4 \pm 2^{\circ}\text{C}$ , but it should be borne in mind that extended post-thaw storage will result in a decline in the content of labile coagulation factors.

### **7.5.2.4: 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 in Table 7.5.2 shall meet the specified values.

**Table 7.5.2 Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted – additional tests**

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control	Within locally defined nominal volume range and within any limits specified for the PI process used
Platelet count <sup>1,2</sup>	(if $\leq 10$ components produced per month then test every available component)	$< 30 \times 10^9/L$
FVIII		$\geq 0.50$ IU/mL
Leucocyte count <sup>2,3</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6/unit$
<sup>1</sup> Units with residual platelet count $> 100 \times 10^9/L$ should only be issued for transfusion under concessionary release		
<sup>2</sup> Pre-freeze in starting component		
<sup>3</sup> Methods validated for counting low numbers of leucocytes must be used		

### 7.5.2.5: 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.

### 7.5.3: Cryoprecipitate, Leucocyte Depleted

The component provides a concentrated source of FVIII, and von Willebrand factor, fibrinogen, FXIII and fibronectin. It is derived from a unit of Fresh Frozen Plasma, Leucocyte Depleted. The plasma from which the Cryoprecipitate, Leucocyte Depleted is produced contains less than  $1 \times 10^6$  leucocytes per component.

#### 7.5.3.1: 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.
- Cryoprecipitate, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing a single donation of Fresh Frozen Plasma, Leucocyte Depleted (see section 7.5.1) at  $4 \pm 2^\circ C$ .
- 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, Leucocyte Depleted 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.
- Cryoprecipitate, Leucocyte Depleted should be administered through a CE/UKCA/UKNI marked transfusion set.

### 7.5.3.2: Labelling

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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, 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 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
- 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*

### 7.5.3.3: 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 vacuum-sealed 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 used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

#### 7.5.3.4: 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 7.5.3 shall meet the specified values.

**Table 7.5.3 Cryoprecipitate, 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)	Within locally defined nominal range
Fibrinogen		>=140 mg/unit
FVIII		>=70 IU/unit
Leucocyte count <sup>1,2</sup>	As per sections 6.3 and 7.1.1	<1 × 10 <sup>6</sup> /unit
<sup>1</sup> Methods validated for counting low numbers of leucocytes must be used		
<sup>2</sup> Pre-freeze in starting component		

#### 7.5.3.5: 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 thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

### 7.5.4: Cryoprecipitate, Pooled, Leucocyte Depleted

The pooled component provides a concentrated source of FVIII, von Willebrand factor, fibrinogen, FXIII and fibronectin. It is derived from units of Fresh Frozen Plasma, Leucocyte Depleted. The plasma from which the Cryoprecipitate, Pooled, Leucocyte Depleted is produced contains less than 1 × 10<sup>6</sup> leucocytes per primary component.

#### 7.5.4.1: 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 is the cryoglobulin fraction of plasma obtained by thawing and pooling five single Cryoprecipitate, Leucocyte Depleted components or pooling five single Cryoprecipitate, Leucocyte Depleted 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 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 components a minimum of 75% of those components tested for the parameters shown in Table 7.5.4 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 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 components. A minimum of 75% of those components tested for the parameters shown in Table 7.5.4 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 should be administered through a CE/UKCA/UKNI marked transfusion set.

#### 7.5.4.2: Labelling

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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\* 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 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

- 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*

#### **7.5.4.3: Storage**

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 be stored at ambient temperature and used within 4 hours.

#### **7.5.4.4: 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 7.5.4 shall meet the specified values.

**Table 7.5.4 Cryoprecipitate, Pooled, 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)	100 – 250 mL
Fibrinogen	Refer to Technical information (section 7.5.4.1) above	$\geq 700$ mg/unit
FVIII		$\geq 350$ IU/unit
Leucocyte count <sup>1</sup>	As per sections 6.3 and 7.1.1	$< 1 \times 10^6$ /unit in the starting component
<sup>1</sup> Pre-freeze in starting component		

#### 7.5.4.5: Transportation

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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.

### 7.5.5: Cryoprecipitate, Pooled, Pathogen Reduced, Leucocyte Depleted

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The component provides a concentrated source of FVIII, and von Willebrand factor, fibrinogen, Factor XIII and fibronectin. It is derived from units of Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted. The plasma from which the Cryoprecipitate, Pooled, Pathogen Reduced, Leucocyte Depleted is produced contains less than  $1 \times 10^6$  leucocytes per component.

#### 7.5.5.1: Technical information

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- 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, Pathogen Reduced, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing and pooling between 6 and 12 single Cryoprecipitate for Neonates and Infants, Pathogen Reduced, Leucocyte Depleted components.
- Plasma should be selected from male donors or screening of female donors for HLA/HNA antibodies should be considered, as a TRALI risk reduction strategy.
- For storage, Cryoprecipitate, Pooled, Pathogen Reduced, Leucocyte Depleted should be rapidly frozen to a core temperature of  $-25\text{ }^{\circ}\text{C}$  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.
- Annual process validation is acceptable for leucodepletion quality monitoring purposes, provided that the primary components, Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted 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, Pathogen Reduced, Leucocyte Depleted components. A minimum of 75% of those components tested for the parameters shown at Table 7.5.5 below shall meet the specified values.
- A secure system must be in place to ensure a full audit trail and the correct identification number is put on the final component pack.
- Cryoprecipitate, Pooled, Pathogen Reduced, Leucocyte Depleted, should be administered through a CE/UKCA/UKNI marked transfusion set.

### 7.5.5.2: Labelling

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The following shall be included on the component label:

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

- Cryoprecipitate, Pooled, Pathogen Reduced, Leucocyte Depleted \* and volume
- the name of the PI system used
- 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 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
- 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 allergy*

*to the compounds used for, or derived from, PI treatment.*

### 7.5.5.3: Storage

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- 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 vacuum sealed over wrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is  $37^{\circ}\text{C}$ ; temperatures between  $33-37^{\circ}\text{C}$  are acceptable.
- Protocols must be in place to ensure that the equipment is regularly cleaned and maintained to minimize 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 used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

### 7.5.5.4: 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 in Table 7.5.5 shall meet the specified values.

**Table 7.5.5 Cryoprecipitate, Pooled, Pathogen Reduced, 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)	100 – 300 mL
Fibrinogen		≥700 mg/unit
FVIII		≥250 IU/mL
Leucocyte count 1,2	As per sections 6.3 and 7.1.1	<1 × 10 <sup>6</sup> /unit
<sup>1</sup> Methods validated for counting low numbers of leucocytes must be used		
<sup>2</sup> Pre-freeze in starting component		

### 7.5.5.5: Transportation

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

### 7.5.6: Human Plasma for Fractionation, Leucocyte Depleted

Plasma that has been obtained from whole blood or by apheresis (as defined in section 7.1.4), containing less than 1 × 10<sup>6</sup> leucocytes per unit.

UK derived plasma may be used for the manufacture of immunoglobulins and albumin for domestic use provided all relevant vCJD risk mitigation measures currently in place for blood components for transfusion are applied and manufacturers submit an application to the MHRA to register the use of UK-sourced plasma including a product specific risk assessment. Manufacture of other blood products such as clotting factors is not currently permitted.

#### 7.5.6.1: Technical information

- All aspects of collection and manufacture, testing and storage should satisfy the requirements defined in the current British Pharmacopoeia monograph on Human Plasma for Fractionation.
- See chapters 3, 4, 5, 9 and 12 for specific details on donor selection, care and testing for Human Plasma for Fractionation, Leucocyte Depleted.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for clinical use.
- Plasma with a volume below 200 mL is not suitable for use.

- Plasma may be selected from both male and female donors. Female donors do not need additional screening for anti-HLA and anti-HNA antibodies.
- When obtained by plasmapheresis, plasma intended solely for the recovery of proteins that are not labile in plasma is frozen using validated conditions by cooling rapidly in a chamber at  $-20^{\circ}\text{C}$  or below as soon as possible and at the latest within 24 h of collection.
- When obtained from whole blood, plasma intended solely for the recovery of proteins that are not labile in plasma is separated from cellular elements and frozen using validated conditions in a chamber at  $20^{\circ}\text{C}$  or below as soon as possible and at the latest within 72 h of collection.
- Human Plasma for Fractionation, Leucocyte Depleted must not be transfused directly to patients.

### 7.5.6.2: Labelling

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For general guidelines, see section 6.6. The following shall be included on the label in eye readable format:

(\* = also in UKBTS approved barcode format)

- Human Plasma for Fractionation, Leucocyte Depleted\*
- Recovered or Source plasma
- the component volume
- the blood component producer's name
- the donation number and, if divided, sub-batch number\*
- the date of collection
- the expiry date of the frozen component\*
- the temperature of storage
- the blood pack lot number\*
- the name, composition and volume of the anticoagulant.
- Not for transfusion

### 7.5.6.3: Storage

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For general guidelines, see section 6.7.

- The component should be stored at a core temperature of  $-20^{\circ}\text{C}$  or below for a maximum of 36 months.
- Although frozen storage temperatures improve the preservation of labile and non-labile proteins, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

### 7.5.6.4: Testing

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- In addition to the mandatory and other tests required for blood donations for Human Plasma for Fractionation, Leucocyte Depleted described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), components should be tested for the parameters shown in Table 7.5.6.
- Total protein testing will be undertaken according to the British Pharmacopeia 2021 – Plasma for Fractionation (*Human Plasma for Fractionation, Ph. Eur. 10.3 monograph 0853*) or using equivalent, validated assays.

**Table 7.5.6 Human Plasma for Fractionation, Leucocyte Depleted – 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)	Stated volume ±10%
Total protein		Mean >=50 g/L
Platelet count <sup>1,2</sup>		<50 × 10 <sup>9</sup> /L
Red cell count <sup>1,2</sup>		<6 × 10 <sup>9</sup> /L
Leucocyte count <sup>2,3</sup>		As per sections 6.3 and 7.1.1
<sup>1</sup> A minimum of 90% of units tested should meet the required value		
<sup>2</sup> Pre-freeze in starting component		
<sup>3</sup> Methods validated for counting low numbers of leucocytes must be used		

More than 90% of leucocyte-depleted components from relevant processes must have less than  $1 \times 10^6$  leucocytes per unit and more than 99% of components must contain less than  $5 \times 10^6$  leucocytes per unit, both with 95% confidence.

Where plasma is collected into one container for final frozen storage the specification must be assessed based on volume ranges of 200 mL to <=400 mL for a single unit equivalent, >400 mL to <=680 mL for a double unit equivalent, and >680 mL for a triple unit equivalent collection.

#### 7.5.6.5: Transportation

For general guidelines, see section 6.11.

The frozen plasma should be stored and transported under conditions validated to maintain a temperature of –20°C or below. Temperature fluctuations in the plasma should be kept to a minimum during storage or transportation. A plasma temperature record during storage and transit of frozen plasma shall be available for inspection.

Short excursions of up to 30 minutes whilst preparing plasma for shipping are permissible.

Exceptional temperature deviations above –20°C, e.g. in the case of equipment failure, on one or more occasions are acceptable so long as the following conditions are met:

- the total period of time above –20°C does not exceed 72 hours
- the temperature does not exceed –15°C on more than one occasion
- the temperature does not exceed –5°C

Where plasma has been subject to temperature deviations during storage or transportation this must be recorded and reported to any third party receiving the plasma.

#### 7.5.7: Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted

Plasma which has been obtained from whole blood and subsequently recovered from the preparation of Cryoprecipitate, Leucocyte Depleted. The plasma from which the Plasma, Cryoprecipitate Depleted, Leucocyte Depleted was made contains less than  $1 \times 10^6$  leucocytes per component.

UK derived plasma may be used for the manufacture of immunoglobulins and albumin for domestic use provided all relevant vCJD risk mitigation measures currently in place for blood components for transfusion are applied and manufacturers submit an application to the MHRA to register the use of UK-sourced plasma including a product specific risk assessment. Manufacture of other blood products such as clotting factors is not currently permitted.

#### 7.5.7.1: Technical information

- All aspects of collection and manufacture, testing and storage should satisfy the requirements defined in the current British Pharmacopoeia monograph on Human Plasma for Fractionation.
- See chapters 3, 4, 5, 9 and 12 for specific details on donor selection, care and testing for Human Plasma for Fractionation, Cryoprecipitate depleted, Leucocyte Depleted.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for clinical use.
- Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted should be held at ambient for no more than 4 hours after processing before being rapidly frozen to a core temperature of  $-25^{\circ}\text{C}$  or below, following locally validated processes.

#### 7.5.7.2: Labelling

For general guidelines, see section 6.6. The following shall be included on the label in eye readable format:

(\* = also in UKBTS approved barcode format)

- Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted\*
- Recovered or Source plasma
- the component volume
- the blood component producer's name
- the donation number and, if divided, sub-batch number\*
- the date of collection
- the expiry date of the frozen component\*
- the temperature of storage
- the blood pack lot number\*
- the name, composition and volume of the anticoagulant.
- Not for transfusion

#### 7.5.7.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of  $-20^{\circ}\text{C}$  or below for a maximum of 36 months.

- Although frozen storage temperatures improve the preservation of labile and non-labile proteins, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

#### 7.5.7.4: Testing

- In addition to the mandatory and other tests required for blood donations for Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted described in Chapter 9, and leucocyte counting (see sections 6.3 and 7.1.1), components should be tested for the parameters shown in Table 7.5.7.
- Total protein testing will be undertaken according to the British Pharmacopeia 2021 – Plasma for Fractionation (*Human Plasma for Fractionation, Ph. Eur. 10.3 monograph 0853*) or using equivalent, validated assays.
- There is no requirement for FVIII testing.

**Table 7.5.7 Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted – 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)	Stated volume ±10%
Total protein		Mean >=50 g/L
Platelet count <sup>1,2</sup>		<50 × 10 <sup>9</sup> /L
Red cell count <sup>1,2</sup>		<6 × 10 <sup>9</sup> /L
Leucocyte count <sup>2,3</sup>	As per sections 6.3 and 7.1.1	<1 × 10 <sup>6</sup> /unit
<sup>1</sup> A minimum of 90% of units tested should meet the required value		
<sup>2</sup> Pre-freeze in starting component		
<sup>3</sup> Methods validated for counting low numbers of leucocytes must be used		

More than 90% of leucocyte-depleted components from relevant processes must have less than  $1 \times 10^6$  leucocytes per unit and more than 99% of components must contain less than  $5 \times 10^6$  leucocytes per unit, both with 95% confidence.

Where Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted is collected into one container for final frozen storage the specification must be assessed based on locally set minimum and maximum volumes.

#### 7.5.7.5: Transportation

For general guidelines, see section 6.11.

The frozen Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted should be stored and transported under conditions validated to maintain a temperature of  $-20^{\circ}\text{C}$  or below. Temperature fluctuations in the plasma should be kept to a minimum during storage or transportation. A plasma temperature record during storage and transit of frozen plasma shall be available for inspection.

Short excursions of up to 30 minutes whilst preparing Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted for shipping are permissible.

Exceptional temperature deviations above  $-20^{\circ}\text{C}$ , e.g. in the case of equipment failure, on one or more occasions are acceptable so long as the following conditions are met:

- the total period of time above  $-20^{\circ}\text{C}$  does not exceed 72 hours
- the temperature does not exceed  $-15^{\circ}\text{C}$  on more than one occasion
- the temperature does not exceed  $-5^{\circ}\text{C}$

Where Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted has been subject to temperature deviations during storage or transportation, this must be recorded and reported to any third party receiving the Human Plasma for Fractionation, Cryoprecipitate Depleted, Leucocyte Depleted.