

RESPONSES TO OPEN CONSULTATION
on Draft Technical Requirements for blood and blood components

ANNEX III
Storage and Freezing

	Subject	Original text	Proposed modification	Justification for modification
PPTA	All Annex III	Storage and Freezing	Storage and Freezing* * = does not apply to plasma intended for fractionation, for which the European Pharmacopoeia Monograph 853 (Human Plasma for Fractionation) applies	Internationally, the European Pharmacopoeia Monograph is already defining storage and freezing for plasma and is well accepted worldwide, respectively already mandatory in all European countries.
Sweden	Title	Storage and Freezing	Change title to Storage, transport and distribution requirements. Replace the wording and the tables as suggested by EBA	To fit the wording of Directive article 29 e) The proposal of EBA reflects the current science.
EMEA	Title	“	STORAGE AND FREEZING* <u>*The conditions of freezing and storage of plasma for fractionation have to comply with the relevant Ph. Eur. monograph, Human Plasma for Fractionation.</u>	Storage and freezing of plasma for fractionation is outside of the scope of the Blood Directive. A cross-reference to the relevant requirements would make it clear that the text does not apply to plasma for fractionation.
France	Title	“	Replace with <i>Storage And Transport Requirements For Liquid And Cryopreserved Components</i>	
Denmark Finland United Kingdom	Title	“	Change the title to: Storage And Transport Requirements For Liquid And Cryopreserved Components Replace the tables with the following (see Appendix).	Rationale: The below layout avoids imprecision and reflects the current science. All storage, including freezing, must be done using approved devices; more specific directions are therefore unnecessary in this Directive and may be in conflict with the devices Directive.
EBA	Title	“	Replace with <i>Storage And Transport Requirements For Liquid And Cryopreserved Components</i>	

France	A. Storage B. Freezing	Tables on the pages 8 - 10	Replace the tables A. and B. with the below tables and text (see Appendix).	The below layout avoids imprecision and reflects the current scene. All storage, including freezing, must be done using approved devices; more specific directions are therefore unnecessary in this Directive and may be in conflict with the Directive 93/42/EEC.
EBA	C. Storage D. Freezing		Replace the tables A. and B. with the below tables and text (See Appendix)	The below layout avoids imprecision and reflects the current scene. All storage, including freezing, must be done using approved devices; more specific directions are therefore unnecessary in this Directive and may be in conflict with the Directive 93/42/EEC.
United Kingdom <i>UK Forum</i>	Cryoprecipitate	Cryoprecipitate and plasma storage time	Is there any evidence to back up only 3 months' storage at -18 - -25? US plasma is stored at this temperature, and although when we import and Methylene Blue treat we will subsequently store at -40°C, it will have been stored at the lower temperature for a period. A 3-month expiry will make it impossible to support an imported FFP programme.	
Greece	Granulocytes	Administered as soon as possible after collection, with maximum storage of 24 hours.	Add: <i>Exposed to an appropriate dose of ionising radiation before transfusion</i>	
Czech Republic	Granulocytes		storage temperature: Wording “if unavoidable“ seems to be problematic, we recommend: “ Not suitable for storage. Keep at +20 °C to +24 °C before use.“	
EMEA	Plasma, fresh frozen	Below -25 °C	Plasma, fresh frozen, <u>for transfusion</u>	To make it clear that this is not for plasma for fractionation.
Spain	Plasma, fresh frozen	Below -25 °C	Below -30°C	Aperture of the freezer

Czech Republic	Plasma, fresh frozen	“	Does this article cover also plasma for industrial processing ? In such a case a “length of storage” should reflect also storage before processing.	
United Kingdom <i>UK Forum</i>	Plasma thawed		– not a recognised product – should just give post-thaw guidance for FFP (which should state max time not just ASAP).	
United Kingdom <i>UK Forum</i>	Platelets (all)		Under transportation temperature states (continuous gentle agitation) This is not possible during transit. Need a statement that will allow 7 day storage of platelets in a validated container / solution if bacterial screening or a licensed pathogen inactivation procedure is used.	
Spain	Platelets concentrate		New translation is needed	The text is not understandable
Italy	Platelets (single unit concentrate,	Transportation temperature Similar to storage temperature (with continuous gentle agitation)	Similar to storage temperature	Continuous gentle agitation is not related to transportation temperature
EUCOMED	Platelets (single unit, concentrate recovered, buffy coat pool, apheresis	5 days (with continuous gentle agitation)	Viability of platelets is preserved up to 7 days under optimal conditions. However, more than 5 days storage of platelets is not presently recommended unless a validated system has assured absence of bacterial contamination	In-line with Council of Europe recommendations
Spain	Platelets concentrate	with continuous gentle agitation	Not needed	Not feasible
United Kingdom <i>UK Forum</i>	Platelets, cryopreserved: apheresis		suggest 10 years for –150°C component storage rather than just >12 months.	
Baxter	Platelets		Platelet storage is allowed for up to 5 days, while some countries already store for 7 days in some conditions.	What are the implications if anybody wants to prolong shelf life?

Greece	Red cells in additive solution, buffy coat removed	+2 °C - +6 °C According to anticoagulant and additive solution. Normally 35 days.)	Delete: ... (Normally 35 days.) <i>Add.: <28 days if irradiated by 25-40 Gy</i>	
Italy	Red cells in additive solution, buffy-coat removed -	Length of storage According to anticoagulant and additive solution. <i>Normally 35 days</i>	According to anticoagulant and additive solution.	Self evident
Greece	Red cells, leukocyte reduced	+2 °C - +6 °C ≤35 days with adenine supplemented anticoagulant. <24 hours if prepared in open system	Add: <i><28 days if irradiated by 25-40 Gy</i>	
Italy	Red cells, leukocyte-reduced	Length of storage < 35 days with adenine supplemented anticoagulant	According to anticoagulant and additive solution	The proposed wording covers all kinds of accepted solutions
United Kingdom <i>UK Forum</i>	Red cells, leukocyte reduced		Typographical error under Transportation temperature +1 °C instead of +2 °C lower limit (also in Storage temp WB for component preparation).	
Italy	Red cells, leukocyte-reduced	Transportation temperature + 1°C - + 10°C	+ 2°C - + 10°C	Transportation temperature should not be lower than storage temperature
Poland	Red cells, leukocyte-reduced	Transportation temperature	Change: 2°C	Change: leukocyte-reduced into leukocyte-depleted
Italy	Red cells, frozen by low glycerol method	Length of storage < 24 hours, use as soon as possible after thawing	< 24 hours, use as soon as possible after thawing <i>if prepared in open system</i>	Current technology allows to carry out the procedure in a closed system.
Italy	Red cells, frozen by low glycerol method	Transportation time Thawed red cells: to be transfused within 24 hours of thawing	Thawed red cells: to be transfused within 24 hours of thawing, <i>if prepared in open system</i>	Current technology allows to carry out the procedure in a closed system.

Italy	Red cells, frozen by high glycerol method	Length of storage < 24 hours, use as soon as possible after thawing	< 24 hours, use as soon as possible after thawing <i>if prepared in open system</i>	Current technology allows to carry out the procedure in a closed system.
Italy	Red cells, frozen by high glycerol method	Transportation time Thawed red cells: to be transfused within 24 hours of thawing	Thawed red cells: to be transfused within 24 hours of thawing, <i>if prepared in open system</i>	Current technology allows to carry out the procedure in a closed system.
United Kingdom <i>UK Forum</i>	Frozen red cells (both types):		Transfuse within 24 hours is repeated in the transport column as well as length of storage column – should be in the former only. HOWEVER, this should also take into account the advance of sterile docking and automated washing such as WBS Haemonetics system which has a validated procedure allowing storage for up to 7 days after deglycerolisation.	
Poland	Red cells frozen.	Transportation time	Cancel the sentence: Thawed red cells .thawing.	
Italy	Red cells, washed	Length of storage < 24 hours if prepared at low temperature < 6 hours if prepared at room temperature	< 24 hours if prepared at low temperature <i>and in open system</i> < 6 hours if prepared at room temperature <i>and in open system</i>	Current technology allows to carry out the procedure in a closed system.
Italy	Red cells, washed	Transportation temperature + 2°C - + 6°C	+ 2°C - + 10°C	No justification to a lower transportation temperature in comparison with all other red cell units.
United Kingdom <i>UK Forum</i>	Red cells, washed		Given as only 6 hours if prepared at RT rather than 24 hours if prepared at low temperature (not further defined). If prepared in a closed system this should be 24 hours for both.	
Italy	Whole blood (for component preparation)	Transportation temperature	+ 2°C - + 10°C	Transportation temperature was not specified

Italy	Whole blood (for component preparation)	Storage temperature + 1°C - + 6°C	+ 2°C - + 6°C	No justification to a lower storage temperature in comparison with all other red cell units. If applied would entail dedicated refrigerators
United Kingdom <i>UK Forum</i>	Whole blood (for component preparation)	:	Typographical error under Storage temperature +1 °C instead of +2 °C lower limit. Unclear why can only hold WB prior to processing (not prior to use as stated) for 8 hours in the cold, but 24 hours at RT for preparation of platelets – should be 24 hours for both. This means we would not be allowed to hold blood overnight as is current practice.	
Poland	Whole blood (for component preparation).	Storage temperature	Change: +2 ⁰ C	
EMEA	Freezing of plasma	Blood product: Time of freezing Plasma A: Frozen within 6 hours of phlebotomy Plasma B: Frozen within 24 hours of phlebotomy Plasma C: Frozen after 24 hours of phlebotomy	<u>Add:</u> <u>The conditions of freezing and storage of plasma for fractionation have to comply with the relevant Ph. Eur. monograph, Human Plasma for Fractionation.</u>	Is there a need for the three types of plasma A, B and C? Storage and freezing of plasma for fractionation is outside of the scope of the Blood Directive. A cross-reference to the relevant requirements would make it clear that the text does not apply to plasma for fractionation.
United Kingdom <i>UK Forum</i>	Freezing		The 3 categories of plasma are not mentioned elsewhere. Prefer a measure of quality rather than time of freezing if this is required.	
WHO Regional Office for Europe	B. Freezing	Platelets	Platelets cryopreserved	The specification would be necessary in order to avoid misinterpretation/ misuse of information by less advised audience
WHO Regional Office for Europe		Red cells	Red cells cryopreserved	The specification would be necessary in order to avoid misinterpretation/ misuse of information by less advised audience

Poland	B Freezing		Cancel: Plasma A, Plasma B, Plasma C. Plasma. Time of freezing: 6 – 18 hours after collection, or rapidly cooled in special device to 20°C - 24°C; can be held for up to 24 hours after collection.	
Spain	Concentrado Hematías en solución de aditivos		Concentrado de Hematías en solución aditiva	Translation error (linguistic)
Italy	Freezing Plasma B	Frozen within 24 hours of phlebotomy	Frozen within 6 - 24 hours of phlebotomy	Within 24 hours would include also plasma A
Italy	Freezing Plasma C	Frozen after 24 hours of phlebotomy	Frozen within 24 - 72 hours of phlebotomy	An upper limit is needed
France Afssaps	Freezing Plasma A Plasma B Plasma C		Delete	
Italy	Freezing Platelets	Frozen within 24 hours	Frozen within 48 hours	The results of NAT testing are not always available within 24 hours. To freeze units before the results are available would entail an expensive waste of resources.
France Afssaps	Freezing Platelets	Frozen within 24 hours	Delete	
France Afssaps	Freezing Red cells	Frozen within 7 days	Delete	

Comments from France Afssaps (not yet incorporated)

France Afssaps	Heading	Storage and freezing	Storage and transport requirements for liquid and cryopreserved blood and blood components
France Afssaps	General comments		The below layout avoids imprecision and reflects the current science. All storage, including freezing, must be done using approved devices; more specific directions are therefore unnecessary in this Directive and may be in conflict with the devices Directive. Ajouter une phrase générale : Les conditions (température et durée) et dispositifs de stockage et de transport doivent être validés et régulièrement contrôlés

France Afssaps	Title	a). liquid storage	
France Afssaps		Red cells, red cells in additive solution, red cells in additive solution buffy-coat removed, red cells leukocytes reduced, red cells washed, whole blood for transfusion and for component preparation	Red cells preparations - Temperature of storage : 2 - 6°C - Maximum storage time : Generally up to 35 days; may be up to 49 days, depending on the bag, additive solution, and other validated conditions.
France Afssaps		Platelets (single unit, concentrate recovered, buffy-coat pool, apheresis)	Platelets preparations - Temperature of storage : 20 - 24°C - Maximum storage time : Generally up to 5 days under validated conditions, e.g. continuous gentle agitation; length of storage may change with the development of validated techniques of preservation of function
France Afssaps		Granulocytes	Granulocytes - Temperature of storage : 20 - 24°C - Maximum storage time : Up to 24 hours.
France Afssaps			Plasma cryodesséché sécurisé - Temperature of storage : 2 - 25°C - Maximum storage time : Up to 24 months. Utiliser immédiatement après reconstitution
France Afssaps			After washing, blood components are generally labelled with a shelf life, depending on the washing process and on the subsequent storage temperature requirements: - red cells washing on manually and unclosed system : shelf life of up to 6 hours - red cells washing on automatically and closed system : shelf life of up to 10 days - platelets and granulocytes : shelf life of up to 6 hours
France Afssaps	Title	b). Cryopreservation	
France Afssaps		Red cells, frozen by low or by high glycerol method	Red cells cryopreserved Storage conditions and duration : up to 10 years or more using validated storage temperature and conditions
France Afssaps		Platelets, cryopreserved: apheresis	Platelets Storage conditions and duration : up to 3 years or more using validated storage temperature and conditions
France Afssaps		Plasma fresh frozen, cryoprecipitate, plasma cryoprecipitate depleted	Plasma and cryoprecipitate Storage conditions and duration : up to 24 months or more in validated storage conditions.

France Afssaps			After thawing, blood components are generally labelled with a shelf life, depending on the thawing process and on the subsequent storage temperature requirements: - red cells thawing on manually and unclosed system : shelf life of up to 24 hours - red cells thawing on automatically and closed system : shelf life of up to 7 days - platelets and plasma: shelf life of up to 6 hours
France Afssaps	Title	B. Transport	
France Afssaps		Transportation temperature and transportation time	Transport of blood and blood components at all stages of the transfusion chain and of fractionation must be under conditions validated to maintain the integrity of the components.

REVISION TO ANNEX III

Proposed by

Denmark, France, Luxembourg, Netherlands, Finland, United Kingdom, EBA *(unless otherwise indicated)*

ANNEX III

STORAGE AND TRANSPORT REQUIREMENTS FOR LIQUID AND CRYOPRESERVED COMPONENTS

A STORAGE

a) Liquid storage

Component	Temperature of storage	Maximum storage time
Red cell preparations and whole blood	2 – 6 °C	Generally up to 35 days; may be up to 49 days, depending on the bag, additive solution, and other validated conditions.
Platelet preparations	20 – 24°C	Generally up to 5 days under validated conditions, e.g. continuous gentle agitation; length of storage may change with development of validated techniques of preservation of function & prevention or eradication of bacterial contamination.
Granulocytes	20 – 24°C	Up to 24 hours

b) Cryopreservation

	Component	Storage conditions and duration
	Red blood cells	up to 10 years or more using validated storage temperature and conditions.
	Platelets	up to 12 months or more using validated storage temperature and conditions.
	Plasma and Cryoprecipitate	24 months at below -25°C; 3 months at -18°C to -25°C.*
France	Plasma and Cryoprecipitate	up to 24 months or more using validated storage conditions
	<i>After thawing, cryopreserved components are generally labelled with a shelf life of up to 12 hours, depending on the thawing process and on the subsequent storage temperature requirements.</i>	
United Kingdom	<i>The label of the thawed component should state the required storage temperature and the length of the shelf life based on validated studies for length of storage under the stated temperature storage conditions.</i>	
France	<i>Cryopreserved components must be thawed and washed using validated procedures. The allowable storage period after thawing and washing will depend on the method used and shall be appropriately validated.</i>	

* add in:- any extension beyond these recommended storage periods require validation

B. TRANSPORT

Transport of blood and blood components at all stages of the transfusion chain must be under conditions validated to maintain the integrity of the product.

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