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98	GRO-C	~~Mr~~ T. SNAPE	15 May 90

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INDEX

This document outlines the requirements for plasma collected and prepared at the Regional Transfusion Centres of England and Wales intended for fractionation at the Blood Products Laboratory, Elstree.

1. DONOR QUALIFICATIONS

1.1 Donors shall be selected according to the current guidelines set out in the National Blood Transfusion Service 'Guidelines for the selection, medical examination and care of Blood Donors'. The latter shall be superseded by the equivalent UK BTS/NIBSC document when formally approved. Donors who state that they may be in a high risk group for contracting AIDS are not acceptable even though they may be found to be HIV-1 antibody negative.

1.2 Where insufficient supplies of antibody specific plasma are available by selection or screening of appropriate donors, immunisation or stimulation of existing antibodies in the donor may be undertaken according to the WHO guidelines and the plasma subsequently collected.

2. COLLECTION OF PLASMA

2.1 Plasma shall be obtained from an uninterrupted donation either by plasmapheresis or from the separation of whole blood. Good Manufacturing Practice shall be employed at all stages of plasma preparation with regular sampling and monitoring being undertaken to demonstrate the integrity of all open systems. The haemoglobin, red cells and platelet content should be reduced as far as possible.

2.2 Containers shall be made of non-reactive plastic. Closures shall maintain a hermetic seal and prevent contamination of the contents. Fill weights shall only be accepted within the stated limits. Acceptable containers, plasma specification codes (PSC) and fill weights are given in Appendix I.

2.3 A UK licenced anti-coagulant shall be added at the time of donation. Anti-coagulants in current use are Citrate Phosphate Dextrose solution (CPD). Acid CPD, CPD 50, CPD A1, Acid Citrate Dextrose (ACD), ACD 1A and Sodium Citrate. Alternative anticoagulants shall be considered for prospective use on the basis of successful pilot scale fractionation trials. The type of anti-coagulant used should be recorded on the despatch sheet.

2.4 The filling line into the pack should be heat-sealed as close as possible to the pack (within 2-3cm).

2.5 Metal clips should not be used to seal the filling line.

2.6 Plasma shall be separated from whole blood within 6 hours of collection and frozen to a core temperature of at least -30°C within 8 hours of collection. Plasma which cannot be frozen within 8 hours of collection will be accepted if frozen within 18 hours of collection. The age (in hours) of the fresh plasma before freezing, either upto 6 hours or upto 18 hours, shall be recorded on the despatch sheet.

Plasma obtained by apheresis shall be frozen as soon as practically possible and certainly within 8 hours of collection.

2.6.1 Separation of antibody specific plasma obtained from whole blood using aseptic technique should be undertaken as soon as possible or when specificity testing permits. When separated the plasma shall be frozen as soon as possible and certainly within 8 hours of separation.

2.7 All single donor packs, International Plasma Packs, (IPP) shall be frozen upright, ensuring that an air space remains between the top of the pack and the plasma, in specifically designed formers. IPP-3 packs shall maintain the 'wedge' shape during and after freezing. The Haemonetics UK Tear Down bag shall be frozen upright between formers to a uniform thickness of 20-25mm and shall not be folded either before or after freezing.

2.8 Each pack shall be securely labelled with a donation number. Tie-on labels are not acceptable. Bar code labels (using 'Codabar' symbology) with eye-readable equivalents are acceptable. Large overstick labels and/or labels fixed across the tear-line of Haemonetics packs interfere with pack opening and shall not be used.

2.9 Each 5L pack shall be prepared from pooled donations with the number of donations per pack recorded on the despatch sheet (each donation having been individually tested as in section 3 prior to pooling). A sample sachet should accompany the pack in the carton.

3. PLASMA TESTING

All plasma shall be checked for appearance and tested to confirm the release criteria are met (as specified in Section 3.1 below) before despatch to BPL. It should be noted that the classification of the plasma according to ABO blood group system is not required except for special trials for which agreed protocols will operate.

3.1 Requirements for all plasma types:

3.1.1 Appearance:

The pack shall be visually inspected and no evidence of damage, leakage, microbial contamination (eg: signs of external soiling), overt haemolysis, heavy fat contamination or unusual labelling (biohazard labels, warning labels etc.) must be found.

3.1.2 Test for antibody to HIV-1:

The donation shall be tested and found to be non-reactive for antibody to HIV-1.

3.1.3 Test for hepatitis B surface antigen:

The donation shall be tested and found to be non-reactive for HBs antigen by a method which detects 1 iu/ml of HBs antigen.

3.2 Requirements for immune plasma:

Immune plasma should be provided only in the form of single donations. The minimum acceptable potency of each donation must be demonstrated using a test method agreed with BPL. BPL will prospectively request samples of immune plasma from individual donations at a frequency to be agreed directly with the supplying RTC. General requirements for the potency testing of specific plasma are given as Appendix II. The requirements for each plasma type are specified below:

3.2.1 Anti-D:

The antibody potency of a plasma sample should be determined using an autoanalyser-based test method. Fractionation requires a minimum pool potency of 50iu/ml and experience has shown that as long as sufficient individual donations in excess of 50iu/ml are provided then individual donations with a minimum potency of 30iu/ml can be accepted.

3.2.2 Anti-cytomegalovirus:

The antibody potency should be determined using a quantitative method such as EIA or CFT that has been agreed with BPL. All donations shall be shown to be of a potency no less than that of a reference sample provided by BPL.

3.2.3 Anti-hepatitis B:

The potency of antibody to hepatitis B surface antigen should be determined using a quantitative method that has been agreed with BPL. The minimum acceptable potency is 10 iu/ml.

3.2.4 Anti-rabies:

As it is not practicable to determine the rabies antibody potency of individual plasma donations, donors should be considered to have adequate concentrations of rabies antibody between one and three months after a second dose of vaccine or between 3 weeks and 3 months after booster doses of vaccine derived from diploid cell vaccine, Merieux. Plasma must not be collected from persons immunised after exposure to infection by rabies virus.

3.2.5 Anti-tetanus:

The antibody potency should be determined using a quantitative method, agreed with BPL, that has been shown to correlate well with the mouse neutralisation test for tetanus antitoxin. The minimum acceptable potency is 6 iu/ml.

3.2.6 Anti-Varicella/Herpes-Zoster (Chickenpox/Herpes-Zoster):

The antibody potency should be determined using a quantitative method such as EIA or CFT that has been agreed with BPL. The donations shall be shown to be of a potency no less than that of a reference sample provided by BPL.

4. STORAGE AND TRANSIT OF PLASMA

4.1 The preferred storage temperature for plasma is -40°C or lower, (as long as the packs withstand lower temperatures) both within the Regional Transfusion Centre and during transit, however, temperatures not exceeding -30° C are acceptable. BPL should be advised of any excursion from the desired storage conditions providing details of temperature and time affected. A record of the ambient temperature of the cold storage transit unit must be handed to the Plasma Receipt staff at the time of delivery.

4.2 Plasma shall be held within the Regional Tranfusion Centre after collection; fresh frozen plasma returned after issue to hospitals will be accepted, under a unique plasma specification code (see Appendix 1), strictly for Research and Development purposes. Time-expired plasma recovered from whole blood returned after issue to hospitals is acceptable if the RTC is satisfied that the blood donation has been stored in a manner which has maintained its fitness for clinical use.

4.3 Frozen packs shall be wrapped in a polythene overwrap and packaged in a standard carton available from BPL. The carton should contain either 10 units (Haemonetics packs) or 20 units (single donation packs excluding specific plasma). The number of units shall be written on the end of each carton and on the plasma despatch sheet. A part filled carton is acceptable in any one delivery as long as the number of donations are clearly indicated on the end of the carton and on the despatch sheet. Each carton must have a batch identification label detailing the centre of origin, carton number and plasma type clearly visible when stacked. Cartons may also be labelled using an agreed barcode system (Code 39). Packing must not result in packs being folded as this causes damage during transit.

5. DOCUMENTATION

5.1 All plasma delivered to the Blood Products Laboratory must be accompanied by a BPL approved despatch sheet, (see Appendix III) typed where possible. The despatch form to be comprised of a four part multi-colour (white, pink, yellow, green) 'no-carbon-required' paper. The green copy to be retained by the RTC and after fractionation of the plasma the pink copy will be returned to the RTC. Only one plasma specification category (PSC) per despatch sheet is acceptable. Computer generated despatch sheets conforming to the above specification are acceptable.

5.2 Despatch sheets shall be completed in full and signed to confirm that the plasma listed conforms to this specification. Initials are not satisfactory.

5.3 Regional Transfusion Centres shall keep a record of plasma donations so that each can be traced to a pack or box number, as listed on the despatch sheet. This information shall be provided to BPL on request. Comprehensive records providing donor traceability and test results appropriate to the specification must be maintained at the RTC for a minimum of 15 years.

5.4 The weight of plasma per delivery (net of packaging) will be given by the RTC on the despatch sheet.

6. QUALITY AUDIT

6.1 All RTCs will participate with BPL in conducting an audit of their manufacturing facilities and procedures.

6.2 Deliveries of plasma to BPL will be checked, weighed and sampled, and tested where appropriate, to confirm compliance with the plasma specification.

7. FAILURE TO MEET SPECIFICATION

7.1 Plasma which does not conform to this specification will not be despatched to BPL unless prior arrangements have been made with the Quality Department Manager.

7.2 The Regional Transfusion Centre shall immediately advise BPL of any information which might compromise one or more plasma donations previously supplied to BPL. BPL shall be advised in the following circumstances:

i) If the donor did not meet the current donor health criteria.
ii) If it is discovered that the HBs antigen or HIV-1 antibody testing has not been done according to agreed procedures.
iii) If the donor may be implicated in an episode of post-transfusion infection.
iv) If the plasma is considered to be unsatisfactory in any other way.

This information, providing confirmation of the problem, is treated in the strictest confidence and should be supplied in writing addressed as follows:

The Director (Plasma Reports)
Blood Products Laboratory
Dagger Lane
Elstree
Hertfordshire
WD6 3BX

Information to be imparted urgently regarding the exclusion of plasma should be provided by telephone.

Telephone: 01-953-6191 extn: GRO-C (Quality Control Unit)
Fax: 01-207-6220

APPENDIX I - PLASMA SPECIFICATION CODES

Plasma Specification Code	Standard Fill Weight	Pack Description	Description
NON-SPECIFIC PLASMA:			
PSC 900/01	250 ±50g	Baxter IPP-3 1645	Triple SAG-M with IPP
		1617	Quadruple SAG-M with IPP
		1864	Standard double pack with IPP
PSC 901/02	170-300g	1737	Triple pack with IPP and platelet
PSC 902/01	<170g		Non-standard collection into Baxter IPP-3
PSC 903/01	>300g		Non-standard collection into Baxter IPP-3
PSC 904/02	450-650g	Haemonetics UK Tear Down bag.	Platelet poor plasma (PPP) collected by PCS, Ultrasite or Haemonetics Model 50.
PSC 905/02	300-500g	Haemonetics UK Tear Down bag	Plasma obtained after platelet removal (PRP) collected by PCS,
PSC 906/01	>650g	"	Non-standard collection of PPP
PSC 907/01	<450g	"	Non-standard collection of PPP
PSC 910/02	500-600g	Baxter Double IPP. EURX 0217	Platelet poor plasma collected by Autopheresis C plasmapheresis machine
PSC 960/01	300-450g	Baxter Double IPP. EURX 0217	Plasma obtained after platelet removal collected by Autopheresis C plasmapheresis machine
PSC 911/01	5.0±0.5kg	5L	Autopheresis C plasmapheresis machine
PSC 912/01	300g-450g	A suitable pack agreed with BPL	Fenwal CS3000

Plasma Specification Code	Standard Fill Weight	Pack Description	Description
NON-SPECIFIC PLASMA cont.			
PSC 913/01	300-450g	Haemonetics UK Tear Down bag	Haemonetics V50 Surge
PSC 914/01	300-450g	A suitable pack agreed with BPL	Cobe Spectra
PSC 915/01	Single donation	Baxter IPP or Haemonetics UK Tear Down bag.	Fresh frozen plasma issued to and returned from hospitals. For R&D purposes only
PSC 916/01	5.0±0.5kg	5L	Pooled fresh plasma frozen within 8 hours of collection (No. of donations/pool to be specified).
PSC 917/01	5.0±0.5kg	5L	Pooled fresh plasma frozen within 8-18 hours of collection (No. of donations/pool to be specified).
PSC 918/02	5.0±0.5kg	5L	Pooled recovered plasma from time-expired whole blood or pooled recovered cryo-supernatant (No. of donations/pool to be specified).
PSC 940/01	300-450g	Baxter Double IPP EURX 0217 or Haemonetics UK Tear Down bag	Manual plasmapheresis machines.
PSC 950/01	Volumes to be determined	Plasma packs to be of an acceptable quality	Novel collection systems and/or anti-coagulants not described above for agreed trial purposes to evaluate plasma quality.

Plasma Specification Code	Standard Fill Weight	Pack Description	Description
SPECIFIC PLASMA:			
PSC 920/01	250±50g	Baxter IPP-3	Single donation of Anti-CMV plasma.
PSC 921/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217.	Anti-CMV plasma collected by apheresis.
PSC 922/01	250±50g	Baxter IPP-3	Single donation of Anti-D plasma.
PSC 923/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217	Anti-D plasma collected by apheresis.
PSC 924/01	250±50g	Baxter IPP-3	Single donation of Anti-HBs plasma.
PSC 925/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217.	Anti-HBs plasma collected by apheresis.
PSC 927/01	250±50g	Baxter IPP-3	Single donation of Anti-rabies plasma.
PSC 928/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217.	Anti-rabies plasma collected by apheresis.
PSC 929/01	250±50g	Baxter IPP-3	Single donation of Anti-tetanus plasma.
PSC 930/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217.	Anti-tetanus plasma collected by apheresis.
PSC 933/01	250±50g	Baxter IPP-3	Single donation of Anti-Varicella/Herpes-Zoster plasma.
PSC 934/02	300-650g	Haemonetics UK Tear Down bag or Baxter Double IPP EURX 0217.	Anti-Varicella/Herpes-Zoster plasma collected by apheresis

APPENDIX II - REQUIREMENTS FOR THE POTENCY TESTING OF SPECIFIC PLASMA

BPL requires that two general specifications are met:

1. Minimum acceptable potency:

   The antibody potency of the plasma should exceed the minimum acceptable potency specified by BPL. This potency is specified in iu/ml if an international standard or reference preparation for the antibody concerned is available, otherwise the minimum acceptable potency is specified in arbitrary units which have been assigned relative to a reference preparation supplied by BPL.

2. Agreed test method:

   The test method used by the Transfusion Centre for the selection of the specific plasma must be agreed with BPL. This formal agreement should be based on an assessment of the suitability of the test method for the specific purpose of the selection of high titre specific plasma. The assessment should include:

   a) The specificity of the method. This should include consideration of the antigenic specificity of the selected antibody, of the immunoglobulin class(es) selected and of evidence of the correlation of the results of the method with other techniques.

   b) The reproducibility of the method.

   The performance of the test method may be assessed with a panel of samples supplied by BPL.

   Once a test method has been agreed, BPL should be provided with a detailed test protocol by the Transfusion Centre. BPL should be notified of any significant modifications of the test procedure and of the date of implementation of these modifications.

APPENDIX III - PLASMA DESPATCH SHEET

BPL Ref no: _____

_____ **TRANSFUSION CENTRE**

BATCH/POOL ISSUE NOTE

Despatched to BPL ELSTREE on _____(date)

COMPLETED AT RTC	COMPLETED AT BPL
Plasma Specification Code PSC_____/____ _____ BOXES/PACKS LISTED BELOW COMPLY WITH THE CURRENT VERSION OF THE BPL PLASMA SPECIFICATION (ref. RMS020) AGE OF PLASMA: UP TO 6 Hrs/UP TO 18 Hrs* ANTICOAGULANT: _____ SIGNED _____ * delete as applicable	Pallet location: _____/_____/_____ Gross weight: _____kg Nett weight: _____kg EXCEPT WHERE INDICATED BELOW THE PLASMA ON THIS FORM IS PASSED FOR FRACTIONATION SIGNED _____ DATE _____

	RTC code/pack no	date prepared	No. of units	titre (specific plasma only)	PLASMA RECEIPT: packs received	QC check	packs found	packs used	comments	PRODUCTION: used in batch
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
21										
22										
23										
24										
25										
		TOTAL							TOTAL	
	NETT WEIGHT (kg)								SIGNED	

Top three copies to accompany plasma to BPL
Bottom copy to be retained by RTC
(Pink copy to be returned to RTC)

Passed to Production _____(date)
Sheet _____ of _____

Fractionated _____(date)

APPENDIX IV - EXPLANATORY NOTES

THE ISSUE, REVISION AND RE-ISSUE PROCEDURES OF THE PLASMA SPECIFICATION

The plasma specification entitled 'Specification for plasma for fractionation' reference number RMS02001.RMS/MARCH, 1989, shall be authorised and issued from Blood Products Laboratory. The definitive document shall be issued on brown photocopy paper from which further copies of similar quality are extremely difficult to make. This has the advantage of restricting/avoiding the circulation of unauthorised copies.

Each centre will be provided with an agreed number of copies. Each copy is given its own unique number and a record will be kept at BPL of the copy numbers and the recipients of said copies.

On revision of the document the reference number will change accordingly, eg: 02001 changes to 02002. The last two digits represents the edition number hence allowing for 99 revisions and this coupled with the month and year provides adequate scope for flexibility.

When a revision has been approved a request will be made for all copies previously issued to be returned. It is the responsibility of the recipients of the specification to ensure that all copies are returned to BPL for disposal. This procedure will avoid the risk of out-of-date specifications remaining in circulation. On receipt of the returned specification the new version will be issued and the same documentation control procedure will be followed.

SECTION 2 - COLLECTION OF PLASMA

Paragraph 2.2

When the British Standard is available plasma containers shall comply with the requirements of BS 2463, 'Transfusion equipment for medical use Part 1 Specification for collapsible containers for blood and blood components'.

Plasma containers made from PVC are not designed to withstand the freezing temperatures required of plasma. The plastic becomes very brittle and is easily fractured. Currenty only plasma packs described in Appendix I are suitable, however, other types of packs presently in use by the transfusion service will be accepted (if undamaged on receipt) for upto 6 months from the date of issue of the specification (until September 1989).

The acceptability of alternative pack types, prepared from a suitable plastic, should be discussed prospectively with the Quality Department Manager, BPL.

Several plasma specification codes have been included to cover both low and high volume plasma donations. It is anticipated that these categories will represent only a small proportion of the plasma delivered to BPL.

Paragraph 2.3

It has been demonstrated that anti-coagulants can have a marked effect upon the recovery of various blood components, therefore the use of alternatives has to be controlled.

SECTION 7 - FAILURE TO MEET SPECIFICATION

Paragraph 7.2

If a donor is implicated in an episode of post-transfusion infection then BPL shall be notified as soon as possible so that either the plasma can be excluded from fractionation or product already prepared can be held or recalled. Depending upon the outcome of any investigation of post-transfusion infection the plasma involved or prepared products will either be destroyed or released for use.

APPENDIX I - PLASMA SPECIFICATION CODES

PSC 913/01

Provision for collecting plasma using the Haemonetics V 50 Surge machine into a Haemonetics UK Tear Down Bag is currently under review.

PSC codes for underfilled hyperimmune plasma packs have been deliberately excluded whilst opening specific plasma packs remains a manual operation.

ADDITIONAL INFORMATION

It is accepted that when obtaining plasma by apheresis into an IPP-3 collection pack then more than one pack will be required. Whilst the same donation number will be provided for these packs it is the responsibility of the Transfusion Centre to advise BPL of the number of packs to exclude in the event of a plasma incident or plasma recall. RTOs should build in a security procedure to ensure that where more than one pack with the same donation is sent for fractionation then BPL will always be advised of the total number to exclude or trace if, and when, necessary.

GLOSSARY

ACD	-	Acid Citrate Dextrose.
anti-HBs	-	antibody to hepatitis B surface antigen.
BPL	-	Blood Products Laboratory, Elstree.
CFT	-	complement fixation test.
CPD	-	Citrate Phosphate Dextrose.
CPDA1	-	Citrate Phosphate Dextrose Adenine.
EIA	-	enzyme immunoassay.
HBs antigen	-	hepatitis B surface antigen.
HIV-1	-	human immunodeficiency virus type 1.
PCS	-	Plasma collection system.
PPP	-	Platelet poor plasma
PRP	-	Platelet rich plasma.
PSC	-	Plasma Specifiction Code.
RTC	-	Regional Transfusion Centre.
WHO	-	World Health Organisation.
UK	-	United Kingdom.