CUTTER SYSTEM
of
PLASMAPHERESIS

Cutter Laboratories, Inc.
Fourth and Parker Streets
Berkeley, California
94710

TABLE OF CONTENTS

109 6868

8 1 0 1 1 2 CS0 a 0 3

FOREWORD

These procedures are divided into five broad sections:

Section 1 General Procedures for Plasmapheresis
Section 2 Specific Procedures and Controls
Section 3 Additional Requirements
Section 4 Forms: Instructions for Completing
Section 5 Equipment

Section 1 assigns responsibilities and delineates the flow of donors, paperwork, blood and plasma throughout the plasma center. Cutter Laboratories suggests these procedures as one way to simply, concisely and expeditiously accomplish the required tasks. It is recognized that physical facilities may involve some limitations on these procedures. In such cases, alteration of these procedures is encouraged providing the basic precepts of the procedures are retained.

R Section 2 gives specific procedural details of each separate task to be performed.

Section 3 gives instructions for alterations in the general procedure for plasmapheresis to provide specific types of plasma or to implement experimental programs.

R Section 4 lists forms and gives instructions for their use.

Section 5 lists types of equipment normally used and gives some precautions in selection and use of equipment. In certain instances, information on additional controls is also provided. Although specific items of equipment may be mentioned by brand name, equipment of equal quality is usually satisfactory.

GRO-C 12/10/80

GRO-C 12/11/80

109 6870

8 1 0 1 1 2 CS0 a 0 5

APPLICABLE REGULATIONS

The following laws and regulations, and all amendments thereto, must be followed by each Plasma Center operating under these procedures:

1. Public Health Service Act; Virus, Serum, and Toxin Act of 1944, Section 351, Regulations of Biological Products.

2. Federal Food, Drug and Cosmetic Act.
   Chapter II - Definitions
   Chapter III - Prohibited Acts and Penalties
   Chapter V - Drugs and Devices
   Chapter VII - General Administrative Provisions

3. Code of Federal Regulations, Title 21, Food and Drugs,
   Chapter 1 - Food and Drug Administration, Department of Health, Education, and Welfare,
   Subchapter C - Drugs: General
   Part 200 - General
   Subpart A - General Provisions
   Section 200.10 - Contract facilities (including consulting laboratories) utilized as extramural facilities by pharmaceutical manufacturers.
   Part 207 - Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution.
   Subpart A - General Provisions
   Section 207.3 - Definitions
   Section 207.7 - Establishment registration and product listing for human blood and blood products.
   Subchapter F - Biologics
   Part 600 - Biological products: General
   Subpart A - General Provisions: All Sections
   Subpart B - Establishment Standards: All Sections
   Subpart C - Establishment Inspection: All Sections
   Part 601 - Licensing
   Subpart A - General Provisions: All Sections
   Subpart B - Establishment Licensing: All Sections
   Subpart C - Product Licensing
   Section 601.20 - Product licenses issuance and conditions.
   Subpart E - Suspension of Licenses and Appeals Procedure: All Sections
   Subpart F - Confidentiality of Information
   Section 601.51 - Confidentiality of data and information in application for establishment and product licenses.
   Part 606 - Current Good Manufacturing Practices for Blood and Blood Components.
   Subpart A - General Provisions: All Sections
   Subpart B - Organization and Personnel: All Sections

GRO-C

109 6871

8101120S0 a 08

Subpart C - Plant and Facilities: All Sections
Subpart D - Equipment: All Sections
Subpart F - Production and Process Controls: All Sections
Subpart G - Finished Product Control: All Sections
Subpart H - Laboratory Controls
Section 606.140-Laboratory Controls
Subpart I - Records and Reports: All Sections
Part 607 Establishment Registration and Product Listing for Manufacture of Human Blood and Blood Products.
Subpart A - General Provisions: All Sections
Subpart B - Procedures for Domestic Human Blood and Blood Product Establishments: All Sections
Part 610 - General Biological Products Standards.
Subpart A - Release Requirements
Section 610.2 - Requests for samples and protocols; official release.
Subpart E - Hepatitis Requirements: All Sections
Subpart F - Dating Period Limitations
Section 610.50 - Date of Manufacture
Section 610.51 - Periods of cold storage
Section 610.53 - Dating periods for specific products.
Subpart G - Labeling Standards.
Section 610.62 - Proper name; package label; legible type.
Part 640 - Additional Standards for Human Blood and Blood Products.
Subpart G - Source Plasma (Human): All Sections

4. All city, county, and state regulations governing plasmapheresis, public health, and business applicable at the plasma center location.

GRO-C

109 6872

8 1 0 1 1 2 CS0 2 0 7

DONOR HEALTH CHECK
Normal Acceptance Values

1. Age - Minimum 18 or as prescribed by state law.

2. Weight - Minimum 110 lbs.

3. Temperature - Minimum 97.6°F, maximum 99.6°F.

4. Pulse - Minimum 50/min., maximum 100/min.

5. Blood Pressure - systolic - minimum 100, maximum 150
   diastolic - minimum 50, maximum 100
   Donors with blood pressure outside these limits may be taken with approval of Medical Director who should initial the results signifying approval.

6. Hematocrit - minimum 38%. (California only - males 41% minimum)

7. Total plasma protein - Minimum 6.0 gm.%.

8. Urinalysis - Negative for sugar and protein.

9. Total protein on serum sample - 6.0-9.0 gm%.

10. Serum protein electrophoresis - Normal appearing pattern with specific components:
    Albumin - 3.5 to 6.0 gm%
    Alpha 1 globulin - 0.1 to 0.4 "
    Alpha 2 globulin - 0.5 to 1.2 "
    Beta globulin - 0.6 to 1.3 "
    Gamma globulin - 0.6 to 1.9 "
    These values have been determined by Reference Laboratory.

11. Syphilis test - Negative.

4/15/76

GRO-C

109 6873

8 1 0 1 1 2 S 0 a n 8

Type and Frequency of Examination

1. Medical History and Physical Examination - no more than one week prior to first donation, or on day of first donation; annually; if, for any reason, six months or longer have elapsed since the last serum sample was collected for Serum Protein Electrophoresis, etc.: whenver advisable: Physican's signature required.

2. Predonation History Questions - on day of each donation; Examiner's initials required.

3. Predonation Vital Signs and Laboratory Examination - on day of each donation; Examiner's initials required.

4. Sample for Total Protein, Serum Protein Electrophoresis and Syphilis test - on day of first donation and every four months thereafter; on day of first donation after absence occurring between four and six months after last sample was collected. Donors returning after six months have elapsed since the last sample was collected must be treated as new donors. (Use same donor number and same donor chart.)

5. Medical Director Review of Serum Protein Electrophoresis and Syphilis Test - within twenty-one days of sample collection; Physician's signature required.

6. Medical Director Review of Donor Chart - every four months of active participation and prior to donation if more than four months but less than six months have elapsed since the last serum sample was collected. Physician's signature required.

R NOTE: In the case of non-English speaking donors. Items 1 and 2 either should be performed by a plasma center employee fluent in the donor's language or should be performed in the presence of a plasma center employee fluent in the donor's language. When an interpreter is employed, that person's identity and reason for participation must be documented in the donor's chart.

GRO-C 5/29/79

GRO-C 5/29/79

4

7/9/79

109 6874

8 1 0 1 1 2 CS0 a 0 9

MAXIMUM VOLUME OF BLOOD
AND
MAXIMUM FREQUENCY OF DONATION

Maximum Amount of Whole Blood Removed from One Donor into One Bag

Donor Weight Pounds	Volume of Blood Out of Donor ml.
110-174	500
175 and above	600

Maximum Amount Whole Blood Removed from One Donor
During One Plasmapheresis or in Any 48 Hour Period

Donor Weight Pounds	Volume of Blood Out of Donor ml.
110-174	1000
175 and above	1200

Maximum Amount Whole Blood Removed from One Donor
During Any 7 Day Period

Donor Weight Pounds	Volume of Blood Out of Donor ml.
110-174	2000
175 and above	2400

GRO-C

109 6875

8 1 0 1 1 2 CS 0 2 1 0

ROUTINE SUBMISSIONS TO CUTTER LABORATORIES

Frozen Plasma and Plasma Packing and Hepatitis Report Forms - weekly or as instructed by Manager Plasma Procurement, Cutter Laboratories.
Plasma Tubing Samples and Plasma Sample Packing Lists on Hyperimmune Plasma - mail weekly
Record of injections on Hyperimmunized Donors - mail weekly
Report of donors diagnosed clinical hepatitis - mail weekly
Serum Samples for Electrophoresis and Serum Sample Packing Lists - mail no less than twice in a seven day period.

ROUTINE SUBMISSIONS TO SCRIPPS-MILES, INC. SPECIAL TESTING LABORATORY

R

Plasma Tubing Samples and Plasma Packing and Hepatitis Report Forms - mail daily

CONTROL LABEL COLORS

Normal Plasma -	Black - N
Tetanus Plasma -	Red - T
Pertussis Plasma -	Green - P
Rabies Plasma -	Pink - B
Anti-HB_S Plasma -	Purple - A
Other Types Plasma -	See Specific Procedures

GRO-C 12/10/80

GRO-C 12/11/80

1/12/81

109 6876

8 1 0 1 1 2 CS0 a 1 1

With the advent of Current Good Manufacturing Practices for Blood and Blood Components, some regulations are now in force which are beyond the scope of Cutter System of Plasmapheresis.

These regulations relate primarily to the subjects noted above. Because of the diversity of the various centers, types of personnel employed, building arrangement, climate, and many other factors, it would be difficult, if not impossible, to create a specific manual covering these subjects; therefore, please refer to the following sections of the Code of Federal Regulations (CFR) and make sure your center is in compliance:

21 CFR 606.20 - Personnel
21 CFR 606.40 - Facilities
21 CFR 606.160(b)(7)(ii) - Record of Responsible Personnel
21 CFR 606.160(b)(7)(iii) - Records of Errors and Accidents
21 CFR 606.160(b)(7)(iv) - Records of Maintenance of Equipment and General Physical Plant

In addition to the above, it is recommended there be a trained cardiopulmonary resuscitation (CPR) team consisting of at least three persons present in the center during plasmapheresis procedures. An alternate will be required to maintain an operative team. There should also be a refresher course scheduled for the team members to maintain competence in CPR.

GRO-C 12/14/77

GRO-C

109 6877

8 1 0 1 1 2 CS 0 a 1 2

PROPER RECORD KEEPING AND ERROR CORRECTION

Over the past several months during inspections of plasmapheresis centers by Corporate Compliance, there have been noted multiple instances of improper error correction on permanent records. The Bureau of Biologics and the FDA are putting increasing emphasis on proper record keeping.

The following points must be kept in mind when making entries onto or correcting errors on all forms, all log books, all test results, and all records:

1. Make all entries on the permanent documents.
   a. DO NOT make records on scraps of paper, memo pads, etc., for later transferring to permanent documents.

2. Make all entries on all documents coincident with, or immediately after, performance of that step, receiving of that information, observance of that test result, etc.

3. Make all entries on all documents in ink.

4. Make all entries on all documents legible.

5. Acceptable method of error correction:
   a. Draw a line through the error such that the words (or figures, etc.) can still be read.
   b. Initial and date the line.
   c. Enter correct information.

6. Unacceptable methods of error correction:
   a. Use of liquid paper, Snopake, White-out or any similiar material that obliterates errors.
   b. Use of felt point pen, of any color, or any similar instrument that obliterates errors.
   c. Use of paper tape, gummed paper labels, or any similar material that covers up errors.

7. Fill in all entry blanks. DO NOT use ditto marks or lines. If a blank is inappropriate for a given step, enter NA (Not Applicable). If a blank becomes inappropriate due to special circumstances, enter NA and a brief description.

9/27/76

6B

GRO-C

109 6878

8101123 0 @13

Subject: General Procedure for Plasmapheresis

Responsibility		Action
Prospective Donor Receptionist	1.	Enters center and identifies self by name.
	2.	Ask if prospective donor is new donor. a. Yes: examine prospective donor's identification for proof of age and positive identity. Acceptable identification includes a driver's license, military ID or any other document containing donor's signature, physical description or picture. Search active, inactive, and terminiated donor files to confirm new donor status. If confirmed, prepare donor chart (see Procedure 2.0.1). b. No: ask for Donor Number. Check donor chart from donor files. Check donor chart and add new entries (see Procedure 2.0.2).
	3.	Send prospective donor and donor chart to Prep. area. a. Alternatively step 13 of this procedure could be performed at this point.
Prep. Technician R	4.	Obtain blood from prospective donor's finger for microhematocrit and total plasma protein (see Procedures 2.1.1, 2.1.2, and 2.1.3) and Donor Coding, if required.
	5.	Take prospective donor's temperature, pulse, and blood pressure. a. Record results of tests on Form 81-9723 (Donor Card). Write your initials in space provided.
	6.	Decide if prospective donor's test results meet normal acceptance values. a. No: inform prospective donor of deficiency and ask person to leave Center. If person asks to see Medical Director, arrange for interview.
	7.	Decide if prospective donor is a new donor. a. Yes: send prospective donor and donor chart to Medical Director for physical examination.
	8.	Decide if donor is due for a physical examination; required every 12 calendar months; after an absence exceeding six months; whenever advisable. a. Yes: send donor and donor chart to Medical Director for physical examination.
Medical Director	9.	Do Medical History and physical examination (see Procedure 2.2.1).
Prep. Technician	10.	Accept donor chart from donors who have successfully completed physical examination.

GRO-C 12/10/80

GRO-C 12/11/80

1/12/81

7

8 1 0 1 1 2 C S 0 a 1 4

109 6879

Responsibility	Action

11. Decide if donor is due for a serum sample for electrophoresis, serum total protein, and syphilis testing; required on all new donors and every four calendar months thereafter.
12. Select proper whole blood bag according to weight of donor.

Weight of donor	Amount anticoagulant	Border on bag label
110-174 lbs.	50 ml.	none
175 - over	60 ml.	black

    a. Visually examine each whole blood bag and attached donor tubing for damage (eg: breakage or incompleteness of seals; abnormal discoloration; holes in film or tubing) or evidence of contamination.
    b. If any evidence of damage or contamination exists, do not use whole blood bag unit. Return to manufacturer (See Procedure 4.0.11).
13. Label whole blood bags with donor's name, Donor Number, Control Number, and date; label test tube for collection of whole blood sample with Control Number if required; distribute other Control Number labels on forms and bags as required; (see Procedure 2.1.4).
14. For Normal and Tetanus plasma affix Donor Code sticker to first whole blood bag if donor is Coded "Non-O". Insure Donor Code sticker does not cover any part of whole blood bag label.
15. Apply fluorescent finger stain, (see Procedure 2.0.4) send donor and labeled whole blood bags to donor room. Retain donor chart or send chart to donor room with donor.

Phlebotomist

16. Assign donor to donor chair or table.
17. Examine both arms for fresh needle marks and select most suitable vein (see Procedure 2.3.4).
18. Identify labeled whole blood bags with donor (see Procedure 2.3.1).
19. Begin preparation of phlebotomy site (see Procedure 2.3.2).
20. Prepare and connect plasmapheresis equipment (see Procedure 2.3.3).
21. Complete preparation of phlebotomy site (see Procedure 2.3.2).
22. Perform phlebotomy (see Procedure 2.3.4).

GRO-C

GRO-C

Subject: General Procedure for Plasmapheresis

Responsibility	Action
	23. Collect first bag whole blood (see Procedure 2.3.5). Observe donor for reaction (see Procedure 2.3.8).
	24. Collect whole blood for serum sample, if required (see Procedure 2.3.6).
	25. Disconnect first bag whole blood and begin Sodium Chloride drip (see Procedure 2.3.7).
	26. Take first bag whole blood to centrifuge area.
R Phlebotomist or Centrifuge Technician	27. Weigh first bag whole blood (see Procedure 2.4.1).
Centrifuge Technician	28. Prepare Source Plasma (Human) label (see Procedure 2.4.2).
	a. Visually examine each plasma pooling bag for damage (eg: breakage or incompleteness of seals; abnormal discoloration; holes in film or tubing) or evidence of contamination.
	b. If any evidence of damage or contamination exists, do not use pooling bag. Return to manufacturer (See Procedure 4.0.11).
	29. Centrifuge first bag whole blood (see Procedure 2.4.3).
	30. Express plasma from centrifuged first bag whole blood (see Procedure 2.4.4).
	31. Make first bag whole blood (now containing red blood cells) available to phlebotomist.
Phlebotomist	32. Obtain bag of red cells from first bag whole blood from centrifuge area.
	33. Return bag of red cells to donor chair or table indicated on bag. Hang bag on IV pole.
	34. Identify bag of red blood cells with donor (see Procedure 2.3.9).
	35. Connect bag of red blood cells to return fitting of administration set and dilute with Sodium Chloride (see Procedure 2.3.10).
	35. Discontinue diluting cells with Sodium Chloride. Agitate bag to obtain smooth suspension. Re-identify bag of red blood cells with donor (see Procedure 2.3.11). Infuse cells into donor only after positive identification has been made.

109 6881

GRO-C

GRO-C

8 1 0 1 1 2 CS 0 a 1 6

Subject: General Procedure for Plasmapheresis

	Responsibility		Action
		37.	Collect second bag whole blood (see Procedure 2.3.5). Observe donor for reaction (see Procedure 2.3.8).
		38.	Disconnect second bag whole blood. Begin Sodium Chloride drip (see Procedure 2.3.7).
		39.	Take second bag whole blood to centrifuge area.
R	Phlebotomist or Centrifuge Technician	40.	Weigh second bag whole blood (see Procedure 2.4.1).
	Centrifuge Technician	41.	Centrifuge second bag whole blood (see Procedure 2.4.3).
		42.	Locate plasma pooling bag labeled with same Donor Number and Control Number as on centrifuged second bag whole blood. Move plasma pooling bag to expressor location.
		43.	Express plasma from centrifuged second bag whole blood (see Procedure 2.4.4).
		44.	Make second bag whole blood (now containing red blood cells) avaliable to phlebotomist.
		45.	Weigh filled plasma pooling bag and complete Source Plasma (Human) label. (see Procedure 2.4.5).
		46.	Place filled labeled plasma pooling bag in a freezer controlled to -20°C or colder (see Procedure 2.4.7). Must be either in separate quarantine freezer or in quarantine area of walk-in freezer clearly separated from plasma ready for shipping.
	Phlebotomist	47.	Obtain bag of red cells from second bag whole blood from Centrifuge area.
		48.	Return bag of red cells to donor chair or table indicated on bag. Hang bag on IV pole.
		49.	Identify bag of red blood cells with donor (see Procedure 2.3.9).
		50.	Connect bag of red cells to fitting of administration set and dilute with Sodium Chloride (see Procedure 2.3.10).
		51.	Discontinue diluting cells with Sodium Chloride. Agitate bag to obtain smooth suspension. Re-identify bag of red blood cells with donor (see Procedure 2.3.11). Infuse cells into donor only after positive identification has been made.

109 6882

GRO-C 12/10/80

GRO-C 12/4/80

8 1 0 1 1 2 C S 0 a 1 7

Subject: General Procedure for Plasmapheresis

Responsibility		Action
	52.	Discontinue phlebotomy and discard used plasmapheresis equipment (see Procedures 2.3.12 and 2.3.13).
	53.	Send donor (and donor chart if present) to reception area.
	54.	Prepare donor chair or table for new donor.
Receptionist	55.	Complete donor records in donor chart (see Procedure 2.0.3).
	56.	Pay donor and ask donor to leave Center.
	57.	Decide if donor chart needs review. a. Yes: send donor chart to Medical Director for review. b. No: file chart.
Medical Director	58.	Review donor chart (see Procedure 2.2.2)
Receptionist	59.	File donor chart.
Centrifuge Technician	60.	Prepare serum samples for total protein, electrophoresis and syphilis testing (see Procedure 2.4.6).
	61.	Prepare hyperimmune and HB_sAg samples for shipping (see Procedures 2.5.1 and 2.5.3).
	62.	Test serum samples for total protein. Record results on Form 81-9723 (Donor Card) in donor's chart (see Procedure 2.4.6). a. Suspend donors having total serum protein below 6.0 gm% or above 9.0 gm%.
R	63.	Test serum samples for RPR. Record results on test sheet (see Procedure 2.5.4) and on form No. 81-9723 (Donor Card) in donor's chart. Suspend donor having positive RPR test until donor is RPR negative.
R	64.	Ship Daily, samples for HB_sAg testing.
R	65.	Ship Twice Weekly, serum samples for total protein and electrophoresis.
	66.	Ship Weekly, hyperimmune plasma samples.
Manager or	67.	Receive written results of HB_sAg test.
R Assistant Manager	68.	Locate positive HB_sAg plasma and any subsequent units in Quarantine area of freezer and promptly destroy. (see Procedure 2.5.2). a. Mark out Control Number of destroyed positive HB_sAg plasma on Plasma Packing and Hepatitis Report Form.
	69.	Remove plasma from Quarantine area. Place completely labeled plasma in shipping area of walk-in freezer.

GRO-C 12/10/80

GRO-C 12/11/80

109 6883

8 1 0 1 1 2 CS0 a 1 8

Subject: General Procedure for Plasmapheresis

Responsibility	Action
Centrifuge Technician	70. Weekly or at other specified intervals prepare frozen plasma for shipping and ship (see Procedure 2.4.7).
	71. Receive results of confirmation test on plasma found to be RIA reactive.
Manager or Assistant Manager	72. If positive, record results of all HB_sAg tests on donor chart and permanently suspend donor.

R

109 6884

GRO-C 12/15/81

GRO-C 12/17/81

11A

8 1 0 1 1 2 C S 0 a 1 9

1. Observe all 10 fingernails of prospective donor under ultraviolet lamp (see Procedure 5.0.2) for bright staining fingers.
2. Observe entire length of prospective donor's exposed arms for recent needle punctures. Scars on donor's arms indicative of past drug addiction, donor not acceptable.
3. If either is present, question prospective donor carefully about possible recent blood or plasma donation. If necessary, telephone other Centers to confirm.
4. Assemble into a folder blank forms:
   Form No. 81-9723 Donor Card (back: 81-9711, Pre-Donation History)
   Form No. 81-9831 Medical History and Physical Examination
   Form No. 81-9745 Plasmapheresis Information and Donor's Consent
5. Assign prospective donor a Donor Number.
6. Record assigned Donor Number, prospective donor's name and other pertinent information in permanently bound Donor Log book.
7. Take donor's photograph. Have donor place his signature on photograph. Permanently attach photograph to prospective donor's folder.
8. Prepare plastic imprinting card if equipment is available. Provide means of attaching plastic imprinting card to donor chart. Keep plastic imprinting card in donor chart at all times when not actually in use for imprinting forms.
9. Use plastic imprinting card, or if not available, write Donor Number and name in block letters on Form No. 81-9711 (Pre-Donation History), on Form No. 81-9723 (Donor Card), and on Form No. 81-9731 (Medical History and Physical Examination). Complete other information at top of forms. Weigh prospective donor to nearest pound with donor dressed as during plasmapheresis. Center personnel must read scale. Write prospective donor's weight and date on Donor Card. Write your initials in space provided.
10. In comments section of Donor Card note serum sample collected and physical examination done. Identify chart folder with either prospective donor's name or Donor Number.
11. Send prospective donor and donor chart to Prep area.

GRO-C

109 6885

8 1 0 1 1 2 CS 0 a 2 0

PROCEDURE 2.0.2

Subject: Check and Prepare Donor Chart - Old Donor

Responsibility: Receptionist

1. Observe all 10 fingers of donor under ultraviolet lamp (see Procedure 5.0.2) for bright staining fingers.
2. Observe entire length of donor's exposed arms for recent needle punctures. Scars on donor's arms indicative of past drug addiction, donor not acceptable.
3. If either is present, question donor carefully about possible recent blood and plasma donation. If necessary, telephone other centers to confirm.
4. Compare photograph in donor chart with donor and compare donor's signature on sign-in sheets with donor's signature on photograph. If comparison cannot be made, ask donor to leave Center.
5. Weigh donor to nearest pound. Donor must be dressed as during plasmapheresis procedure. Center personnel must read scale.
6. On Form No. 81-9723 (Donor Card) record date and donor's weight. Write your initials in space provided.
7. Ask donor predonation history questions on Form 81-9711 (see Procedure 4.0.2). Question donor out of hearing range of other donors. Carefully phrase questions to obtain maximum information. Use common names of diseases and conditions prevalent in area. Record donor's responses by checking appropriate boxes. Write your initials in space provided.
8. Determine, from Form No. 81-9723 (Donor Card) if:
   a. Donor has donated within past 48 hours. If yes, ask donor to leave Center.
   b. Donor has already donated twice within a seven-day period. If yes, ask donor to leave Center.
   c. Four calendar months have elapsed since last review of donor chart by Medical Director. If yes, note M.D. review in comments section of Form 81-9723.
   d. Twelve calendar months have elapsed since last physical examination was done. If yes, note physical examination due in comments section of Form 81-9723.
   e. Four calendar months have elapsed since last serum sample for total protein, electrophoresis, and syphilis determinations were taken. If yes, note "collect serum sample" in comments section of Form 81-9723.
   f. More than four calendar months, but less than six calendar months have elapsed since last serum sample for total protein, electrophoresis, and syphilis determination was taken then:
      (1) Donor may be allowed to donate <u>after</u> medical director approves donation in writing on Form No. 81-9723 (Donor Card) and,
      (2) Collect serum sample for total protein, electrophoresis, and syphilis test during donation.

GRO-C

109 6886

8 1 0 1 1 2 CS 0 a 2 1

Subject: Check and Prepare Donor Chart - Old Donor

Responsibility: Receptionist

g. More than six months have elapsed since last serum sample for total protein, electrophoresis, and syphilis test were taken, then donor must be processed as a new donor except:
(1) The old donor chart will be used and,
(2) The old donor number will be used.

h. Donor has lost a unit of red cells or donated a unit of whole blood within the past 8 weeks. If yes, ask donor to leave the center, UNLESS
(1) The donor is examined by Medical Director and certified, in writing, by Medical Director on Form 81-9723 (Donor Card), to be acceptable for further plasmapheresis before expiration of the 8-week period, AND
(2) The donor possesses an antibody that is
(i) transitory
(ii) of a highly unusual or infrequent specificity, or
(iii) of an unusually high titer, AND
(3) The antibody and necessity for plasmapheresing the donor is documented on form 81-9723 (Donor Card).

GRO-C 3/M/77

GRO-C 8/31/77

109 6887

8 1 0 1 1 2 CS0 a 2 2

PROCEDURE 2.0.3

Subject: Complete Donor Chart

Responsibility: Receptionist

1. Following Donation:
   a. Ask donor for name and Donor Number when donor appears for payment.
   b. Obtain donor chart.
   c. Review entries for current donation on all forms for completeness.
   d. Complete any deficiencies noted in donor chart, contacting other Center personnel for information if necessary.
   e. Ask concerning donor's general health and well being.
   f. Check donor's arm to make sure phlebotomy site has not opened.
   g. Inform donor of suspensions, terminations, etc. if any.
   h. Inform donor of next allowable donation date.
   i. Add to donor chart serum protein electrophoresis results.
   j. Add to donor chart titer results on hyperimmune donors.
2. When donor leaves center after no donation due to health reasons or after physician review:
   a. Check to determine if reason for either permanent rejection or temporary deferral of donation is clearly documented on Form Nos. 81-9723 (Donor Card), 81-9711 (PreDonation History) or 81-9731 (Medical History and Physical Examination), (See Procedures 4.0.1, 4.0.2, 4.0.4, respectively).

GRO-C

109 6888

810112 CS0a23

PROCEDURE 2.0.4

Subject: Application of Fluorescent Finger Stain

Responsibility: Prep Technician

1. Apply finger stain to designated finger with a wooden applicator stick, not cotton tipped.
2. Dip stick in finger stain and place liberal drop on donor's finger nail near cuticle. Stain will flow around cuticle.
3. Push cuticle back in a number of places so that stain runs underneath cuticle.
4. Make sure donor does not wipe off stain before drying.
5. If donor is missing designated finger, use same finger on opposite hand. Make entry on Form No. 81-9723 (Donor Card) noting this action.

GRO-C

109 6889

8 1 0 1 1 2' GS 0 a2 4

PROCEDURE 2.1.1

Subject: Puncture Finger and Obtain Blood in Capillary Tube

Responsibility: Prep Technician

1. Select a finger on donor's hand that is relatively clean and free of callous. If donor's hands are visibly dirty, ask donor to wash hands in restroom.
2. Hold donor's finger firmly.
3. Vigorously scrub side of donor's finger with sponge containing 70% Isopropyl Alcohol.
4. Remove protective covering from point of a sterile, disposable lancet. Once exposed, do not touch lancet to any surface other than donor's finger.
5. Hold donor's finger firmly and puncture scrubbed side of finger with sterile lancet. Puncture finger deeply enough to get a free flow of blood. Do not puncture finger while donor has thermometer in mouth.
6. Wipe blood and any excess alcohol from donor's finger with a dry sterile sponge.
7. Squeeze donor's finger gently causing blood to flow freely from puncture.
8. Touch tip of a heparinized capillary tube to freely flowing blood.
9. Fill heparinized capillary tube approximately three-fourths full. Do not fill so full that column of blood is longer than maximum scale divisions on hematocrit reading device. Do not allow air bubbles to enter capillary tube. If necessary, repuncture donor's finger after again scrubbing with a sponge containing 70% Isopropyl Alcohol.
10. Wipe donor's finger with sponge containing 70% Isopropyl Alcohol.
11. Ask donor to hold dry sponge firmly on puncture until bleeding is stopped.
12. Hold filled capillary tube horizontally and perpendicular to a tray of sealing clay.
13. Push the filled end of the capillary tube into sealing clay with a twisting motion. Clay will form an effective seal in capillary tube.
14. If desired, sealed, filled capillary tube may be held vertically in a numbered slot or compartment in sealing clay holder.
15. Provide a suitable way of positively identifying a filled capillary tube with correct donor and/or correct donor chart.
16. When sealing clay becomes filled with holes, smooth out to a uniform thickness with a tongue depressor, or finger covered with a rubber or plastic finger cot or glove.

4/15/76

GRO-C

109 0890

81C112 CS0 25

Subject: Microhematocrit Determination

Responsibility: Prep Technician

1. Keep microhematocrit centrifuge clean at all times (see Procedure 5.0.3).
2. Keep rubber gasket against which capillary rests undamaged.
3. Place a filled capillary tube (see Procedure 2.1.1) in a numbered position in head of microhematocrit centrifuge.
4. Provide a suitable way of positively identifying a filled capillary tube with correct donors and/or correct donor chart.
5. Operate microhematocrit centrifuge according to manufacturer's instructions with particular reference to time settings and all safety precautions.
6. Using scale on microhematocrit centrifuge head or an auxillary scale, place bottom of red cell pack (red cell-clay interface) on zero line.
7. Moving scale or capillary tube, whichever is appropriate to measuring device used, place top of plasma (plasma-air interface) on 100% line.
8. Determine which line on scale most nearly matches top of red cell pack (red cell-plasma interface) and from labeled percentage on the line determine microhematocrit value. Occasionally a white layer will be noted between top of red cell pack and bottom of plasma. This is a buffy coat (mixture of white blood cells and platelets). In this case, measure top of red cell pack (red cell-buffy coat interface).
9. Record observed value in appropriate space on Form No. 81-9723 (Donor Card). Write your initials in space provided.
10. Proceed immediately to total plasma protein determination.

Control Procedure

R 1. Before initial use, after repairs or adjustments, or at least annually.
   a. Fill two capillary tubes, (see Procedure 2.1.1).
   b. Operate centrifuge for a 3 minute spin and obtain readings.
   c. Respin same capillary tubes for 1 additional minute and obtain readings as above.
   d. Respin same capillary tubes again for 1 additional minute and obtain readings as above.
   e. Maintain a bound log book in area of microhematocrit centrifuge use. Make entries:
      (1) Date
      (2) Serial number of microhematocrit centrifuge.
      (3) Total time capillary tubes spun.
      (4) Results obtained as a result of each total time.
      (5) Decide microhematocrit time setting to be used. Time for use is that minimum time interval necessary to achieve maximum packing of red cells, i.e.: minimum hematocrit reading.

GRO-C 6/11/80

GRO-C

109 6891

8 10112 CS0 a 26

Subject: Microhematocrit Determination

(6) Write that time in large letters next to date on which test done.
(7) Technician doing microhematocrit determination signs initials next to recorded time to be used.

2. Before initial use, after repairs or adjustments, and quarterly.
   a. Check timer by observing the elapsed time equipment operates under influence of timer with suitable watch. Must be within ± 10% of equipment manufacturer's specifications.
   If timer is outside of above specified limits, equipment must not be used for testing of donors until equipment is adjusted and found to meet specified limits by further testing.

GRO-C 6/16/80
GRO-C 6/16/80

109 689

PROCEDURE 2.1.3

Subject: Total Plasma Protein Determination

Responsibility: Prep Technician

1. Gently break capillary tube 1 mm. away from the red cell-plasma interface toward open end of tube.
2. Hold pre-standardized refractometer in a horizontal position with cover plate closed over surface of prism. Face of prism and cover plate must be clean and lint free (see procedure 5.0.4).
3. Touch unbroken end of capillary to exposed portion of prism at end of cover plate. Allow plasma to enter space between cover plate and prism by capillary action. Tilt or gently shake capillary tube to begin plasma flow. Never strike prism with capillary tube. Never lift cover plate before reading.
4. Place finger on nameplate and press cover plate gently, but firmly.
5. Expose covered prism to bright window, fluorescent or incandescent light source. If necessary to obtain maximum contrast between light and dark boundary, tilt instrument slightly with respect to light source.
6. Focus scale by rotating eyepiece. Read total protein value directly at point where dividing line between light and dark boundary crosses scale.
7. Record total protein value on Form No. 81-9723 (Donor Card). Write your initials in space provided.
8. Swing cover plate off prism and over body of refractometer.
9. Wipe both surfaces with soft cloth or tissue moistened with water. Dry both surfaces with soft cloth or tissue. Wet surfaces may cause a false low reading on next sample. Fuzzy light and dark boundary results from improper cleaning. Never use sharp or hard objects or gritty cleaning compounds for cleaning. Never use alcohol for cleaning. Avoid scratching either surface.

Adjustment of Refractometer

1. The only adjustment permitted is zero setting.
2. Use only good quality distilled water (Sterile Water for Injection USP is ideal) stored in a closed glass container.
3. Bring refractometer and water to 70-85°F.
4. Fill a microhematocrit capillary tube with water.
5. Take a reading as described above.
6. Reading must be 1.000 on Urine Specific Gravity scale or 1.333 on Refractive Index scale.
7. Adjustment is required if reading deviates by more than 1/2 a scale division.
8. Push jeweler's screw driver through cement seal.
9. Turn clockwise to increase reading, turn counter-clockwise to decrease reading. Final motion must be in clockwise direction.
10. Repeat reading with new capillary tube and water.
11. Seal hole with caulking compound, obtainable from refractometer manufacturer.

GRO-C

109 6893

Subject: Total Plasma Protein Determination

Responsibility: Prep Technician

Control Procedure

1. Daily - Use good-quality distilled water (Sterile Water for Injection USP is ideal) stored in a closed glass container.
   a. Check Zero adjustment.
2. Record of Control Procedure.
   a. Maintain a bound log book in area of refractometer use. Make daily entries:
      (1) Date
      (2) Serial number of refractometer
      (3) Result of reading for zero adjustment and initials of technician obtaining result.
      (4) Adjustment of refractometer and initials of person making adjustment.
      (5) Note in detail any repair of instrument.
   b. Each working day, each technician doing refractometer determinations tests refractometer being used that day for zero adjustment.

Trouble Shooting

1. Check zero setting any time refractometer is dropped, jarred, or transported more than a few feet prior to again using for measurement of donor total plasma protein.
2. Scratched or pitted prism surface may cause erroneous results. Return refractometer to manufacturer for repair.
3. Following transit, jarring, or dropping, an air bubble may appear as you look into refractometer. Hold refractometer vertically, eyepiece down, shake slightly. Air bubble will reenter a trap where it is held during normal operation. Air bubble is required to be in trap for temperature compensation and accurate total protein reading.

GRO-C

PROCEDURE 2.1.4

Subject: Label Whole Blood Bags, Test Tube for Whole Blood Sample, and Required Forms

Responsibility: Prep Technician
Alternate Responsibility: Receptionist

R 1. Prior to issuance, insure all numbers on Control Number set are identical, and Control Number set is sequential with other Control Number sets in use.
2. Except for labels designated for whole blood bags, it is not intended that the specific label indicated will be for the use indicated.
3. The chart demonstrates there are more than sufficient labels for all uses.

C 00112
SOULES, DAVID E.

4. Name, Donor Number, and date are applie as indicated with e mechanical imprinte If not, print block letters.

	658410		Second whole blood bag
Plasma pooling container	658410	658410	Plasma Packing List & HB_sAG Report Form
Serum Sample Packing List	658410	658410	Serum (electrophoresis) sample
Plasma (tubing) sample (antibody tests)	658410	658410	Plasma Sample Packing List (antibody tests)
	658410	658410	Donor's forehead or arm
RPR (syphilis) test sheet	658410	658410	Donor Card
Hepatitis (tubing) sample (HB_sAG test)	658410	658410	

658410

109 6895

First whole blood bag

GRO-C 10/29

GRO-C 11/5/7

21

SOULES DAVID E.
C 00112

1/22/80

PROCEDURE 2.2.1

Subject: Perform Medical History and Physical Examination

Responsibility: Medical Director

1. Receive from Prep Technician partially completed donor chart.
2. Determine if prospective donor is new donor.
   a. Make sure prospective donor has read Form No. 81-9745 (Plasmapheresis Information and Donor's Consent) Prospective donors who are blind or are otherwise unable to read the form must have entire text read to them in the language in which they are fluent (tape recording of complete text OK). Person reading text or operating tape recorder must sign consent form as so doing.
   b. Explain to prospective donor hazards of plasmapheresis particularly that of a hemolytic transfusion reaction if prospective donor is given red blood cells of another donor.
   c. Determine if prospective donor has completely understood procedure including risks involved.
   d. Give prospective donor an opportunity to sign Form No. 81-9745 (Plasmapheresis Information and Donor's Consent) making sure donor has a clear opportunity to refuse. If donor refuses to sign, ask person to leave Center.
   e. Witness donor's signature on Form No. 81-9745.
3. Determine if donor is old donor appearing for an annual examination because a period exceeding 6 months has elapsed since the last sample, Serum Protein Electrophoresis, etc. was collected.
4. Perform Medical History and Physical Examination, recording result on Form No. 81-9731 (Medical History and Physical Examination) and following guidelines set forth for completion of Form No. 81-9731 (see procedure 4.0.4).
5. Determine if prospective donor meets qualifications of a plasmapheresis donor. If not, ask person to leave Center and return appropriately marked donor chart to Reception area.
6. Determine if prospective donor meets qualifications for any hyperimmune program.
   a. Ask donor to read appropriate Immunization Information and Donor's Consent (see procedures 3.0.1, 3.0.2, 3.0.3). Prospective donors who are blind or are otherwise unable to read the form must have entire text read to them in the langu in which they are fluent (tape recording of complete text OK). Person reading text or operating tape recorder must sign cons form as so doing.
   b. Explain to donor the hazards of hyperimmunization program contemplated (see procedures 3.0.1, 3.0.2, 3.0.3).
   c. Determine if prospective donor has completely understood risks involved.
   d. Give donor an opportunity to sign appropriate Immunization Information and Donor's Informed Consent form making sure donor has a clear opportunity to refuse.
   e. Witness donor's signature.
7. Send qualified donor and donor's chart to Prep area.
8. Frequency of Medical History and Physical Examination.
   a. New donors. On day of first donation or within one calendar week prior to first donation.
   b. Old donors. Once every 12 calendar months from day of first donation for donors experiencing continued participation, or

2/20/79

GRO-C 2/9/79

GRO-C 2-2-

PROCEDURE 2.2.1

Subject: Perform Medical History and Physical Examination

Responsibility: Medical Director

prior to the first donation following a lapse of participation resulting in six months or more elapsing since the last sample for Serum Protein Electrophoresis, etc. was collected, or whenever it appears appropriate from observations of Medical Director or other Center personnel, and on day of first donation following a period of non-participation due to suspension by Medical Director for medical reasons.

GRO-C 2/9/79

GRO-C 2-6-79

PROCEDURE 2.2.2

Subject: Review Donor Chart

Responsibility: Medical Director

1. Receive from Reception Area those donor charts scheduled for review.
2. Review accumulated laboratory data and collection records appearing on:
   a. Form No. 81-9711 (Pre-donation History).
   b. Form No. 81-9723 (Donor Card).
   c. Results of total protein on serum sample.
   d. Results of serum electrophoretic tests, including tracing.
   e. Results of tests for syphilis.
3. Serum protein electrophoresis.
   a. Total protein value on serum sample must be no less than 6.0 gm% and no greater than 9.0 gm%.
   b. Acceptable values for plasmapheresis donors as determined by Cutter Laboratories, Inc: R

Albumin -	3.5 to 6.0 gm%
Alpha 1 globulin -	0.1 to 0.4 "
Alpha 2 globulin -	0.5 to 1.2 "
Beta globulin -	0.6 to 1.3 "
Gamma globulin -	0.6 to 1.9 "

   c. The serum protein electrophoresis results must be reviewed by the physician and his signature and statement of acceptance or non-acceptance must appear on every electrophoresis pattern. Donors may only be accepted when their electrophoresis results fall within the normal range in section 3 (b). If the value of any protein fraction is reported outside this established range, the donor must be removed from the plasmapheresis program until another serum sample is drawn, retested and reported to be within the acceptable range. The physician at the plasma center may not make an exception to abnormal values and allow a donor to continue on the plasmapheresis program on this basis.
   d. Abnormally high or low readings, difficulty in separating the five major components or patterns with sharp spikes should be investigated further. This may lead to the accidental discovery of some underlying disease, eg: myeloma.
   e. Abnormal patterns such as bisalbuminemia are sufficient reason for terminating donors.
   f. Any inquiries concerning serum electrophoretic patterns should be directed to Dr. Ralph Rousell, Cutter Laboratories, Inc. R
4. Syphilis test.
   a. Donor with positive syphilis serology must be suspended and not allowed to donate plasma.
   b. If, after treatment, a donor's positive syphilis test becomes negative, donor may be reinstated.
   c. Biological false positive reactions may occur in such diseases as infectious mononucleosis, malaria, lupus erythematosus, vaccinia and virus pneumonia. If donor's private physician can

109 6898

GRO-C

GRO-C

4/7/80

Subject: Review Donor Chart

Responsibility: Medical Director

provide signed documentary evidence that an FTA (Fluorescent Treponemal Antibody) or TPI (Treponema Pallidum Immobilization) test on donor is negative, and if medical director has determined that apparent biological false positive reaction is not result of an underlying disease that would disqualify donor from plasmapheresis program, then donor may continue on plasmapheresis program. All signed documentary evidence leading to the conclusions mentioned above must be included in donor's permanent chart.

5. Determine if results of these data and records show continued suitability of the donor.
   a. If they do, write the words "Donor suitable for continued plasmapheresis" in next available space on Form 81-9723 (Donor Card) beginning at extreme left of card, sign your name in your own handwriting and indicate date on which such determination was made.
   b. If they do not, write the words "Donor NOT suitable. DO NOT bleed unless suitability reestablished" in next available space on Form No. 81-9723 (Donor Card) beginning at extreme left of the card, sign your name in your own handwriting, and indicate date on which such determination was made. In following space indicate reason for your decision including a date on which donor may be reexamined for suitability.

6. Return donor charts to Reception Area.
7. Frequency of Review of Donor Chart.
   a. On receipt of results of serum electrophoresis and syphilis tests on samples drawn no earlier than 21 days previously.
   b. Every 4 calendar months for donors experiencing continued participation or prior to first donation following a lapse of participation which results in between four and six calendar months having elapsed since the last sample for Serum Protein Electrophoresis, etc. was collected, or whenever it appears appropriate from observations of Medical Director or other center personnel, and prior to first donation following a period of non-participation due to suspension by Medical Director for medical reasons. Donors returning on which no serum electrophoresis sample has been collected within the past six months shall be processed as new donors. (use same donor number).

109 0027

GRO-C 09-28

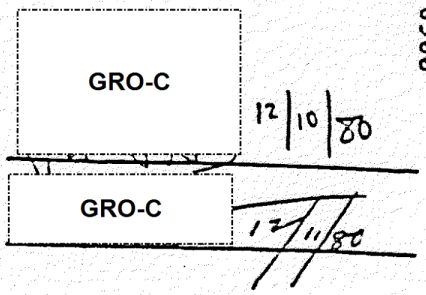
GRO-C 10/6/78

PROCEDURE 2.2.3

Subject: Record Batch Numbers and Lot Numbers of Supplies in Use Daily

Responsibility: Phlebotomist and Centrifuge Technician

1. At the beginning of each working day, record in a bound log book:
   a. Date
   b. Batch numbers, if applicable, and lot numbers of supplies in use that day.
   c. First control number issued for each type plasma to be drawn that day.
2. Supplies whose batch numbers and lot numbers are to be recorded are:
   a. Attached Double Bleeding Plasmapheresis Units (record numbers for both 50ml and 60ml citrate bags).
3. Supplies whose lot numbers are to be recorded are:
   a. Saftifilter® Blood Administration Set
   b. Sodium Chloride for Injection, USP
   c. Plasma Pooling Bag
4. If, during a working day, new supplies are issued bearing new batch numbers and/or lot numbers, record in log book.
   a. Date
   b. New batch number and/or lot number of supplies issued.
   c. First control number issued for each type plasma that will be drawn using new batch number and/or lot number equipment.



PROCEDURE 2.3.1

Subject: Identify Labeled Whole Blood Bags with Donor

Responsibility: Phlebotomist

1. Assign donor to table or chair and receive labeled blood bags.
2. Assist donor to become comfortable on table or chair assigned.
3. Write table or chair identification number or letter on both whole blood bags.
4. Ask donor's name and Donor Number. As donor recites information, verify information on whole blood bag labels.
5. Check to confirm that Control Number on each whole blood bag and on test tube for whole blood collection for serum sample (if any) are duplicates of Control Number affixed to donor.
6. Show labels on each whole blood bag to donor and ask donor to verbally confirm name and number as belonging to donor.
7. Ask donor to read aloud entire Control Number.
8. While donor reads Control Number, read Control Number affixed to donor to assure it is a duplicate of Control Number read by donor.
9. Read aloud donor name and number on label of each whole blood bag.
10. Ask and receive verbal confirmation that donor name and number belong to donor.
11. In the case of persons with insufficient vision to participate in this procedure, another center employee must partidipate in this procedure on behalf of the donor. This employee's identity and participation should be entered on the donor card.
12. In the case of non-English speaking donors, this procedure must be performed by a phlebotomist fluent in donor's language.
13. Any uncertainties or inconsistencies with any portion of this procedure will be resolved by Medical Director or his designate.
14. Proceed to prepare phlebotomy site (see procedure 2.3.2) and prepare and connect plasmapheresis equipment (see procedure 2.3.3) after this entire procedure has been satisfactorily completed.

R

109 6901

GRO-C 5/29/79

GRO-C 5/29/79

7/9/79

PROCEDURE 2.3.2

Subject: Prepare Phlebotomy Site

Responsibility: Phlebotomist

1. Examine both exposed arms and select site for phlebotomy (see Procedure 2.3.4)

R 2. Scrub phlebotomy site with Tincture of Green Soap NF for a minimum of 30 seconds if using gauze or dental plug, or for a minimum of 60 seconds if using cotton sponges. An alternate, equivalent, cleanser may be employed if used in accordance with manufacturer's directions.

R 3. Remove soap by surgical scrub with 70% Isopropyl Alcohol.

4. Apply Tincture of Iodine, USP, or equivalent, using a spiral motion starting at center of phlebotomy site and proceeding outward. Cover an area at least 2 inches in diameter.
   a. Allow iodine to dry. While waiting for iodine to dry, prepare and connect plasmapheresis equipment (see Procedure 2.3.3).

5. Remove iodine with 70% Isopropyl using a spiral motion starting at center of phlebotomy site and proceeding outward until iodine is removed.

6. Betadine type materials may be used provided proper solutions are employed and manufacturer's directions for use are followed:
   a. Betadine Surgical Scrub may be substituted for Tincture of Green Soap NF providing a 5 minute scrub is employed.
   b. Betadine Solution may be substituted for Tincture of Iodine USP providing solution is left on arm for at least 1 minute. Betadine Solution should not be allowed to dry.
      1) Betadine Solution does not require removal before performing phlebotomy.

7. The Frepp/Sepp Kit™, manufactured by the Marion Scientific Corporation, may be used provided the manufacturer's directions for use are followed
   a. Frepp™ surgical scrub may be substituted for Tincture of Green Soap NF providing a 30-second scrub is employed.
   b. Sepp™ (Povidone Iodine) Antiseptic Swab may be substituted for Tincture of Iodine USP. Use as specified in 6b above.

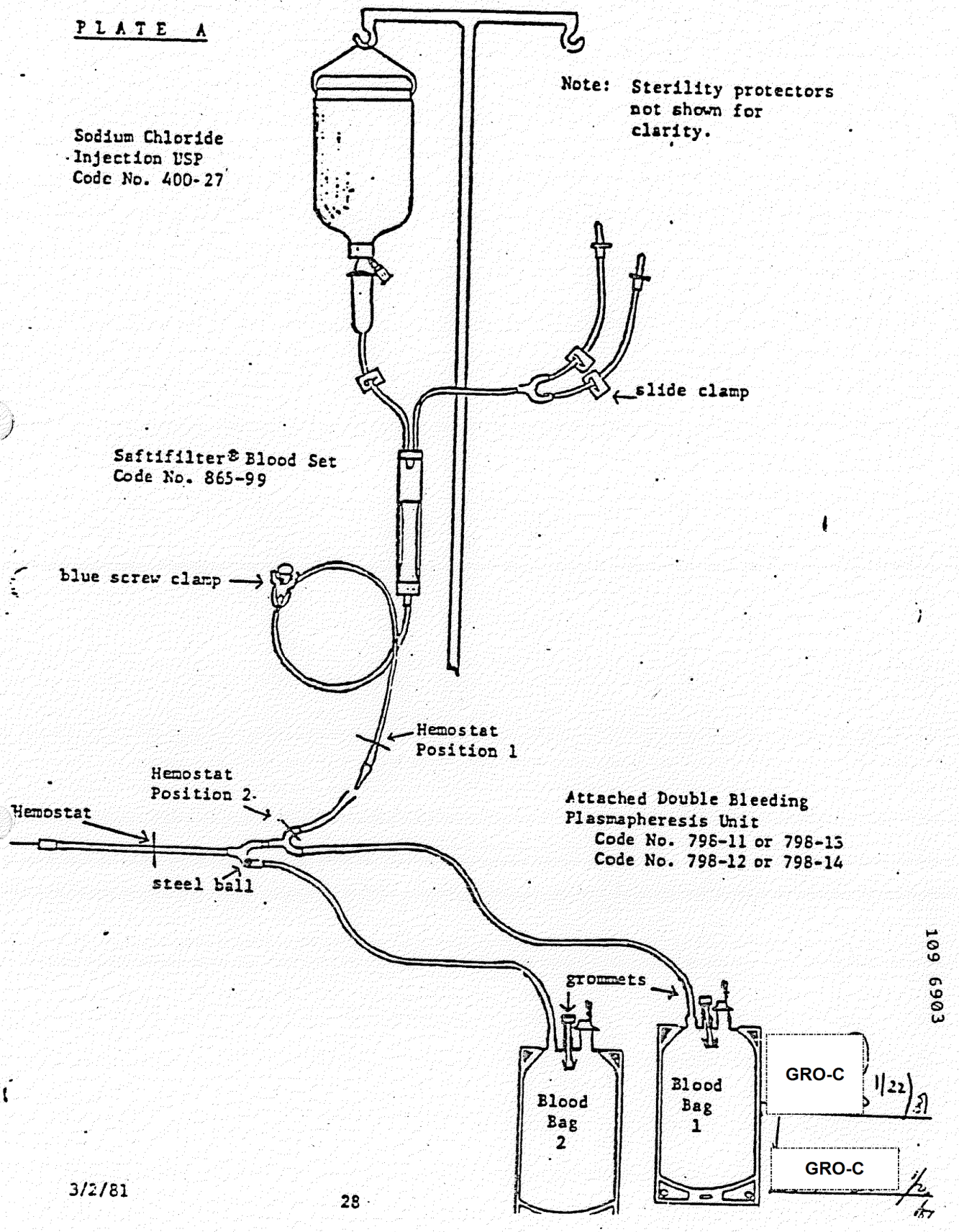
8. Perform phlebotomy (see Procedure 2.3.4).

9. Precautions:
   a. Sterile cotton balls, dental plugs or gauze sponges with sponge forceps may be used for all applications. Cotton tipped applicators may be used for all applications except the soap scrub.
   b. Solutions containers and sponge forceps are washed and sterilized at least once each week.
   c. Stand sponge forceps in a container of 70% Isopropyl Alcohol in between use.
   d. Maintain a record of sterilization runs indicating results of sterility test controls, e.g.: sterilizer tape or Diak controls (see Procedure 5.0.9).
   e. Sterile strip packaged Cepti-Seal SEPP™ may be used if desirable.
   f. If phlebotomy cannot be performed immediately following site preparation, place a sterile gauze pad over phlebotomy site.

GRO-C 9/24/79

GRO-C 9/24/79

PLATE A



109 6903

3/2/81

PROCEDURE 2.3.3

Subject: Prepare and Connect Plasmapheresis Equipment

Responsibility: Phlebotomist

See facing page for Plate A.
Make all connections aseptically.

1. Secure one each of the following equipment:
   a. Sodium Chloride Injection USP, Code No. 400-27 or ~~400-30~~.
   b. Saftifilter® Administration Set, Code No. 865-99.
2. Connect Sodium Chloride and Administration Set.
   a. Close both slide clamps on legs of Administration Set adjacent to blood inletting spikes.
   b. Stand bottle base down on a solid flat surface.
   c. Remove tear off aluminum seal and aluminum dust cover from stopper assembly.
   d. Remove sterility protector from spike on drip chamber of Administration Set.
   e. Insert spike into target area of stopper on Sodium Chloride bottle without twisting.
   f. Invert bottle immediately and observe solution for air bubbles and turbidity. If bubbles are absent or solution is turbid, discard entire set up.
3. Hang set up on IV pole at donor location.
4. Fill Administration Set with Sodium Chloride.
   a. Squeeze flexible filter barrel and establish fluid level just below top of filter.
   b. Remove sterility protector from male luer fitting on Administration Set and allow Sodium Chloride to flow out of fitting.
   c. Apply hemostat at Position 1 and proceed immediately to next step.
5. Connect Administration Set and Double Plasmapheresis Set.
   a. Clamp hemostat at Position 2.
   b. Remove sterility protector from female luer fitting on donor set.
   c. Connect male and female luer fittings.
   d. Release hemostats at Positions 1 and 2 allow solution to flow just past the first plastic Y.
   e. Clamp hemostat at position 2.
   f. Seal plasma transfer legs of each blood bag by folding tubing in half and firmly applying a grommet to each leg. Do not crimp gromm
6. Prepare to Collect Bag of Whole Blood (see Procedure 2.3.5) after performing Phlebotomy (see Procedure 2.3.4).
7. Use set up as soon after insertion of spike into stopper assembly as possible. In no case is more than one hour to elapse between inserting spike in stopper and administration of Sodium Chloride to donor.

GRO-C 6/13/78

GRO-C 6/14/78

109 6904

8/28/78

PROCEDURE 2.3.4

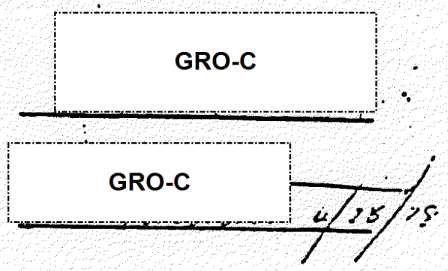
Subject: Perform Phlebotomy

Responsibility: Phlebotomist

1. Use only medial cubital vein, medial cephalic vein, or cephalic vein lying in the region of the ante-cubital fossa.
2. Place a tourniquet on donor's arm at least 4-6 inches above prepared phlebotomy site.
3. Ask donor to clench and unclench fist several times.
4. Ask donor to keep fist clenched during phlebotomy.
5. Clamp hemostat to line between donor needle and first "Y" fitting.
6. Remove sterility protector from phlebotomy needle on donor set.
7. NEVER touch prepared phlebotomy site (see Procedure 2.3.2) with anything other than a sterile needle prior to performing phlebotomy.
8. Insert needle through skin and into vein in one smooth motion, threading needle into vein.
9. Immediately remove hemostat from line between donor needle and first "Y" fitting.
10. Tape needle into place on donor's arm.
11. Proceed immediately to Collect Bag of Whole Blood (see Procedure 2.3.5).
12. Record identity of phlebotomist in comments section of Form No. 81-9723 (Donor Card) (see Procedure 4.0.1).

Precaution:

In the event second venipuncture becomes necessary release tourniquet, secure new equipment and begin again if donor is willing.



7/17/78

PLATE B

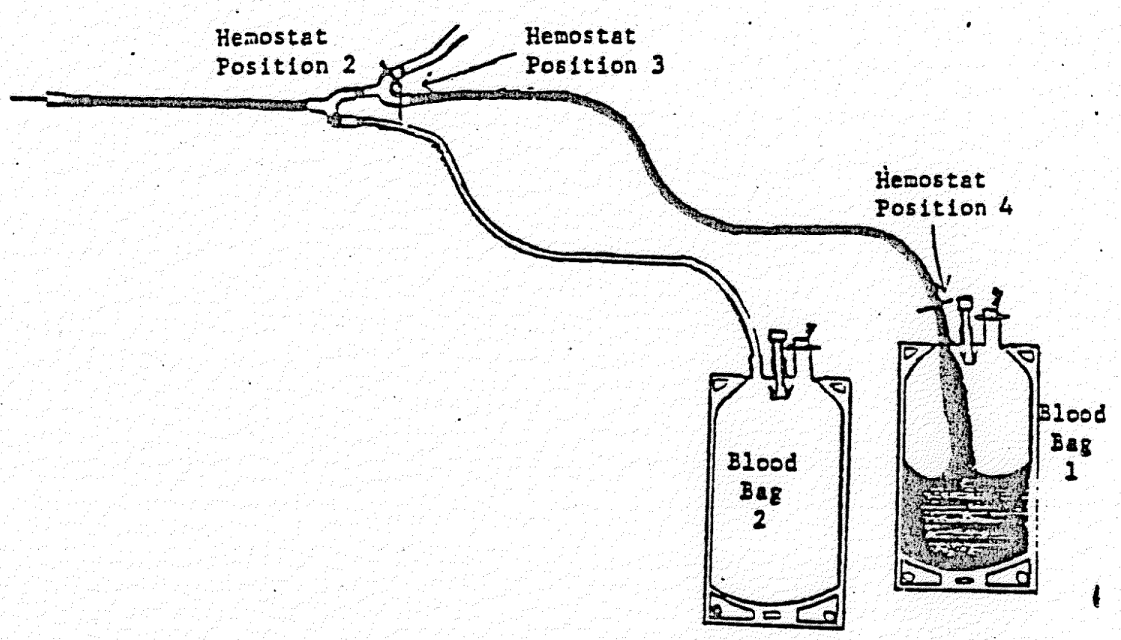
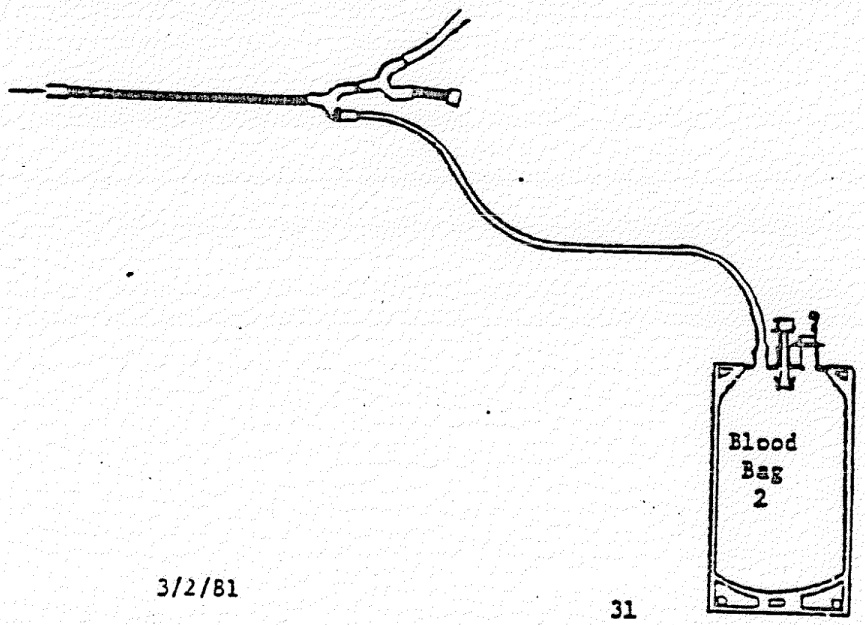


PLATE C



109 6906

GRO-C 1/22/81

GRO-C 1/26/81

PROCEDURE 2.3.5

Subject: Collect Bag of Whole Blood

Responsibility: Phlebotomist

See facing page for Plates B and C.

1. Decide if amount of whole blood to be collected is 500ml. or 600ml. Collect 500ml. if blood bag label has no border and 600ml. if blood bag label has black border.
2. Adjust vacuum collecting device or automatic cut-off scale (See Procedure 5.0.5) to collect required amount of whole blood.
3. First whole blood bag.
   a. Insert blood bag 1 into vacuum collecting device or hang blood bag onto automatic cut-off scale. Position blood bag 2 so it does not interfere with functioning of vacuum collecting device or automatic cut-off scale.
   b. Perform phlebotomy (See Procedure 2.3.4).
   c. Start mixing and vacuum switches on vacuum collecting device or agitate blood bag hung on automatic cut-off scale. Note: When latter device is used it is necessary to periodically manually mix blood and anticoagulant in blood bag at sufficient intervals to prevent clotting.
   d. When vacuum collecting device or automatic cut-off scale signifie completion of whole blood collection, release tourniquet, releas hemostat at position 2 and clamp hemostat at position 3, unless test tube of whole blood is to be collected.
   e. Proceed immediately to disconnect bag of whole blood (see Procedure 2.3.7) or collect test tube of whole blood (see Procedure 2.3.6), whichever is applicable.
4. Second whole blood bag.
   a. Close slide clamp on administration set adjacent to drip chamber.
   b. Move steel ball in Y adjacent to donor needle to permit flow of blood into blood bag 2.
   c. Reapply tourniquet.
   d. Start mixing and vacuum switches on vacuum collecting device or agitate blood bag hung on automatic cut-off scale. Note: When latter device is used it is necessary to periodically manually mix blood and anti-coagulant in blood bag at sufficient interval to prevent clotting.
   e. When vacuum collecting device or automatic cut-off scale signifie completion of whole blood collection, release tourniquet, move steel ball in Y to original position.
   f. Proceed immediately to disconnect bag of whole blood (See Procedure 2.3.7).

GRO-C 6/13/78

GRO-C 6/14/78

8/28/78

109 6997

Subject: Collect Bag of Whole Blood

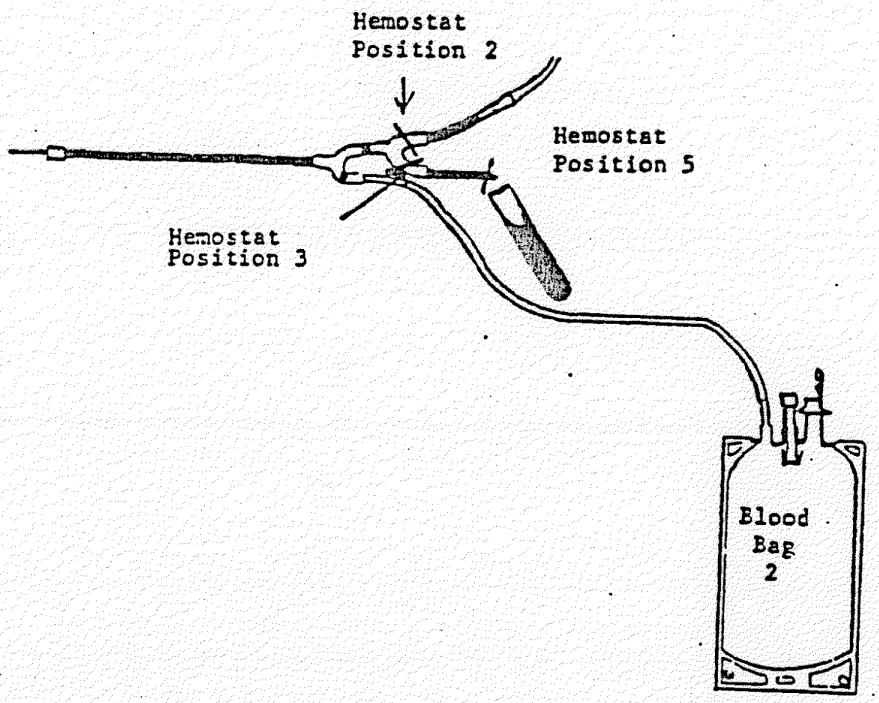
Responsibility: Phlebotomist

Precaution:

1. Do not collect second bag whole blood if red cells from first bag whole blood cannot be returned to donor. In this event discontinue phlebotomy (see Procedure 2.3.12).
2. In the event of clotting in needle or donor tubing, preventing withdrawal of blood, DO NOT attempt to flush clots out with either blood or Sodium Chloride. Discontinue phlebotomy (see Procedure 2.3.12), secure new equipment and begin again if donor is willing.

GRO-C

PLATE D



GRO-C 1/22/81

GRO-C 1/26/81

3/2/81

109 6909

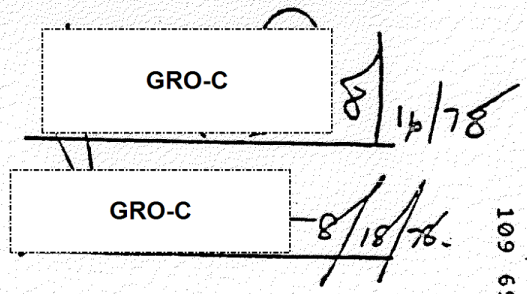
PROCEDURE 2.3.6

Subject: Collect Test Tube of Whole Blood for Serum Sample

Responsibility: Phlebotomist

See facing page for Plate D.

1. Apply hemostat at position 3.
2. Remove filled blood bag from vacuum collecting device or plasmapheresis cut-off scale.
3. Strip donor tubing from hemostat toward bag whole blood.
4. Double blood-free tubing over and hold with fingers to maintain tubing blood-free.
5. Apply grommet to folded tubing and seal.
6. Cut blood-free tubing between hemostat and grommet but nearer hemostat.
7. Hold Control Number labeled test tube so that blood may flow from cut end of donor set into test tube.
8. Release hemostat at position 3 and allow blood to flow freely into test tube.
9. Allow test tube to fill to within 1 inch of top.
10. Apply hemostat at position 3.
11. Remove tourniquet.
12. Remove hemostat from position 2.
13. Strip blood from tubing into test tube in ONE operation.
14. Immediately apply hemostat at position 5 to maintain tubing air-free.
15. Adjust flow of Sodium Chloride to slow drip with blue screw clamp after flushing blood from tubing.
16. Fold cut blood bag tubing over close to Y and hold with fingers to maintain tubing blood-free.
17. Apply grommet to folded tubing.
18. Remove hemostat from position 5 and seal tubing with grommet.
19. Remove hemostat from position 3.
20. Trim off blood-free length of tubing.
21. Insert blood bag 2 into vacuum collecting device or hang blood bag onto plasmapheresis cut-off scale.
22. Take Control Number labeled test tube of whole blood and blood bag 1 to Centrifuge area.
23. Alternatively, a B-D Vacutainer® or comparable blood collection system may be used, provided the manufacturer's directions for use are followed.



109 6910

8/28/78

PROCEDURE 2.3.7

Subject: Disconnect Bag of Whole Blood and Begin Sodium Chloride Drip.

Responsibility: Phlebotomist

See Plate B & C

1. Remove filled blood bag from vacuum collecting device or automatic cut-off scale.
2. First Whole Blood Bag:
   a. Adjust flow of Sodium Chloride to a slow drip with the blue screw clamp after flushing blood from tubing.
   b. Double blood bag tubing over close to Y and hold with fingers to maintain tubing blood free.
   c. Apply grommet to folded tubing and seal.
   d. Strip blood bag tubing from grommet toward bag whole blood.
   e. Double blood bag tubing over close to blood bag and hold with fingers to maintain tubing blood-free.
   f. Apply grommet to folded tubing and seal.
   g. Cut donor tubing between grommets but near grommet close to the Y.
   h. Insert blood bag 2 into vacuum collecting device or hang bag 2 onto automatic cut-off scale.
3. Second Whole Blood Bag
   a. Open slide clamp on administration set adjacent to drip chamber.
   b. Adjust flow of Sodium Chloride to a slow drip with blue screw clamp after flushing blood from tubing.
   c. Double blood bag tubing over close to Y and hold with fingers to maintain tubing blood free.
   d. Apply grommet to folded tubing and seal.
   e. Strip blood bag tubing from grommet toward bag whole blood.
   f. Double blood bag tubing over close to blood bag and hold with fingers to maintain tubing blood-free.
   g. Apply grommet to folded tubing and seal.
   h. Cut donor tubing between grommets but near grommet close to the Y.

4. Trim off blood-free length of tubing and take bag of whole blood to Centrifuge area.

Precaution:

1. In the event of clotting in needle or donor tubing, preventing flow of saline, whole bood, or red cells, DO NOT attempt to remove or dislodge clot by stripping donor tubing. Discontinue phlebotomy (see Procedure 2.3.12), secure new equipment and begin again if donor is willing.

1069 6911

GRO-C 8/16/78

GRO-C 8/18/78

PROCEDURE 2.3.8

Subject: Symptoms and Treatment of Donor Reactions

Responsibility: Medical Director and All Personnel

For any donor reaction or injury while donor is on Center premises, or if reported to Center after donor has left premises, write specific details of reaction or injury, all steps taken and all treatment accorded donor including names of personnel involved and outcome of event on Form No. 81-9723 (Donor Card) in donor's permanent chart.

Medical Director will sign and post standing orders for treatment of donor reactions in his absence. If different from that contained in this procedure, submit one copy to Cutter Laboratories.

This Procedure is written as a guideline for your center. The Medical Director should decide the treatment provided for donor reactions.

In the unlikely event a fatality occurs as a complication of, or associated with, plasmapheresis (including, but not limited to, drawing of blood and returning of red cells) notify Director, Bureau of Biologics by telephone as soon as possible. Within seven days, a written report of a detailed investigation of all facts surrounding the incident must be submitted to the Director, Medical Operations, Cutter Laboratories with a copy to the Manager, Plasma Procurement, Cutter Laboratories.

GRO-C 1-13-78

GRO-C 1-20-78

PROCEDURE 2.3.8

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

In the event of a donor receiving the wrong red cells, within 7 days a written report of a detailed investigation of all facts surrounding the incident must be sent to the Director of Medical Operations, Cutter Laboratories with a copy sent to the Manager, Plasma Procurement. This report should include donor's actions, physical findings and appearance during problem; action taken by Medical Director and other Center personnel; action taken by and results obtained of outside health care facility; status of donor following all aspects of all treatment; probable cause of error as determined by Medical Director and Center Manager; action taken by Medical Director and Center personnel to prevent recurrence of problem.

HEMOLYTIC TRANSFUSION REACTION

Description

The greatest danger of plasmapheresis is the transfusion of the wrong red blood cells to the donor possibly resulting in a hemolytic transfusion reaction. It should be continually stressed that the single most important concept is PREVENTION by carefully rechecking information on the bleeding bag, name of donor, etc., before infusion of red cells is initiated. Close observation during the early stages of infusion is MANDATORY. Early recognition of the signs and symptoms of a hemolytic reaction may prevent life-threatening sequelae.

Signs

1. Primary:
   (Usually begins after 50 ml. or less of red cells have been given.)
   Symptoms may include throbbing headache, severe lumbar pain, precordial chest pain, dyspnea (difficult breathing), anxiety, nausea, restlessness, and hives.

2. Secondary:
   May include flushed face then cyanosis (bluish discoloring of skin), distended neck veins, initial slowing of pulse followed by a rapid thready beat, cold and clammy skin, chills and fever.

3. Tertiary:
   Shock and hemorrhage. (Onset of any of these signs is sufficient reason for stopping flow of red cells to donor immediately.)

GRO-C 1-18.

GRO-C 1-20?

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

Procedures

1. Immediate Actions:

R If a hemolytic transfusion reaction is even remotely suspected, stop the flow of red cells to donor without awaiting further signs. Apply tourniquet, disconnect administration set from double plasmapheresis set and clear suspect incompatible blood by allowing about 5cc of donor's blood to back-flush pheres set. Apply hemostat near female connector to stop blood flow. Remove tourniq and aseptically connect new saline filled administration set and saline bottle. Start a saline drip to maintain an open IV.

a. Do not discard transfused bag of red cells. Hold for possible evaluation under step 2e of this procedure.
b. Call Medical Director immediately.
c. Recheck all donor identification and blood types.
d. Without delay, carefully draw a fresh specimen of blood from donor's other arm into a sodium citrated vacutainer or similar tube. Centrifuge and examine supernatant plasma for hemoglobin. Not even a faint tinge is seen in the absence of intravascular lysis. In severe reactions, plasma is pink.
e. If it can be obtained immediately, examine a fresh sample of urine for hemoglobin.
f. Knowing the results of the test for elevated plasma hemoglobin (and elevated urine hemoglobin if possible) and in combination with clinical signs and symptoms, the Medical Director decides, without delay, whether the diagnosis of acute hemolytic transfusion reaction is likely.

2. For Positive Hemolytic Transfusion Reaction:

a. Immediately infuse 30 grams of mannitol intravenously (300ml of 10% mannitol) to provide renal tubule protection and to initiate diuresis. This 30 grams of mannitol should be infused intravenously during 8-10 minute interval. Maintain open IV with Sodium Chloride Injection.
b. Monitor and record vital signs.
c. Call hospital and alert an Internist.
d. Keep IV open with Sodium Chloride Injection during transport to hospital.
e. Take transfused bag of red cells to hospital for direct and indirect Coombs test during laboratory study of reaction by hospital laboratory. Also take test tube of whole blood as sample of pretransfusion donor's blood if collected that day, and tube drawn above in Procedure 1.d.
f. If hypotension is occurring DO NOT treat it with vasopressors as they may not be effective in the presence of hypovolemia. Place donor in

GRO-C 8/8/79
GRO-C
GRO-C 8/9/79

CSO

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

a position such that feet are elevated above head if necessary. If Medical Director feels hypovolemia is contributing to the condition of the donor than a consideration of infusion of Plasmanate® (Plasma Protein Fraction) or 5% Albumin may be appropriate, administered at a rate of 10 ml per minute or slower.

3. Negative Plasma and Urine Hemoglobin Tests:

   a. Recheck all identification and blood types to affirm red cells belong to same donor.
   b. Decision to continue auto-transfusion AFTER all symptoms subside rests with Medical Director.
   c. Release donor from Center only upon the express approval of Medical Director.

4. While responding to suspected incompatible red blood cell transfusion someone in the phlebotomy area should:

   a. Stop all other red blood cell infusions on other donors, and start saline drip for these other donors.
   b. DO NOT start any more red blood cell infusions until suspected incompatible red blood cell transfusion matter is resolved.
   c. Recheck identity of all red blood cell bags before starting to reinfuse them back to donors.

HEMATOMA

Description

In plasmapheresis a hematoma is a focal extravasation of blood which soon clots to form a solid mass due to traumatic injury or rupture of the vein the needle is in.

Signs

1. A dark colored disfiguration at venipuncture site.

2. A visible, tumorlike swelling at venipuncture site.

GRO-C MD 1-3-75

GRO-C 1-5-79

109 69

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

Procedures

1. Remove tourniquet and withdraw needle from arm.
2. Place 3 or 4 sterile gauze flats over hematoma.
3. Apply firm digital pressure for 7 to 10 minutes with phlebotomy site held above donor's heart level.
4. DO NOT bend arm.

HYPOTENSION

Uncomplicated

1. Syncope

   a. Description

      (i) Syncope is temporary loss of consciousness caused by a rapid change in blood volume or composition which, if not treated, can develop into a state of cardiac arrest.
      (ii) Syncope can also result from psychological factors.

   b. Signs

      (i) Decrease in blood pressure.
      (ii) Change in skin pallor.
      (iii) Skin becomes cold and clammy in appearance.
      (iv) Dizziness or lightheadedness.
      (v) Unclear vision resulting in rolling eyes.
      (vi) Unconsciousness.

   c. Procedures

      (i) If blood is being drawn from donor, discontinue procedure.
      (ii) Notify Medical Director.
      (iii) Keep IV set open with Sodium Chloride solution.

GRO-C 1-3-75

GRO-C 1-5-79

109 6916

P 1 1 1 CS0 5 1

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

(iv) Measure vital signs every 5 minutes until donor recovers; i.e., blood pressure, pulse, and respiration.
(v) Place donor flat on back with both legs elevated above head.
(vi) Loosen tight clothing.
(vii) Pass aromatic spirits of ammonia under donor's nose; donor should respond by coughing. Test ammonia on yourself before using on donor. Ammonia that is too strong may injure nasal membranes; ammonia that is too weak is not effective.
(viii) Apply cold compresses to donor's forehead or back of neck.
(ix) Maintain an adequate airway. If necessary, place padded tongue blade between donor's teeth to prevent chewing or biting of tongue and, under the supervision of the Medical Director insert a nonbreakable oropharyngeal airway.

2. Nausea and/or Vomiting

a. Signs

The signs of nausea and/or vomiting may occur as a symptom of hypotension.

b. Procedures

(i) Make donor as comfortable as possible, check blood pressure and pulse.
(ii) If only nauseated, instruct donor to breathe slowly and deeply. Continue donation if only slight nausea with normal blood pressure and pulse. If there is hypotension or persistent nausea and/or vomiting, discontinue withdrawal of blood and open saline line to slow drip rate. Continue saline drip until Medical Director has assessed the situation.
(iii) Apply cold compresses to donor's forehead. If donor vomits, provide emesis basin and have cleansing tissue or a cold towel ready. Clean excessive vomitus from donor's nasal and oral cavity to prevent choking.
(iv) Give donor a paper cup of water to rinse out mouth.
(v) Anti-emetics, such as Tigan (200 mg/ampule) and IV fluids, such as 5% Dextrose solution, are given only by Medical Director if no underlying pathology is suspected.

GRO-C 1-3-78

GRO-C 1-5-78

109 6917

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

Complicated

1. Cardiovascular Collapse

a. Collapsed Vein(s)

(i) Description

The main cause of collapsing veins would be because too rapid a change in total blood volume causing too great a decrease in total blood volume (hypovolemia) and resulting in a severe drop of systolic and diastolic blood pressure.

(ii) Signs

(1) Donor might complain that he senses or feels like his arm is going to sleep.
(2) Change in skin color of arm.
(3) Rapid decrease in both systolic and diastolic blood pressure.
(4) Dizziness, light-headedness, then unconsciousness (fainting).

(iii) Procedures

(1) Immediately stop withdrawal of whole blood from donor and monitor blood pressure and pulse.
(2) Alert Medical Director of situation.
(3) Infuse remainder of Sodium Chloride solution into donor's arm to raise blood pressure. Maintain Sodium Chloride for injection solution until Medical Director has evaluated the situation.
(4) Transport donor to hospital if necessary after alerting hospital about the situation.

b. Cardiorespiratory or Cardiopulmonary Arrest

(i) Description

Uncommonly, a donor may have a severe cardiovascular reaction to the plasmapheresis procedure which may precipitate an immediate cardiac arrest followed by respiratory arrest.

GRO-C 1-3-78

GRO-C 1-5-78

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

(ii) Signs

(1) Unconsciousness.
(2) Heart stops.
(3) Breathing stops.

(iii) Procedures

(1) IMMEDIATELY call CPR team and have them administer resuscitation.
(2) Stop withdrawal of blood but keep IV open with return of Sodium Chloride solution to donor, even during emergency treatment period and during transport to hospital.
(3) Inform Medical Director immediately while resuscitation is being performed.
(4) Occasionally, a sharp blow over the heart at the apex of the sternum will restore an effective heart beat. Otherwise, external cardiac compression with ventilation is indicated.

(A) If donor is on a mattress, place cardiac resuscitation board beneath donor.
(B) If donor is on chair, place donor flat on his back on the floor.

(5) Begin CPR with mouth-to-mouth resuscitation and external chest compression according to current CPR standards.
(6) Administer 0.5 ml 1:1000 aqueous epinephrine IV or intracardiac (by use of spinal needle) and sodium bicarbonate solution as necessary.
(7) Maintain CPR during transport to nearest hospital. CPR team and Medical Director must accompany donor to hospital.

2. Anaphylactic Shock

a. Description

An acute generalized reaction occurring within minutes after the administration of foreign material such as hypersensitization vaccines or toxoids.

GRO-C 1-3-78

GRO-C 1-5-78

109 6919

8 1 0 1 1 1 CS0 a 55

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

b. Signs

(i) Shock
(ii) Laryngeal edema
(iii) Asthma
(iv) Urticaria
(v) Pruritis
(vi) Erythema

c. Procedures

(i) The donor should be placed in a position with the feet elevated above the head.
(ii) Establish an IV line with a saline drip to maintain blood pressure.
(iii) Monitor blood pressure, pulse and respiration. Maintain oxgenation by mechanical ventilation if required.
(iv) Epinephrine 1:1000 0.2 to 0.5 cc subcutaneously immediately with small repeated doses at 15 minute intervals depending on the donor's condition. Do not give intravenously.
(v) Antihistamine intravenously, e.g., diphenhydramine (Benadryl) 50 mg. or parabromdylamine (Dimetane) 10 mg. injected slowly.
(vi) Intravenous infusion of Dextrose in water should be piggybacked to the saline in order to add further medication, such as a pressor agent, e.g., methoxamine (Vasoxyl) 20 mg., phenylephrine (NeoSynephrine) 10 mg., or L-norepinephrine.
(vii) Direct injection of hydrocortisone (Solu-Cortef) 100 to 200 mg. into the intravenous tubing with a further 500 mg. per liter for infusion. Though steriods act slowly, they are essential when a shock-like state has developed.
(viii) If the airway is inadequate, caused by laryngeal edema, tracheostomy may be indicated and intermittent positive pressure with oxygen and a bronchodilator such as aminophylline should be used if bronchospasm is noted.
(ix) When condition warrants, transport donor to hospital.

HYPERSENSITIVITY SKIN REACTIONS

1. Serum Sickness

a. Description

Delayed hypersensitivity reaction following injection of a serum.

GRO-C 1-3-78
GRO-C 1-5-78

2/13/76

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

b. Signs

(i) Urticaria
(ii) Pruritus
(iii) Fever

c. Procedures

(i) Antihistamines by mouth such as promethazine (Phenergan) 25 mg., diphenhydramine (Benadryl) 50 mg., tripelennamine (Pyribenzamine) 50 mg., may be given. Hydroxyzine (Atarax) 50 mg. may be more useful if urticaria and pruritus predominate (see below).
(ii) Prednisone 10 mg. every 6 hours until symptoms subside; then gradually taper the dose over a period of 2 weeks.
(iii) Epinephrine 1:1000, 0.3 cc subcutaneously every 3 hours as required.
(iv) Transport to hospital.

2. Laryngeal or Gottic Edema

a. Description

Excessive accumulation of fluid in the glottis or larynx region.

b. Signs and Symptoms

(i) Choking and speech difficulty.
(ii) Increasing respiratory distress.

c. Procedures

(i) Aqueous epinephrine (1:1000) 0.3 cc subcutaneously every 10 minutes for first hour or until symptoms subside.
(ii) Give antihistamines intravenously once, then orally every 6 hours.
(iii) For increasing respiratory distress or cyanosis, early tracheostomy may be indicated and intermittent positive pressure with oxygen and a bronchodilator such as aminophylline may be necessary.
(iv) Transport donor to hospital.

GRO-C 1-3-78

GRO-C 1-5-78

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

3. Urticaria

a. Description

A skin condition characterized by the appearance of intensely itching wheals or welts with elevated, usually white centers and a surrounding area of erythema.

b. Signs

(i) Hives or nettle rash
(ii) Itching
(iii) Wheals or welts
(iv) Erythema

c. Procedures

(i) Hydroxyzine (Atarax) 25 to 50 mg. every 4 hours followed by rest.
(ii) Use of calamine, Caladryl, or starch bath for topical therapy.
(iii) If condition does not respond, use epinephrine and steroids as outlined under "Serum Sickness."
(iv) If condition warrants, transport donor to hospital at Medical Director's discretion.

ARTERIAL PUNCTURE

Description

Puncturing of artery when performing phlebotomy.

Signs

1. Rapid infiltration of tissues with blood.

2. Spurting of blood around needle at phlebotomy site.

GRO-C 1-3-78

GRO-C 1-5-78

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

Procedures

1. Withdraw needle and apply firm "point" pressure over puncture site for at least 5 minutes or longer if necessary.
2. Elevate arm and keep it above heart level.

HYPERVENTILATION

Description

Breathing too fast.

Signs

1. Tingling sensation in mouth, fingers, or toes.
2. Faint muscular twitching spasms of hands.

Procedures

1. Calm verbal reassurance.
2. Possibly rebreathing into a paper bag will provide prompt relief.
3. If symptoms persist, discontinue plasmapheresis.

CONVULSIONS AND SEIZURES

Description

Convulsions are violent involuntary paroxysm of the voluntary muscles. Seizures are sudden attacks on a person's body.

Signs

1. Extreme muscular contractions.
2. Severe flexion spasms.

GRO-C 1-3-78

GRO-C 1-5-79

8 1 0 1 1 2 3 0 a 5 0

109 6923

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

3. Extension of the arms and legs.

4. A fit.

Procedures

1. If standing, prevent donor from falling so that the person will not injure himself. If donor is in phlebotomy position, hold down donor on chair or bed if possible.

2. Call for more help.

3. Second person should then withdraw needle and aid in controlling donor's movements.

4. Do not appempt to restrain movements of donor's extremities completely, but focus on preventing donor from injuring self or you.

5. Quickly remove dentures (if present) and establish an adequate airway. Place padded tongue blades between donor's upper and lower jaw to prevent chewing or biting of tongue and insert nonbreakable oropharyngeal airway under Medical Director's supervision.

6. Notify Medical Director as soon as possible. At Medical Director's discretion the following therapy may be administered:

   a. Delirium tremens - Immediate treatment consists of administering 100 mg. diphenylhydantoin (Dilantin) I.M. to control the seizure.
   b. Idiopathic Epileptic Seizures - 10 mg. IV of diazepam (Valium) usually stops the attack within minutes; however, 100 mg. of diphenylhydantoin or 50 to 100 mg. of sodium phenobarbital (Luminal Sodium) may be given I.M. as well for an anticonvulsant.

7. Transfer donor to hospital at Medical Director's discretion.

EMERGENCY SUPPLIES

A suggested list is given below. All supplies should be readily available. Check all medical supplies at least monthly for outdating.

GRO-C 1-3-78

GRO-C 1-5-78

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

1. Aromatic Spirits of Ammonia.
2. Oropharyngeal airway, plastic or hard rubber.
3. Oxygen and Ambubag.
4. Sterile gauze flats.
5. Sterile needles, 20 gauge 2 inches and 25 gauge 3/4 inch, and spinal needle.
6. Sterile hypodermic syringes, 2 ml and 10 ml sizes.
7. Emesis basin or equivalent.
8. Padded tongue blades.
9. Sterile suture tray with surgical supplies for tracheostomy.
10. Cardiac resuscitation board.
11. Drugs and intravenous solutions:

    a. Sodium citrated vacutainers.
    b. 10% Mannitol.
    c. Methoxamine, phenylephrine, or L-norepinephrine.
    d. Sodium Chloride for Injection, U.S.P.
    e. Plasmanate® or 5% albumin.
    f. Tigan (Trimethabenzamine 200 mg. ampules).
    g. Sodium bicarbonate solution.
    h. Benadryl (Diphenhydramine hydrochloride 10 and 50 mg. ampules).
    i. Epinephrine (1:1000) 1 ml ampules and 1:100 as well.
    j. 100 mg. diphenyldantoin (Dilantin).
    k. Calamine, Caladryl or starch bath.
    l. 100 mg. sodium phenobarbital (Luminal).
    m. 1 or 2% lidocaine.
    n. Parabromdylamine (Dimetane) 10 mg.
    o. 5% dextrose solution.
    p. 100-200 mg hydrocortisone (Solu-Cortef) and prednisone.

GRO-C

3-12-79

109 6925

Subject: Signs of, and Guideline Procedures for, Donor Reactions

Responsibility: Medical Director and All Personnel

q. Aminophylline.
r. 25 mg. promethazine (Phenergan) or 50 mg. Tripelennamine (pyribenzamine) or 50 mg. hydroxyzine (Atarax). Chlorotrimeton.

HOSPITAL ARRANGEMENTS

Prior arrangements are made with a specialist in internal medicine, a physician in charge of emergency room, and administrators of a hospital in the vicinity of the center to provide emergency care for donors if required. To assure continuation of arrangements, contact and consultation with hospital personnel is made every six to twelve months. Keep on file details of arrangements made. Make sure all personnel are aware of location of file.

GRO-C 1-3-78

GRO-C 1-5-78

8 1 0 1 1 CSU a 6 2

0926

PROCEDURE 2.3.9

Subject: Identify Bag of Red Blood Cells with Donor

Responsibility: Phlebotomist

1. Secure donor's complete attention.
2. Remove bag of red cells from IV pole and hold. If procedure is interrupted rehang bag of red cells on IV pole.
3. Ask donor to state aloud donor's name and Donor Number.
4. Verify label information as donor audibly responds.
5. Confirm that Control Number on bag is duplicate of Control Number affixed to donor.
6. Show bag label to donor.
7. Ask donor to verbally confirm name and Donor Number as belonging to donor.
8. Ask donor to read aloud entire Control Number from bag label.
9. Read Control Number affixed to donor as donor reads aloud Control Number on bag label to assure they are duplicates.
10. Read aloud to donor, donor name and Donor Number on bag label.
11. Ask donor for verbal confirmation that name and Donor Number read aloud belong to donor.
12. In the case of persons with insufficient vision to participate in this procedure, another plasma center employee must participate in this procedure on behalf of the donor. This person must record their initials on bag label and on comments section of form 81-9723 (Donor Card).
13. In the case of non-English speaking donors this procedure must be performed by a phlebotomist fluent in donor's language.
14. Write your initials on bag label signifying that entire identification has been completed.
15. Immediately connect bag of red blood cells to Sodium Chloride and dilute (see Procedure 2.3.10).
16. Record your initials on comments section of Form 81-9723 (Donor Card).
17. Any uncertainties or inconsistencies with any portion of identification procedure are brought to the attention of Medical Director or his designate, who will take appropriate action.

GRO-C 2/9/79

GRO-C 2-6-79

109 6927

2/20/79

PROCEDURE 2.3.10

Subject: Connect Bag of Red Blood Cells to Sodium Chloride and Dilute

Responsibility: Phlebotomist

Note: Make all connections aseptically.

1. Remove white recipient cap from spike entry port on blood bag with a firm vertical tug.
2. Remove sterility protector from spike on one leg of administration set.
3. Immediately insert spike on adminstration set into spike entry port on blood bag with a gentle twisting motion. Seat spike only to shoulder of taper; seating to flange could cause bag to be punctured.
4. Hang bag on IV pole in as low a position, relative to position of Sodium Chloride bottle, as permitted by length of plastic tubing. Do n allow tubing or bag to come in contact with donor's feet.
5. Open completely slide clamp below drip chamber and slide clamp on leg of administration set to be used.
6. Allow 75-100 ml. of Sodium Chloride to flow into bag of red blood cells
7. Close completely slide clamp below drip chamber and slide clamp on leg of administration set used.

Note: Once either blood bag is attached to administration set, blood bag remains permanently attached to administration set.

GRO-C 6/13/78

GRO-C 6/14/78

6/26/78

40

CSO

109 692E

PROCEDURE 2.3.11

Subject: Mix Red Blood Cells and Sodium Chloride, reidentify bag of diluted red blood cells with donor and infuse

Responsibility: Phlebotomist

1. Gently agitate bag to obtain smooth suspension.
2. Secure donor's complete attention.
3. Ask donor to state aloud donor name and donor number.
4. Verify label information as donor audibly responds.
5. Show bag label to donor.
6. Ask donor to verbally confirm name and donor number as belonging to donor.
7. In the case of persons with insufficient vision to participate in this procedure, another plasma center employee must participate in this procedure on behalf of the donor. This person must record their initials on bag label and on comments section of form 81-9723 (Donor Card).
8. In the case of non-English speaking donors this procedure must be performed by a phlebotomist fluent in donor's language.
9. Write your initials on bag label signifying that reidentification has been completed.
   a. Do not infuse red blood cells if any question concerning reidentification is present.
10. Hang bag on IV pole on a level with sodium chloride bottle.
11. Open completely slide clamp on bag leg of administration set.
12. Open completely screw clamp or roller valve on administration set.
13. Infuse diluted red blood cells into donor.
14. Record your initials in comment section of form 81-9723 (Donor Card).
15. Allow bag to empty as completely as possible.
16. Use adequate sodium chloride to flush filter and tubing on administration set to return to donor as many red cells as possible.
17. First bag of red blood cells:
    a. Close completely slide clamp on bag leg of administration set.
    b. Close completely screw clamp or roller valve on administration set.
    c. Proceed immediately to collect second bag of whole blood (see procedure 2.3.6).
18. Second bag of red blood cells.
    a. Close completely slide clamp on bag leg of administration set.

Precautions:

1. Time interval between start of withdrawal of a bag of blood until that bag's diluted red blood cells are completely reinfused into original donor should be no longer than one hour and preferably less than 1/2 hour.

GRO-C 5/2/79

5/31/79

GRO-C 5/3/79

109 6929

41 [illegible] 30 [illegible] 85

Subject: Mix Red Blood Cells and Sodium Chloride, reidentify bag of diluted red blood cells with donor and infuse

Responsibility: Phlebotomist

2. In the event of clotting in needle or donor tubing, preventing flow of saline or infusion of diluted red cells, DO NOT attempt to flush clots out with either blood or sodium chloride. Discontinue phlebotomy (see procedure 2.3.12), secure new equipment and begin again if donor is willing.

3. The identification and reidentification of red blood cells with correct donor is the single most important and crucial task performed in plasmapheresis. More damage can be done to donor by giving back wrong red blood cells than by any other error or combination of errors conceivable. Be careful! Be alert! Be accurate! Be sure!

GRO-C 5/2/79

GRO-C 5/3/79

Subject: Discontinue Phlebotomy

Responsibility: Phlebotomist

1. Open completely slide clamp between drip chamber and filter on administration set.
2. Use adequate sodium chloride to flush filter and tubing on administration set to return to donor as many red blood cells as possible.
   a. If no sodium chloride remains, allow filter and tubing on administration set to drain as completely as possible.
3. Remove tape anchoring phlebotomy needle in place.
4. Place a sterile gauze pad over the site of phlebotomy.
5. Withdraw needle in one smooth motion simultaneously applying pressure through sterile gauze pad to puncture wound at phlebotomy site.
6. Instruct donor to firmly hold gauze pad in place with arm elevated above heart level for 3-5 minutes.
7. Remove all used plasmapheresis equipment from immediate area of donor (see Procedure 2.3.13).
8. When satisfied that puncture wound has closed and will not reopen, either strap gauze firmly in place with tape or apply bandaid.

Precaution:

1. Following discontinuation of phlebotomy, each donor is to be observed to be steady, walk and feel normal. If any donor feels weak or has problems, appropriate action is to be taken by Medical Director or his designate. Incident is to be noted on form 81-9723 (Donor Card). Review of donor's status at time of incident and/or prior to next donation is at Medical Director's discretion.
2. Whenever a donor suffers a significant loss of red blood cells, e.g., broken or leaky blood bag, defaced label, etc., donor will be detained at center for at least one hour under periodic supervision of Medical Director. During this time appropriate liquids will be offered to donor. Donor's blood pressure, pulse rate and general well-being will be monitored periodically. Donor may leave center when dismissed by Medical Director. Make appropriate notation on Form 81-9723 (Donor Card). See Procedure 2.3.14 regarding further plasmapheresis.
3. Occasionally a donor may experience difficulties before, during or after the actual plasmapheresis procedure. Such difficulties may include, but are not limited to, DTH or other adverse reactions (see Procedure 2.3.8), clotting of blood in tubing or needle sufficient to prevent withdrawal of blood or reinfusion of red cells, accidents such as falling, or any other incident which is not a part of a normal uncomplicated center visit. Should such arise, a full description of incident or difficulties, including, but not limited to, its causes, action of center personnel, effect on donor, treatment and disposition of donor, will be noted in the appropriate spaces on Form 81-9723 (Donor Card) and signed by those conducting the investigation. Depending on the nature of the problem, it may be advisable for Medical Director to examine donor prior to donation at donor's next visit.

GRO-C 6/14/78

GRO-C 6/14/78

PROCEDURE 2.3.13

Subject: Discard Used Plasmapheresis Equipment

Responsibility: Phlebotomist

1. Remove from used plasmapheresis equipment all non-disposable items, eg.: hemostats.
2. Bend, break or cut phlebotomy needle to prevent any possibility of future use.
3. Discard used equipment in plastic lined waste receptacles.
4. Clean donor bed or chair after every donation.
5. Arrange for frequent removal of discarded plasmapheresis equipment from Donor Area.
6. Make sure discarded plasmapheresis equipment is secure from pilferage prior to garbage pickup.

GRO-C 6/13/78

GRO-C 6/14/78

109 6932

CS0 68

PROCEDURE 2.3.14

Subject: Loss of Whole Blood or Red Cells

Responsibility: All Personnel

1. If, for any reason, a unit of red cells cannot be returned to donor, or if donor gave a unit of whole blood:
   a. Document details of red cell loss or whole blood donation in next available space on Form No. 81-9723 (Donor Card), and,
   b. Document temporary suspension of donor from plasmapheresis for a period of eight weeks, UNLESS:
      (1) Donor is examined by medical director and certified, in writing by medical director, on Form No. 81-9723 (donor Card), to be acceptable for further plasmapheresis before expiration of the eight-week period, AND
      (2) The donor possesses an antibody that is transitory, or of a highly unusual or infrequent specificity, or of an unusually high titer, AND
      (3) The antibody and necessity for plasmapheresing the donor is documented on Form 81-9723 (Donor Card).

Precaution: Examination by medical director must not be limited to return of hematocrit and total protein to normal levels. Consideration must be given to effect on donor's health if a second unit of red cells cannot be returned to the donor within the eight-week period.

109 6933

GRO-C

GRO-C

PROCEDURE 2.4.1

Subject: Weigh Whole Blood

R Responsibility: Centrifuge Technician or Phlebotomist

1. On each donor weigh both bags of whole blood each time donor donates.
2. Record in a permanent record book:
   a. Date of collection
   b. Control Number of donor
   c. Identification of chair or table associated with vacuum collecting device or plasmapheresis cut-off scale (see Procedure 5.0.5)
   d. Weight of donor in pounds
   e. Either gross weight of bag in grams or volume, in milliliters, of whole blood collected
      (1) Milliliters of whole blood determined by reference to conversion table (see Procedure 5.0.8)
   f. Action taken to recalibrate vacuum collecting device or plasmapheresis cut-off scale if required due to under or over drawing
R g. Initials of person weighing whole blood bag
R 3. If whole blood weight is determined by centrifuge technician, phlebotomist or other specified person must be notified whenever the amount of whole blood collected exceeds that permitted.
R 4. Readjustment of vacuum collecting device or plasmapheresis cut-off scale is made by phlebotomist or other specified person.
5. If first whole blood bag is inadvertently overdrawn, readjust or recalibrate collecting device before collecting second bag whole blood. Reduce amount of whole blood drawn in second whole blood bag so that total amount of whole blood drawn from donor does not exceed 1000 ml or 1200 ml whichever is appropriate to donor's body weight.
6. Maximum amount of whole blood drawn per bag is 500 ml or 600 ml, whichever is appropriate to donor's body weight. (see appropriate Conversion Chart for gross weight.)

GRO-C

GRO-C

11/24/80

109 6934

3/27/74

PROCUREDURE 2.4.2

Subject: Prepare Source Plasma (Human) Label for Plasma Pooling Bag

Responsibility: Centrifuge Technician

1. Select a blank Source Plasma (Human) Label legibly stamped with center name and address.
2. Observe donor identification label on bag whole blood.
3. Write on Source Plasma (Human) label Center Code, Donor Number, collection date, check box for type of plasma or write plasma type on line designated OTHER: e.g. anti-HB_s. Check box for amount anti-congulant, and circle type of HB_sAg to be done.
4. Proceed to balance (see Procedure 2.4.3) and centrifuge bag whole blood (see Procedure 2.4.3).
5. Apply partially completed Source Plasma (Human) label to empty plasma pooling bag, leaving at least 1 1/4" space above the label for application of Source Plasma (Human) Salvaged label over the words "Source Plasma (Human)" should that become necessary.

GRO-C 2/9/79

GRO-C 02/13/79

3/27/79

1 1 1 CSO a 7 1

4/15/76

PROCEDURE 2.4.3

Subject: Centrifuge Whole Blood

Responsibility: Centrifuge Technician

1. Make sure balancing scales read zero with nothing on either pan. If not, adjust scales to obtain zero reading.
2. Balance bag whole blood against another bag whole blood or water filled balance bag. Rubber weights used to achieve balance must be clean and dry.
3. Observe centrifuge cups to make sure weights from previous centrifugation have all been removed.
4. Place balanced bags whole blood into opposing centrifuge cups with weights on bottom of bag.
   a. Centrifuge cups must be clean and dry.
5. Make sure bags whole blood are placed in centrifuge cups so that side seams of bags are parallel with pivots on yoke of centrifuge head and fittings are on top of bag.
6. If head is shielded, attach shield cover firmly to head.
7. Close cover of centrifuge, set speed control and timer, activate centrifuge. (see procedure 5.0.7 for settings).
8. Centrifuge stops automatically when timing cycle completed. Never slow or stop centrifuge manually.
9. Open centrifuge cover; if present remove shield cover without disturbing centrifuge head.
10. Grasp centrifuged bag whole blood by top fittings and gently lift free of centrifuge cup.
11. Proceed to express plasma (see procedure 2.4.4).
12. Remove all weights from centrifuge cup, making sure weights and centrifuge cups are clean and dry.
13. Close centrifuge cover while centrifuge not in use to prevent frost build up in chamber.
14. If bag whole blood leaks or breaks in centrifuge cup, entire head, all centrifuge cups and shield, if present, are thoroughly cleaned and dried before centrifuging other bags whole blood.

Control Procedure

1. Daily
   a. For each centrifuge in use each working day when centrifuge is under full load, observe and record in a bound log book:
      (1) Date
      (2) Serial number of centrifuge
      (3) Speed in revolutions per minute (rpm) of centrifuge as indicated on centrifuge tachometer when at speed.
      (4) Setting on rpm control.
      (5) Chamber temperature as indicated on centrifuge thermometer when centrifuge is at speed.

4/15/76

GRO-C

109 6936

Subject: Centrifuge Whole Blood

Responsibility: Centrifuge Technician

(6) Setting on temperature control
(7) Setting on brake control
(8) Separation of red cells and plasma adequate
(9) Note in detail any repairs effected.

2. As necessary - defined as, on receipt of new equipment, whenever trouble with equipment produces unacceptable separation of red cells and plasma on several runs, and after equipment repair eg: motor replacement, brake rectifier replacement, but not to include replacement of brushes.
   a. Check speed with tachometer; record as revolutions per minute (rpm). Must be within ± 10% of setting on rpm control and rpm shown on tachometer.
   b. Check timer by observing elapsed time equipment operates under influence of timer with suitable watch. Must be within ± 10% of equipment manufacturer's specifications.
3. If either daily or as necessary equipment checks indicate equipment is not functioning properly, equipment must not be used to separate donors' red cells and plasma until equipment is repaired and found to be acceptable by further testing.

GRO-C

PROCEDURE 2.4.4

Subject: Express Plasma from First Bag Whole Blood

Responsibility: Centrifuge Technician

See Facing page for Plate E.

1. Gently, so as not to disturb red cell pack, place bag of centrifuged whole blood in clean expressor positioned so that label can be easily read.
2. Express plasma from centrifuged first bag whole blood.
   a. Remove grommet from, and apply hemostat to, blood bag tubing.
   b. Allow expressor to exert pressure on blood bag.
   c. Match information on labeled first bag whole blood with information on labeled plasma pooling bag.
   d. Remove sterility protector from female luer fitting on blood bag.
   e. Remove sterility protector from male luer fitting on plasma pooling bag. Use longest pooling bag line.
   f. Aseptically connect blood bag and pooling bag fittings.
   g. Remove hemostat and express plasma.
   h. Remove one Control Number label from blood bag and apply to pooling bag.
   i. If available, remove Donor Code sticker from blood bag and apply to front of pooling bag. Insure Donor Code sticker covers no part of Source Plasma (Human) label.
   j. Remove a second Control Number label from blood bag and apply to pooling bag tubing approximately 8" from luer fitting.
   k. For hyperimmune plasma only remove a third Control Number label from blood bag and apply to pooling bag tubing approximately 4" from second Control Number label.
   l. When plasma is fully expressed into pooling bag, apply hemostat to pooling bag tubing.
   m. Heat-seal blood bag tubing.
   n. Release pressure of expressor.
   o. Make bag red cells available to phelbotomist for reinfusion.
   p. Heat-seal pooling bag tubing near luer fitting and as necessary to obtain required number of plasma tubing samples. Seal tubing in order shown in Plate E.
   q. Set one 8" sample aside for HB_sAg testing.
   r. Strip remaining plasma into pooling bag or collect second tubing sample (NLT 4") for antibody determination, whichever is applicable.
   s. Set second tubing sample aside for antibody determination (titering). (See Procedure 2.5.3).
   t. If a back-up HB_sAg sample is required, it should be taken from this pooling bag line. If necessary, the sample for antibody determination can be taken from second pooling bag line.

GRO-C 1/10/79

GRO-C 1/10/79

Subject: Express Plasma from First Bag Whole Blood

Responsibility: Centrifuge Technician

Precautions:

1. When nearing completion on expressing plasma from whole blood bag, do not allow white buffy coat layer (white cells and platelets) or red cells to enter plasma pooling bag tubing.
2. Do not exert any pressure, eg: hand pressure, to expressor plate other than that exerted by expressor spring to prevent red cell contamination of plasma.
3. During separation of plasma each bag is observed for leakage. If noted, stop separation of plasma, destroy bag of whole blood, mark plasma pooling bag PC (possibly contaminated). On Form No. 81-9723 (Donor Card), in comments section opposite Control Number, write information relative to destruction and non return of donor's red cells.
4. If any donor identification labels come off whole blood bag or are defaced or smeared as to cause any doubt of identification of red cells with donor, the entire bag or bag whole blood or red cells are destroyed. On Form No. 81-9723 (Donor Card), in comments section opposite Control Number, write information relative to destruction and non return of donor's red cells.
5. Plasma from donors whose plasma is habitually chylous in not acceptable. Consider returning whole blood to donor and terminating donor's participation.

GRO-C

109 6939

PROCEDURE 2.4.5

Subject: Express Plasma from Second Bag Whole Blood and Complete Source Plasma (Human) Label on Plasma Pooling Bag

Responsibility: Centrifuge Technician

See Plate E

1. Gently, so as not to disturb red cell pack, place bag of centrifuged whole blood in clean expressor.
   a. Position bag so that label is visible and can be easily read.
2. Express plasma from centrifuged second bag whole blood.
   a. Remove grommet from, and apply hemostat to, blood bag tubing.
   b. Allow expressor to exert pressure on blood bag.
   c. Match information on labeled second bag whole blood with information on labeled plasma pooling bag.
   d. Make sure Control Number labels on second blood bag and pooling bag are identical.
   e. Remove sterility protector from female luer fitting on blood bag.
   f. Remove sterility protector from male luer fitting on plasma pooling bag.
   g. Aseptically connect blood bag and pooling bag fittings.
   h. Remove hemostat and express plasma.
   i. Remove a Control Number label from the blood bag and apply to pooling bag.
   j. When plasma is fully expressed into pooling bag, apply hemostat to pooling bag tubing.
   k. Heat-seal blood bag tubing.
   l. Release pressure of expressor.
   m. Make bag red cells available to phlebotomist for reinfusion.
   n. Strip plasma in tubing into plasma pooling bag.
   o. Heat seal tubing near pooling bag.
   p. Remove one Control Number from plasma pooling bag and place in sequence on Form No. 81-9709 (Plasma Packing and Hepatitis Report Form).
   q. Weigh plasma pooling bag and convert weight to nearest milliliter.
   r. Write volume on partially completed plasma pooling bag label and on Form No. 81-9709 (Plasma Packing and Hepatitis Report Form).
   s. Immediately freeze plasma. (See Procedure 2.4.7).

Precautions:

1. When nearing completion on expressing plasma from whole blood bag, do not allow white buffy coat layer (white cells and platelets) or red cells to enter plasma pooling bag tubing.
2. Do not exert any pressure, eg: hand pressure, to expressor plate other than that exerted by expressor spring to prevent red cell contamination of plasma.

GRO-C 1/10/79

GRO-C 1/10/79

109 6940

Subject: Express Plasma from Second Bag Whole Blood and Complete Source Plasma (Human) Label on Plasma Pooling Bag.

Responsibility: Centrifuge Technician

3. During separation of plasma each bag is observed for leakage. If noted, stop separation of plasma, destroy bag of whole blood, mark plasma pooling bag PC (possibly contaminated). On Form No. 81-9723 (Donor Card), in comments section opposite Control Number, write information relative to destruction and non return of donor's red cells.
4. If any donor identification labels come off whole blood bag or are defaced or smeared as to cause any doubt of identification of red cells with donor, the entire bag or bag whole blood or red cells are destroyed. On Form No. 81-9723 (Donor Card), in comments section opposite Control Number, write information relative to destruction and non return of donor's red cells.
5. Plasma from donors whose plasma is habitually chylous is not acceptable. Consider returning whole blood to donor and terminating donor's participation.

9/5/75

GRO-C

109 6941

PROCEDURE 2.4.5.1

Subject: Remove Red Cell Contamination From Pooled Plasma

Responsibility: Centrifuge Technician

NOTE: This procedure is designed to be performed on red cell contaminated plasma pooled from two units of whole blood and is not to be used on plasma pooled from a single unit whole blood.

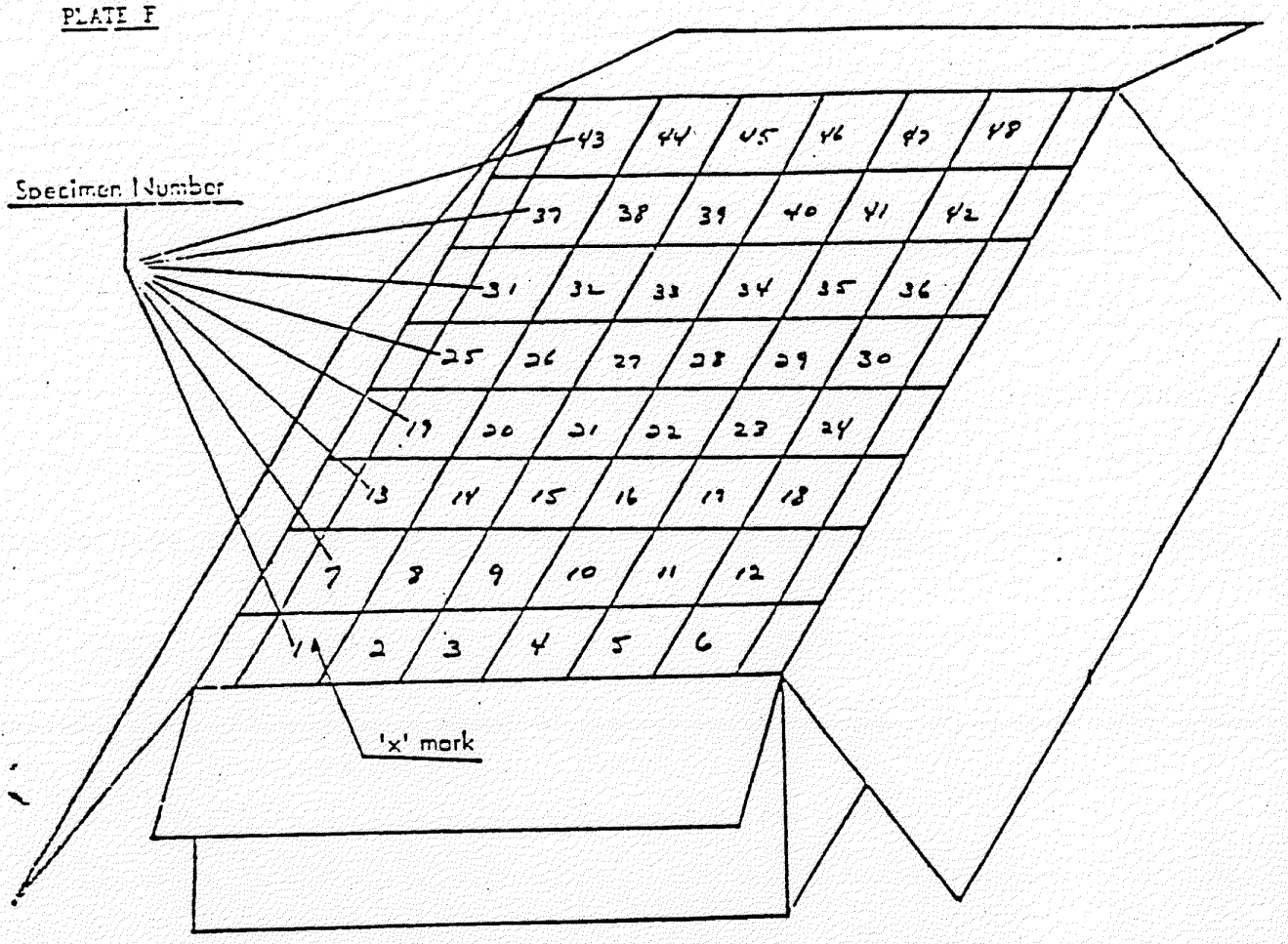
1. Strip plasma from second plasma expressing leg into pooling bag, apply hemostat close to pooling bag to keep tubing blood or plasma-free.
2. Heat seal tubing approximately 4 inches from hemostat.
3. Fold plasma-free tubing close to pooling bag and apply grommet to doubled-over tubing. Remove hemostat.
4. Heat-seal other pooling bag line close to pooling bag.
5. Centrifuge red cell-contaminated plasma (see Procedure 2.4.3).
6. Prepare Source Plasma (Human) label for second pooling bag (see Procedure 2.4.2).
7. Express plasma from first pooling bag.
   a. Make sure information on both pooling bag labels is identical.
   b. Allow expressor to exert pressure on first plasma pooling bag.
   c. Remove sterility protector from male luer fitting on longest line of second pooling bag.
   d. Aseptically cut first pooling bag tubing close to heat-seal and insert male luer fitting firmly into cut end of tubing.
   e. Remove grommet and express plasma.
   f. When plasma is fully expressed into second pooling bag apply hemostat to tubing.
   g. Release pressure of expressor.
8. Transfer Control Number labels and Donor Code sticker from first pooling bag to second pooling bag.
9. Heat-seal tubing close to first pooling bag.
10. Discard first pooling bag.
11. Strip plasma from tubing into second pooling bag and heat-seal tubing close to bag; ALTERNATIVELY,
12. If original plasma tubing samples are contaminated with red cells. new plasma tubing samples must be obtained, (see Procedure 2.4.4).

GRO-C

GRO-C

109 6942

PLATE F



Using the Specimen No. from the packing list, proceed as follows:

A. Mark an 'x' on the inner box partition in the front left corner compartment(as above) - Insert Specimen 1.

B. Moving from left to right, fill in the row with specimens, following the same number sequence as assigned on the packing list.

C. The second and remaining rows should be filled similarly, moving from left to right, as shown above.

PROCEDURE 2.4.6

Subject: Prepare Serum Samples for Shipping

Responsibility: Centrifuge Technician

See facing page for Plate F.

1. Allow blood to completely clot in test tube of whole blood collected for serum samples.
2. Allow sufficient time after clotting for clot to retract ie: pull away from test tube wall.
3. Ring the clot by inserting a clean wooden applicator stick into test tube between clot and tube wall. Move applicator stick completely around inside wall of tube effectively separating clot from tube wall.
   a. Use a separate applicator stick for each clot.
4. Centrifuge tubes to effectively separate clot from serum.
   a. Make sure tubes are balanced properly to prevent breakage.
5. Select a clean dry vial and cap (see Procedure 5.0.6).
6. Gently pour or pipette, with a pasteur pipette, at least 2 milliliters of serum into vial without allowing red cell contamination.
7. Perform a total protein determination on each serum sample by the method described in Procedure 2.1.3.
   a. Record result on Form No. 81-9723 (Donor Card) and Form No. 81-9751 (Serum Sample Packing List).
   b. If total protein value is less than 6.0 gm%:
      (1) Temporarily suspend donor from further plasmapheresis until total protein value on a new serum sample is 6.0 gm% or greater.
      (2) Discard sample. Do not send to Cutter Laboratories for serum protein electrophoresis testing.
   c. If total protein value is greater than 9.0 gm%:
      (1) Temporarily suspend donor from further plasmapheresis until total protein value on a new serum sample is 9.0 gm% or less.
      (2) Discard sample. Do not send to Cutter Laboratories for protein electrophoresis testing.
   d. When donor's new serum sample has been taken and tested to be within 6.0 - 9.0 gm% range:
      (1) Send serum sample to Cutter Laboratories for serum protein electrophoresis testing.
      (2) Reinstate donor and continue regular plasmapheresis.

GRO-C 1/1

GRO-C 1/11/80

PROCEDURE 2.4.7

Subject: Freeze Source Plasma (Human)

Responsibility: Centrifuge Technician

1. Either of two freezing methods may be employed, quick-freeze or regular freeze. Quick-Freeze is preferred.
2. Quick-Freeze
   a. Immediately place all units of plasma in a quick-freeze unit operated at -30°C or below. If quick-freeze unit is full and plasma therein is not frozen, transfer coldest units to walk-in freezer in order to make room for unchilled plasma.
   b. Position plasma pooling bags so that they freeze wrinkle-free.
   c. Transfer units of plasma to a freezer operated at -20°C or below in an area of that freezer clearly marked as a Quarantine area.
3. Regular Freeze
   a. Immediately place all units of plasma in a freezer operated at -20°C or below in an area of that freezer where most rapid freezing will occur.
   b. Position plasma pooling bags so that they freeze wrinkle-free. NEVER freeze plasma pooling bags in shipping cartons.
4. When solidly frozen, plasma pooling bags may be placed in shipping cartons. (See Procedure 2.4.8) and stored in Quarantine area of freezer (See Procedure 2.4.7.1).

NOTE: Units of plasma should not be exposed to room temperature any longer than absolutely necessary.

GRO-C 12/5/78

GRO-C 12/7/78

109 6945

PROCEDURE 2.4.7.1

Subject: Storage of Plasma Prior to Shipping

Responsibility: Centrifuge Technician

1. Place frozen plasma pooling bags in shipping cartons (see Procedure 2.4.8) in Quarantine area of freezer.
2. Quarantine methods.
   a. Preferably a separate freezer operating at or below -20°C and labeled as "Quarantine Freezer, Do Not Ship Plasma". See Procedure 5.0.10 for temperature documentation.
   b. As an alternative, a portion of walk-in freezer operating at -20°C or below, set aside for use only as a Quarantine area and labeled as "Quarantine Area, Do Not Ship Plasma". If this method is used, Quarantine area must be separated from remainder of freezer by a physical barrier so that personnel packing plasma cannot inadvertently include plasma stored in Quarantine area in plasma shipment.
3. Plasma will remain in Quarantine area until HB_sAg tests have been completed and all HB_sAg reactive and/or positive units of plasma have been removed and destroyed. (See Procedures 1.0 #68, 2.5.1, 2.5.1.1, 2.5.1.2, and 2.5.2) R
4. When step 3 has been completed, remove plasma from Quarantine area. Store plasma in portion of walk-in freezer reserved for plasma to be shipped. (See Procedure 2.4.8.)
5. Plasma that is continuously stored at -20°C or below is designated as and shipped as Source Plasma (Human). See Procedure 2.4.8 for shipping instructions.
6. Plasma that is not continuously stored at -20°C or below and does not exceed +10°C is designated as and shipped as Source Plasma (Human) Salvaged, except that plasma exposed to temperatures not to exceed -5°C for less than 72 hours need not be labelled Source Plasma (Human) Salvaged. (See Procedure 2.4.9 for shipping instructions.) R
7. Plasma that is not continuously stored at -20°C or below and does exceed +10°C must remain in quarantine until disposition of plasma is obtained from Bureau of Biologics.

GRO-C 12/10/80

GRO-C 12/11/80

CSO 9946

CSO 83

PROCEDURE 2.4.8

Subject: Prepare Frozen Source Plasma (Human) for Shipping

Responsibility: Centrifuge Technician

1. Line empty carton, in which Sodium Choloride for Injection USP was received, with a clean seamless polyethylene bag, size 24 x 24 inches.
2. Apply shipping labels to both ends of carton.
   a. Make sure color of shipping label corresponds to type of plasma shipped in carton (see page 6 for Control Number label colors and Plasma Types).
3. For Normal and Tetanus plasma Coded "Non-O" only: apply Donor Code sticker to Code box or top right hand corner of shipping label.
4. Write carton number given on Plasma Packing and Hepatitis Report Form in block numbers one inch high in Carton Number box or immediately above Week Number box.
5. Write Week Number in Week Number box.
6. Place bags of solidly frozen plasma in properly numbered and labeled carton while consulting correct Plasma Packing and Hepatitis Report Form
R and store cartons at -20°C or colder until time of shipment.
7. On day of shipping:
   a. Inspect temperature recorder charts for entire length of time plasma was in freezer to insure plasma was continuously stored at -20°C or colder; if not, see Procedure 2.4.9.
R b. Ensure carton is effectively sealed for shipment.
   c. Affix "Less Than Standard Packing" label on any case containing less than twelve units.
   d. On trucker's Bill of Lading write:

MONITOR AND MAINTAIN TEMPERATURE
AT -5°C OR BELOW
ALL BAGS FROZEN AT

_____ _____
(time) (date)

_____
(signature)

8. Affix copy of trucker's Bill of Lading to photocopies of Form No. 81-9707 (Plasma Packing and Hepatitis Report Form) and retain on permanent file.
9. Affix originals of Plasma Packing and Hepatitis Report Forms for all plasma
R in shipment to last carton of Normal Plasma, Code X and ship to destination designated by and method designated by Manager of Plasma Procurement, Cutter Laboratories.
   a. If one or more types of hyperimmune plasma are to be shipped to a destination different from the destination designated for Normal Plasma affix originals of Form 81-9709 for all such hyperimmune plasma to last carton of one type of plasma only.

GRO-C 5/22/80

GRO-C 5/30/80

Subject: Prepare Frozen Source Plasma (Human) for Shipping

Precautions:

1. DO NOT ship any plasma on which HB_sAg tests are incomplete.

2. DO NOT ship any HB_sAg negative plasma drawn from a donor who has donated previous units on which the HB_sAg testing is incomplete.

GRO-C 12/10/80

GRO-C 12/10/80

109 6948

1 11 CS. 6 85

PROCEDURE 2.4.9

Subject: Prepare Frozen Source Plasma (Human) Salvaged for Shipping.

Responsibility: Centrifuge Technician and Manager

1. Definition of Source Plasma (Human) Salvaged:
   a. Any Source Plasma (Human) that has been stored at temperatures higher than -20°C but below +10°C or that has experienced during shipping temperatures higher than -5°C but below +10°C.
      (1) Temperatures are those shown on recorder chart for plasma stored in Center freezer. (see Procedure 5.0.10).
   b. R Plasma stored in freezer wherein temperature rises above -20°C but not more than -5°C for less than 72 hours, need not be placed in Source Plasma (Human) Salvaged category provided reason for temperature rise is documented on recorder chart (see Procedure 5.0.10) and provided plasma remains hard frozen.
2. Notify Cutter Laboratories when plasma falls into Source Plasma (Human) Salvaged category.
   R a. Phone Plasma Procurement Administrator (415) 420-5019, with information:
      (1) Date and time temperature rose above -20°C.
      (2) Date and time temperature returned to -20°C.
      (3) Quantity of each Plasma Type (see Procedures 3.0.1, 3.0.2, and 3.0.3), with dates and Week Number of plasma collection, number of cartons, beginning and ending Control Numbers, for all Plasma to be designated Source Plasma (Human) Salvaged.
      (4) Maximum temperature reached by freezer.
      (5) Statement of cause of temperature rise and corrective action taken.
   b. At the option of Cutter Laboratories, instructions will be given to ship plasma or retain plasma in Center.
   c. If maximum temperature reached is above +10°C, Center manager or owner must notify Bureau of Biologics of occurrence and request release of plasma for shipment. All plasma in freezer must be quarantined in freezer and not shipped until release is obtained.
3. Shipping of Source Plasma (Human) Salvaged.
   a. Procedure 2.4.8 will be followed except as noted below.
   b. Plasma Pooling Bags
      (1) Remove each unit of plasma from carton and carefully apply Source Plasma (Human) Salvaged label (Form No. 81-9710) over Source Plasma (Human) label so that only the words Source Plasma (Human) are covered.
      (2) On each Source Plasma (Human) Salvaged label check the box "Storage Temperature Exceeded -20°C" using a black permanent marking pen.
      (3) Replace unit of plasma in original carton.
   c. Cartons
      (1) Mark each carton label with word "Salvaged" immediately after words "Source Plasma (Human)" using a black permanent marking pen.
      (2) Cartons will not be split.
      (3) Cartons may require renumbering as i

GRO-C 12/11/80

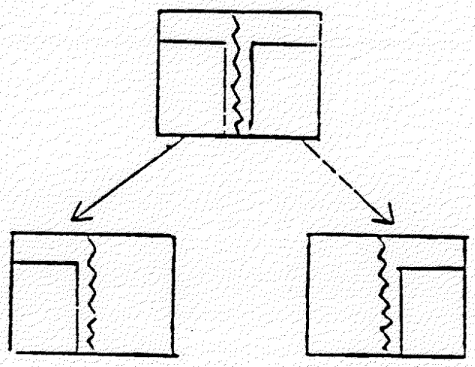
GRO-C 12/11/80

Subject: Prepare Frozen Source Plasma (Human) Salvaged for Shipping.

Responsibility: Centrifuge Technician and Manager

d. Plasma Packing and Hepatitis Report Form (Form No. 81-9709).
   (1) Write Source Plasma (Human) Salvaged on top of each Plasma Packing and Hepatitis Report Form if all cartons listed are designated as Source Plasma(Human) Salvaged using a black permanent marking pen. Be sure to so label Plasma Packing and Hepatitis Report Form before making photocopies for retention on permanent file (see Procedure 2.4.8).
   (2) File complete information as given in 2. above with Plasma Packing and Hepatitis Report Form listing plasma designated as Source Plasma (Human) Salvaged.

e. If only part of plasma drawn during a single Week Number is to be designated as Source Plasma (Human) Salvaged:
   (1) Cut Plasma Packing and Hepatitis Form with scissors isolating carton designated Source Plasma (Human) Salvaged from carton designated as Source Plasma (Human).
   (2) Tape each part onto a blank Plasma Packing and Hepatitis Report Form thus creating two new sheets that list Source Plasma (Human) Salvaged separately from Source Plasma (Human):



   (3) Complete each new Plasma Packing and Hepatitis Report Form as Specified in Procedure 2.4.8 and above.
   (4) Renumber all cartons as required so that all Source Plasma (Human) Salvaged cartons are numbered 1 through ? and all Source Plasma (Human) cartons are numbered 1 through?, within designated Week Number(s).

GRO-C

PROCEDURE 2.5.1

Subject: Prepare HB_sAg Test Plasma Samples for Shipping

Responsibility Centrifuge Technician

1. Check Control Number labels on plasma tubing samples with Control Number labels on Form No. 81-9709 (Plasma Packing and Hepatitis Report Form) (see Procedure 4.0.8). Control Number should be fastened around tubing so that the two ends of the label adhere to each other and cannot adhere to another piece of tubing or become detached. Labels should be about 1" from one end, not in the middle, and not at both ends.
2. Make clear photocopy of completed Form No. 81-9709 and give to Center Manager.
3. Start a new cardboard sample support for each Plasma Packing and Hepatitis Report Form. Fill cardboard sample support to match completion of Form No. 81-9709(Plasma Packing and Hepatitis Report Form) including beginning and ending Control Numbers.
4. Insert plasma tubing samples into cardboard sample support in the same order the Control Numbers appear on Form 81-9709, so that the Control Number labels are all at the same end of the plasma tubing samples.
5. Take two paper towels and fold into a 2" wide strip. Place over one end of plasma samples to absorb any leaking plasma. Repeat with two additional towels over other end of samples.
6. Fold flaps of cardboard sample support inward over paper towels and secure tabs in slots.
7. Insert no more than two filled cardboard sample supports into polyethylene bag. Exclude air from polyethylene bag. Fold open end of polyethylene bag at least twice and securely tape to the back of cardboard sample support to provide a watertight seal. Do NOT insert Form 81-9709 into polyethylene bag.
8. Place cardboard sample supports in polyethylene bag and corresponding Form No. 81-9709 into manila envelope.
9. Thoroughly seal manila envelope.

R 10. Mail plasma tubing samples to testing facility DAILY.

GRO-C 12/10/80

GRO-C 12/10/80

109 6951

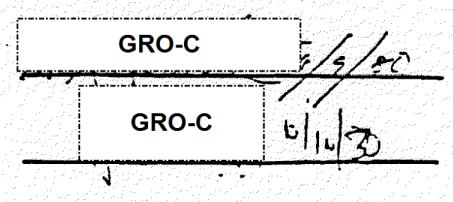
1 - 11 - CS0 a 8

PROCEDURE 2.5.1.1

Subject: HB_sAg Test Results

Responsibility: Center Manager or Assistant Manager Only

1. Receive telephone call from testing laboratory.
   a. Testing laboratory will telephone if any test is determined to be HB_sAg reactive.
   b. Consult appropriate Donor Chart to determine if there were any units of plasma donated subsequent to the unit of plasma found reactive.
   c. Mark the appropriate unit(s) of plasma as reactive on photocopy of Plasma Packing and Hepatitis Report form and draw a single line through entry. Initial and date line. Locate photocopies for any subsequent units and line them out as well.
   d. Immediately quarantine reactive unit of plasma and any subsequent units of plasma in a separate freezer operating at -20°C or colder or in a clearly marked sealed or lockable container in the quarantine area of the freezer. Label outside of container "Possibly HB_sAg Positive Plasma, DO NOT SHIP".
   e. Provide a system to prevent further plasmapheresis of donor until results of confirmation tests are known.
2. Receive Plasma Packing and Hepatitis Report Form from testing laboratory containing HB_sAg test results.
   a. Compare original Plasma Packing and Hepatitis Report forms with appropriate photocopies to ascertain that testing is complete on all samples listed.
   b. Handling individual units of plasma on which HB_sAg testing is incomplete, i.e. marked "QNS" or "sample missing".
      (1) Remove unit and any subsequent units drawn from same donor from original carton(s) and quarantine in container labelled "Possibly HB_sAg Positive Plasma, DO NOT SHIP".
   c. Discard photocopy of Plasma Packing and Hepatitis Report Form.
   d. Handling plasma initially reported as QNS, sample missing or reactive but later found to be negative.
      (1) Remove unit and any subsequent units drawn from same donor from quarantine and return to original carton(s), if available.
      (2) If original cartons have been shipped, add unit(s) to another Plasma Packing and Hepatitis Report Form of the same Plasma Type and Donor Code and ship on next regular shipment. In space headed HB_sAg Result write "Confirmation Test Negative". Initial and date statement.
      (3) Attach photocopy of "HB_sAg Negative" test results to Plasma Packing and Hepatitis Report Form containing the appropriate unit(s).
      (4) Reinstate donor to active donor status.



109 6952

e. Handling plasma initially reported as reactive and found to be positive on confirmation tests, i.e. HB_sAg positive plasma.
   (1) Remove unit and any subsequent units drawn from same donor from quarantine and destroy promptly (see Procedure 2.5.2).
   (2) Record positive HB_sAg test on Donor Chart and permanently reject donor.
   (3) Update permanent reject files.

3. Sort quarantined plasma
   a. Transfer all plasma with negative HB_sAg results from quarantine area of freezer to portion of walk-in freezer reserved for plasma to be shipped.
   b. Ship complete week numbers on next regular shipping day, or as directed by Manager, Plasma Procurement, Cutter Laboratories.
   c. Retain in quarantine area of freezer all plasma with incomplete test results, any plasma drawn subsequently from the same donor.

Records.

Retain, on permanent file, photocopies of completed Plasma Packing and Hepatitis Report Forms and original results of confirmation tests as received from testing laboratory.

Precaution:

Checking of original Plasma Packing and Hepatitis Report Forms with retained photocopy of Plasma Packing and Hepatitis Report Forms is a vital step in this procedure, and must be done promptly and carefully!

GRO-C 5/9/80

GRO-C 6/10/80

Subject: Report of donor reported to have, or to have had, clinical, serum, or infectious hepatitis or discovered to have been tested as HB_sAg positive in the past.

Responsibility	Action
All Personnel	1. Receive report from any source that an active donor has, or has had, clinical, serum or infectious hepatitis or has been tested as HB_sAg positive in the past.
	2. Notify the Center Manager or Assistant Center Manager immediately so he/she can investigate validity of report.
Center Manager or Assistant Center Manager only.	3. If validity of report is established record information on Donor Chart and permanently terminate donor; update permanent reject files.
	4. Report of plasma (shipped) drawn from a donor who, while denying a history of hepatitis and testing HB_sAg negative, is discovered to have had clinical, serum, or infectious hepatitis or to have been tested as HB_sAg positive in the past.
R	a. Promptly report by phone to Q.A. Plasma Procurement Administrator, (415) 420-5151. Report must include: (1) Donor number and name. (2) Agency reporting hepatitis. (3) Date report received by Center. (4) Date of diagnosis or HB_sAg positive test. (5) Control Number, date of drawing, Plasma Type, Donor Code and Week Number in which drawn, of all plasma units drawn subsequent to diagnosis, or plasma units drawn since donor tested positive for HB_sAg that have been shipped. (6) Number of carton(s) in which unit(s) shipped. (7) Date shipped and destination.
R	5. Prepare a report on Center letterhead confirming all information given, mail to Q.A. Plasma Procurement Administrator, Cutter Laboratories, Inc. Fourth & Parker Streets, Berkeley, CA 94710.
	6. Quarantine all available plasma units on hand pending receipt of instructions for final disposition thereof from Director of Plasma Procurement, Cutter Laboratories.

109 6954

GRO-C 12/10/80

GRO-C 12/11/80

8 1 0 1 1 2 CS0 a g 1

PROCEDURE 2.5.1.3

Subject: Obtain sample of plasma for HB_sAg testing after plasma has been frozen.

Responsibility: Center Manager or Assistant Center Manager

Note: Only in the event that HB_sAg test samples are lost, and all attempts to find them have failed, can the following procedure be used to obtain an additional plasma sample for test purposes.

A. Identify, thaw and sample unit of plasma.
1. Locate all units of plasma for which the samples were lost.
2. Remove plasma from freezer and place in a refrigerator with a temperature setting of 2° to 8°C.
3. Monitor and record temperature of refrigerator frequently while plasma is thawing.
   Caution: Plasma must not be allowed to reach a temperature in excess of 10°C at any time. Once plasma begins to thaw, all equipment must be ready to proceed with resampling as rapidly as possible.
4. Obtain sterile vials with lids which will hold at least 5cc's of plasma.
5. Label a vial with a Control Number corresponding to each unit of plasma to be sampled.
6. Obtain a sterile 5cc disposable syringe and sterile disposable 20 gauge needle for each unit of plasma to be sampled.
7. When plasma is thawed, remove one unit of plasma at a time and thoroughly agitate the bag to obtain a uniform mixture.
8. Lay unit of plasma on a flat surface in a clean isolated lab area other than the centrifuge lab.
9. Put on protective gloves and wear them throughout the entire procedure.
10. Aseptically attach sterile needle to sterile syringe leaving needle protector in place.
11. Select longest tubing end on the plasma pooling bag and swab with a sterile gauze pad moistened with 70% Isopropyl Alcohol.
12. Remove excess alcohol with dry sterile gauze and proceed to next step immediately.
13. Remove needle protector and insert needle into sterile portion of tubing near hemoclip (do not contaminate entry site with fingers).
14. Draw approximately 5cc's of plasma into syringe.
15. After drawing sample, withdraw needle and bend tubing over on itself so that the hole in the tubing is sealed.
16. Place hemoclip on folded tubing.
17. Seal hemoclip.

8-24-77
GRO-C
6-10-77

Subject: Obtain sample of plasma for HB_sAg testing after plasma has been frozen.

Responsibility: Center Manager or Assistant Center Manager

18. Aseptically express plasma from syringe into properly labeled sterile vial.
19. Bend needle then discard needle and syringe. (See Procedure 2.3.13).
20. All plasma which has been resampled, must be labeled as Source Plasma (Human) Salvaged. (See Procedure 2.4.9). R
21. Return unit of plasma to freezer immediately, before proceeding to sample another unit.
22. When all sampling is complete, clean entire area before using lab for normal purposes.
23. Prepare samples for mailing to testing laboratory using a suitable mailer to avoid breakage.
24. Prepare copies of Form 81-9709 (Plasma Packing and Hepatitis Report Form) from copies of original submission to testing laboratory.

B. Because the samples being submitted for testing are not the normal tubing samples and because the paperwork are not originals, a typewritten explanation must accompany the samples to explain why the samples and paperwork are different. Keep a copy of the letter and of the Plasma Packing and Hepatitis Report Form on file.

GRO-C 11/26/81

GRO-C 11/2/81

10/26/81

54E 8 1 1 1 CS0 8 8 3

rev 6956

PROCEDURE 2.5.2

Subject: Destruction of HB_sAg Positive Plasma or other Unacceptable Plasma

Responsibility: Laboratory Technician

1. Equipment.
   a. Sixteen quart canner with pressure gauge, such as Sears, Roebuck and Company model 670.46000. Similiar equipment is satisfactory provided equipped with an aneroid type pressure gauge. Equipment using only a weight regulator is NOT satisfactory.
   b. Heavy duty electric hot plate with continuous rheostat regulator. Equipment with preset push button regulators is not satisfactory.
2. Procedure.
   a. Remove bag of plasma from freezer and allow to thaw; may require 24 hours or longer.
   b. Remove, from bag of plasma, Control Number label and place in log book described below. Write in log book Donor Number of donor of plasma, date plasma collected and date destroyed.
   c. Place bags on wire rack in canner. A maximum number of 5 bags may be run at same time. Cleaning of canner will be facilitated if bags of plasma are first placed in a plastic roasting bag before placing in canner. Add a minimum of 1 qt. and a maximum of 2 qts. water containing 1 cup washing soda (Na_2CO_3).
   d. Lock top of canner in place.
   e. Apply high heat to canner by means of hot plate. Record in log time of day heating begun.
   f. Reduce heat sufficiently to maintain no less than 15 psi. Record in log time of day 15 psi is reached and heat reduced.
   g. Record in log pressure showing on gauge in psi at 30, 60 and 120 minutes after reducing heat.
   h. Turn off heat after 120 minutes. Record in log time of day heat turned off. Allow canner and contents to come to room temperature.
   i. Unlock top of container and remove contents.
   j. Place contents in heavy duty plastic bag, sealing top of bag to form water-tight seal.
   k. Discard in regular trash receptacle.
   l. Clean canner after each use. Pay particular attention to rubber seal on lid. Follow closely canner manufacturer's recommendations with respect to maintainence of pressure gauge, soft plugs and other safety devices.
3. Log Book Contains Following Information.
   a. Control Number label of destroyed bag of plasma.
   b. Donor Number of donor of plasma.
   c. Date plasma collected.
   d. Run number - composed of year, Center Code and a sequential number, eg: 77XX0001.
   e. Date of run.
   f. Informative details of run as described in procedure above.
   g. Signature of person performing destruction of plasma.

GRO-C

3/3/77

Subject: Destruction of HB_gAg or Other Unacceptable Plasma

Responsibility: Laboratory Technician

4. Write on Form 81-9723 (Donor Card) in the appropriate donor's chart, opposite Control Number label of plasma destroyed, "Plasma Destroyed Run No. _____", eg: 77XX0001.
5. Physical removal of unacceptable units of plasma from freezer, destruction of plasma, documentation of plasma destruction in log book and donor's chart must be done by one person, preferably Laboratory Technician, and verified by another, preferably Center Manager. Thus two signatures must appear in log book and donor's chart.
6. Alternate Procedure:

R

   a. Autoclave at 15 psi steam pressure, 121.5°C (251°F) for 2 hours after stated temperature and pressure reached.
   b. If alternate procedure used, record specified information in log book changing informative details of run to include (1) time heat first applied, (2) time required temperature and pressure achieved, (3) time temperature and pressure reduced.

GRO-C 12/11/80

GRO-C 12/1/80

109 6958

CSO

PROCEDURE 2.5.3

Subject: Prepare Hyperimmune Plasma Samples for Shipping

Responsibility: Centrifuge Technician

1. Check Control Number labels on plasma tubing samples with Control Number labels on Form No. 81-9190 (Plasma Sample Packing List). Control Number should be fastened around tubing so that the two ends of the label adhere to each other and cannot adhere to another piece of tubing or become detached. Labels should be about 1" from one end, not in the middle, and not at both ends.
2. Start a new cardboard sample support for each Plasma Sample Packing List. Fill cardboard sample support to match completion of Form No. 81-9190 (Plasma Sample Packing List) including beginning and ending Control Numbers.
3. Insert plasma tubing samples into cardboard sample support in same order the Control Numbers appear on Form 81-9190, so that the Control Number labels are all at the same end of the plasma tubing samples.

R 4. Take two paper towels and fold into a 2" wide strip. Place over one end of plasma samples to absorb any leaking plasma. Repeat with two additional towels over other end of samples.

R 5. Fold flaps of cardboard sample support inward over paper towels, and secure tabs in slots.

6. Insert no more than two filled cardboard sample supports into polyethylene bag. Exclude air from polyethylene bag. Fold open end of polyethylene bag at least twice and securely tape to the back of card-

R board sample support to provide a watertight seal. Do NOT insert form 81-9190 into polyethylene bag.

7. Place cardboard sample supports in polyethylene bag and corresponding Form No. 81-9190 into 13" x 10" manila envelope.
8. Thoroughly seal manila envelope.
9. Apply shipping label (see Procedure 4.0.9) to front of manila envelope marking an "X" in Bio Control box.
10. Mark shipping label for Hepatitis B Antibody plasma samples: "Type A".
11. Mark shipping label for Rabies plasma samples: "Type B".
12. Mail plasma tubing samples WEEKLY by First Class Mail.
13. Plasma samples which contain red blood cells, buffy coat, are excessively chylous or are contaminated with bacteria or mold will give false test results and will not be tested.

GRO-C 3/18/80

GRO-C 3/21/80

109 6959

C 1 1 1 CS0 2 96

PROCEDURE 2.5.4

Subject: RPR (Syphilis) Test

Responsibility: Laboratory Technician

1. RPR tests will be done in a Test Laboratory segregated from other center activities.
2. Materials and Reagents.
   a. RPR Card antigen suspension, 20 g. needle and dispensing bottle.
   b. Plastic coated cards with ten 18 mm. circle spots each.
   c. Dispenstirs.
   d. Card Test Rotator, Model 300.
   e. RPR positive control card.
3. Preparation for RPR test.
   a. Secure RPR test sheet.
   b. Arrange serum samples to be tested in same order as listed on RPR test sheet.
   c. Expose serum samples to be tested by removing caps from vial. Be sure not to mix-up caps and vials.
4. Perform RPR test, read and record results of RPR test on RPR test sheet according to instructions from manufacturer of equipment and reagents. Record lot number of all reagents and equipment used on RPR test sheet. A complete description of test procedure may be found in "Manual of Tests for Syphilis, 1969" U.S. Department of Health, Education, and Welfare, Disease Program, Atlanta, Georgia 30333, Public Health Service Publication No. 411. Can be obtained from U.S. Government Printing Office, Washington, D.C.
   a. Use RPR positive control card on each day test is run. Record results of control tests on RPR test sheet.
   b. At least once each week, determine revolutions per minute (rpm) of serologic rotator by method recommended by manufacturer and record results on RPR test sheet on day performed.
   c. Label RPR antigen dispensing bottle with Lot No. and expiration date of antigen.
   d. Discard all used reagents and equipment as recommended by manufacturer.
5. Replace caps on same vials from which removed.
6. Sign and date RPR test sheet. Preserve completed RPR test sheet as a permanent record.
7. Place results of RPR test on each donor each time run on Form No. 81-9723 (Donor Card) in each donor's chart (see Procedure 1.0 #6).
   a. If RPR test is positive do not permit donor to donate again until donor's acceptability has been reestablished, (see Procedure 2.2.2).
   b. Ship unit of plasma if HB_sA_g test is negative.
      NOTE: Issuance of the first unit of RPR positive plasma collected from a donor is permitted; relabeling is not required.

GRO-C 12/4/78

GRO-C 12/5/78

8 1 1 1 C80 a 07

109 6960

Subject: Tetanus Toxoid Immunization and Tetanus Immune Plasma. Additional Requirements

Responsibility	Action
Medical Director	1. Selection of Donors. a. Determine if donor is acceptable plasmapheresis donor. (see Procedures 2.2.1, 2.2.2, 4.0.4). b. No more than 1 week before first immunization injection, determine that: (1) Donor has received a basic series of injections for primary immunization against tetanus, preferably more than 12 months previously. Veterans of US Armed Forces may be assumed to meet this requirement. (2) Donor has no history of untoward reactions to immunization. c. Determine if donor meets these requirements (1) Yes. Enroll donor in Tetanus program (see Procedure 2.2.1). (2) No. Do not enroll donor in Tetanus program. 2. Reactions to Tetanus Immunization. a. More common in people who have received a basic tetanus series and in those over 25 years of age. b. May include rash, hives, mild fever, swelling of glands, transient dizziness, local erythema and swelling; reactions are infrequent. Anaphylaxis has been known to occur but with an extremely low frequency. c. Maintain followup on each donor receiving toxoid on day of injection and on donor's next visit to Center to determine if reaction has occurred. If reaction does occur, write appropriate comments on Form 81-9723 (Donor Card) in donor's chart for day injection given. d. Treat donors as necessary with epinephrine (1:1000) and diphenhydramine 50 mg. if required. e. If donor has significant reaction, take appropriate action to prevent donor from receiving further injections.

GRO-C

GRO-C 11/30/77

109 6961

8 1 0 1 1 2 CS 0 a e e

Subject: Tetanus Toxoid Immunization and Tetanus Immune Plasma, Additional Requirements

Responsibility	Action
	3. Donor Health Status. a. Annual Physicial Examination (see Procedure 2.2.1). (1) Review injection history to determine compliance with frequency and number of injections and history of reactions. (2) Review increased frequency of upper respiratory infections (more than one every 2 months), lymph node enlargement, hepatosplenomegaly and review central nervous system more thoroughly than for donor of Normal plasma. b. Review Donor Chart (see Procedure 2.2.2). (1) Review abnormality of serum electrophoresis with particular emphasis on difficulties in separation of alpha 2 and beta globulin.
Medical Director or Designated Trained Individual	4. Immunization of Donor. a. Determine if donor has been approved for immunization (see Procedures 2.2.1, 4.0.4) and has consented to procedure (see Form No. 81-9746 Tetanus Immunization and Donor's Informed Consent). b. Use Tetanus Toxoid, fluid, obtained from a commercial manufacturer and administered in accordance with the manufacturer's direction insert except for dosage, frequency and route of administration. c. Inject intramuscularly following acceptable medical practices. DO NOT inject intravenously. Medical Director must be present whenever donors are being immunized. d. Provide injection information: (1) Use blank sheet of paper 8 1/2 X 11" with Center name and address at top.

R

GRO-C 1/2/79

GRO-C 1/3/79

1 11 CS0 a 99

109 6962

Subject: Tetanus Toxoid Immunization and Tetanus Immune Plasma, Additional Requirements

Responsibility	Action

(2) Next write statement "On _____ (enter date given), the donors listed below received _____ (enter name of manufacturer) Tetanus Toxoid injections, Code_____ (enter code letter), dose _____ (enter ml.) Lot No. _____".

AL 00003	AL 00040
AL 00401	AL 01036
AL 00010	etc.

(3) Include Center Code as part of Donor Number as shown. Be sure Donor Numbers are legible and accurate.

(4) Add information in (2) above on the sheet for each day's injections, including date and Lot No.

(5) Record same information in Comments section of Form No. 81-9723 (Donor Card).

(6) For each week, use one sheet (if sufficient) and mail weekly to Manager, Plasma Procurement, Cutter Laboratories, Inc.

e. Inject before or after but not during plasmapheresis.

f. Retain donor in Center for at least 15 minutes after injection to observe for anaphylaxis.

R

5. Number and Frequency of Immunizations.

a. Give first injection on day donor is enrolled in program. Inject no more than 1.0 ml intramuscularly. Booster - First year: inject no more than 1.0 ml intramuscularly at intervals of no less than 3 months. No more than four injections will be given the first year. After first year - as for first year, but no more than 3 times per year and at intervals of no less than 3 months.

b. Titer values will be mailed to center for inclusion in donor's chart on a regular basis following submission of plasma tubing samples.

c. Acceptable titer following booster is average titer of 15 or higher. If donor's titer averages 10 or less on three consecutive sample donor is boostered, if eligible, or removed

GRO-C 4/24/80

GRO-C 4/24/80

GRO-C 4/30/80

:/25/80

61

81111 CSCW 00

Subject: Tetanus Toxoid Immunization and Tetanus Immune Plasma, Additional Requirements

Responsibility	Action
	from program and not given further injections of tetanus toxoid. Such removals will appear on the Suggested Action Report. In some instances marginal donor (eg: titer 10-15) may be temporarily suspended because of an over supply of tetanus plasma. Such suspension will appear on Suggested Action Report as "Remove, other", code 24 (See Procedure 3.0.7).
R	d. If donor's titer falls below 15 and time interval is proper to give donor a booster, Medical Director examines donor to ascertain if donor's past histo: and present physical condition are acceptable. If so, Medical Director approves booster injection by signing Form No. 81-9723 (Donor Card). Booster injection is then given.
Receptionist or Prep Technician	6. Convert Normal Donor to Tetanus Donor.
	a. Plasma collected six days or less after toxoid injection is classified as Normal plasma (Black Control Number labels, plasma type N).
	b. Plasma collected more than six days after toxoid injection is classified as Tetanus plasma (Red Control Number labels, plasma Type T).
	c. On subsequent donations plasma will be classified as Tetanus plasma until donor is removed from program by Suggested Action Report or due to being classified as nonresponsive.
	d. Following removal from program, plasma from subsequent donations will be classified as Normal plasma unless donor is enrolled in another hyperimmunization program (see Procedures 3.0.2 - 3.0.6).

GRO-C 4/12/79

GRO-C 4/26/79

109 6964

Subject: Tetanus Toxoid Immunization and Tetanus Immune Plasma Additional Requirements.

Responsibility		Action
Centrifuge Technician	7.	Plasma Tubing samples must be collected on Tetanus plasma (see Procedure 2.4.4), and stored under refrigeration (2 to 8°C or 32 to 46°F). prior to mailing.
HB_sAg Test Technician	8.	Plasma tubing samples on Tetanus plasma must be sent to Cutter Laboratories weekly. (see Procedure 2.5.3). Collect one plasma tubing sample weekly starting seven days after the first injection. Interpret results as in 5c. above.
Centrifuge Technician	9.	Make sure shipping label on carton of frozen plasma is red.

GRO-C

TETANUS IMMUNIZATION INFORMATION AND DONOR'S INFORMED CONSENT

Before participating in the Tetanus Immune Globulin program you should understand the significance of Tetanus Immune Globulin to the immunization program in which you will participate.

Under the Tetanus Immune Globulin program you will receive injections of tetanus toxoid. The amount and the concentration under the program may be greater than the total amount and concentration which a person receives in normal or routine immunization. The maximum number of injections you will receive during the first year is four, administered not less than three months apart. The maximum number of injections you will receive during the second and subsequent years is three, administered not less than three months apart. The first injection is given when you begin participation in the program. After you receive this injection, your body will probably produce antibodies in your blood plasma. If the quantity of antibodies in your blood plasma does not reach an acceptable level or if the quantity falls below an acceptable level you will be either removed from the Tetanus Program or given another injection. Through these antibodies you will become immunized against the disease of tetanus (lockjaw).

When your plasma is withdrawn by plasmapheresis a portion of your antibodies becomes the source of the product, Tetanus Immune Globulin, which is used to protect people who have been exposed to tetanus infection through cuts or puncture wounds.

The Tetanus Immune Globulin produced from your plasma gives the medical profession a much safer product to use on humans than any product which can be manufactured from other sources. This i why the Tetanus Immune Globulin program is so important.

There are some risks in receiving an injection of tetanus toxoid under this program. There may be a stinging sensation immediately after the injection. I a few cases, a mild to moderate soreness redness or swelling at the injection sit may occur. Rarely, the arm itself could swell up or a swelling of the lymph nodes may occur and may be noticed as a lump under the arm. It is rare but possible for reactions involving the whole body or symptoms similar to flu such as headache, aching muscles and fever to occur. While extremely uncommon neurological disorders have been reporte following the injection of almost all immunizing products. Even though it is rare, the possibility of such a disorder exists and must be appreciated.

We ask that you sign the statement below to indicate that you have read and understood this paper and agree to participate. Ask any questions that occur to you about this Tetanus Immune Globulin immunization program.

DONOR CONSENT

I have read and I understand the above information on immunization with tetanus toxoid I give my consent and agree to participate in the Tetanus Immune Globulin Program.

To the best of my knowledge I have answered or will answer fully and honestly the questions asked me concerning my health as a donor.

I agree that I will not give blood or plasma donations or receive injections of any ki without advising the Medical Director in charge of this donor center when I next present myself for a donation or an injection. Furthermore, I agree to advise the Medical Direct of any reaction during or following tetanus immunization. I understand that I am free to withdraw my consent and not receive further tetanus toxoid at any time.

READ THIS ENTIRE DOCUMENT AND DO NOT SIGN IT UNLESS YOU UNDERSTAND IT

Signature of Donor	Date	Witness	Date
		GRO-C	6/20/79
81-9746	6/20/79	GRO-C	6/21/79
	62	GRO-C	6-21-79

[illegible] 2.2.2

Subject: Pertussis Vaccination and Hyperimmune Plasma.
Additional Requirements

Responsibility	Action
Medical Director	1. Selection of donors a. Determine if donor is acceptable plasmapheresis donor (see Procedures 2.2.1, 2.2.2, 4.0.4). b. Donor must not be currently donating plasma of another hyperimmune type or have received other hyperimmunization injection within past seven days. c. Examination more detailed than for donation of normal plasma to ensure: (1) Donor has no history of convulsions or central nervous system disease or injury; important due to reports of encephalopathy following vaccination. (2) Donor has no history of allergy or allergy-like (autoimmune) diseases, e.g. glomerulonephritis, rheumatoid arthritis, rheumatic fever, etc.; important due to reports of allergic vasculitis following vaccination. d. Determine if donor meets these requirements. (1) Yes. Enroll donor in Pertussis program (see Procedure 2.2.1). (2) No. Do not enroll donor in Pertussis program. 2. Reactions to Pertussis Vaccination. a. Local inflammatory reaction commonly seen within 24 hours of vaccination. b. Occasionally irritability, loss of appetite and vomiting occur. c. Occasionally a systemic reaction with fever and malaise or convulsions occurs. d. Rarely encephalopathy occurs. e. Rarely allergic vasculitis occurs. f. A nodule may appear and persist for several weeks at site of injection. This is due to insoluble aluminum phosphate adjuvant. Nodule should be allowed to recede spontaneously. g. Maintain followup on each donor receiving vaccine to determine if reaction has occurred h. If reaction does occur, write appropriate comments on Form No. PI-9723 (Donor Card) in donor's chart for day injection given.

GRO-C

9/3/70

63

[illegible]

109 6997

Subject: Pertussis Vaccination and Pertussis Immune Plasma, Additional Requirements

Responsibility	Action
	i. Treat donors as necessary for reaction. j. If donor has significant reaction, take appropriate action to prevent donor from receiving further injections.
	3. Donor Health Status. a. Annual Physical Examination (see procedure 2.2.1). (1) Review injection history to determine compliance with frequency and number of injections and history of reactions. (2) Review increased frequency of upper respiratory infections (more than one every 2 months), lymph node enlargement, hepatosplenomegaly and review central nervous system more thoroughly than for donor of Normal plasma. b. Review Donor Chart (see procedure 2.2.2). (1) Review abnormality of serum electrophoresis with particular emphasis on difficulties in separation of alpha 2 and beta globulin.
Medical Director or Designated Trained Individual	4. Vaccination of Donor. a. Determine if donor has been approved for vaccination (see proceedures 2.2.1 and 4.0.4) and has consented to procedure (see Form No. 81-9747 Pertussis Immunization Information and Donor's Informed Consent). b. Use only Pertussis Vaccine, Non-Adsorbed, manufactured by Lederle Laboratories, supplied by Cutter Laboratories, or Pertussis Vaccine Adsorbed, manufactured by Michigan Dept. of Public Health, supplied by Cutter Laboratories. c. Maximum dose per injection is 0.5ml. d. Inject intramuscularly only, following acceptable medical practices. DO NOT inject intravenously. Medical Director must be present whenever donors are being vaccinated. e.. Provide Injection information. (1) Use blank sheet of paper 8 1/2 x 11" with Center name and address at top. Use a separate sheet from other types of injections.

GRO-C 3-21-79

GRO-C 2/13/79

CSO W 5

109 6968

Subject: Pertussis Vaccination and Pertussis Immune Plasma. Additional Requirements

Responsibility	Action

(2) Next, write statement "On _____ (enter date given), the donors listed below received injections of Pertussis Vaccine, Non-Adsorbed manufactured by Lederle Laboratories, Code B, dose 0.5ml, Lot No. _____:" OR write: "On_____ (enter date given), the donors listed below received injections of Pertussis Vaccine, Adsorbed, manufactured by Michiga Department of Public Health, Code E, dose 0.5ml, Lot No. _____:"

AL 00003 AL 00040
AL 00401 AL 01036
AL 00010 etc.

(3) Include Center Code as part of Donor Number as shown. Be sure Donor Numbers are legibl and accurate.

(4) Add information in Item (2) above on sheet for each day's injections, noting date and Lot No.

(5) Record same information in comments sectior of Form No. 81-9723 (Donor Card).

(6) For each week, use one sheet (if sufficient and mail weekly to Manager, Plasma Procurement, Cutter Laboratories, Inc.

f. Inject after plasmapheresis.

g. Retain donor in Center for at least 15 minutes after injection to observe for anaphylaxis.

5. Number and Frequency of Vaccinations.

a. Give first injection on day donor is enrolled i program.

b. Injections may be repeated on days 7 and 14.

R c. In addition to the primary series of three injections described above, donor may receive booster injections of no more than 0.5ml, intra muscularly, maximum three times a year.

d. Subsequent booster injections or removal from program are done on the basis of donor's titer results and suggestions to Medical Director by means of a weekly Suggested Action Report (see Procedure 3.0.7).

GRO-C 4/21/81

GRO-C 5-27-81

GRO-C 5/29/81

Subject: Pertussis Vaccination and Pertussis Immune Plasma. Additional Requirements

Responsibility		Action
R		e. Acceptable titer is 100 or greater. When Donor's titer falls to 50 or lower and remains at 50 or lower for 2 consecutive titer determinations, give booster if donor is eligible. If donor is not eligible, remove donor from program.
		f. When decision is made to give donor a booster, Medical Director examines donor to ascertain if donor's past history and present physical condition are acceptable. If so, Medical Director approves booster injection by signing Form No. 81-9723 (Donor Card). Booster injection is then given.
Receptionist or Prep Technician	6.	Convert Normal Donor to Pertussis Donor
		a. Plasma collected from donors undergoing immunization is classified as Normal plasma (Black Control Number labels, plasma type N) until primary immunization is complete.
		b. On subsequent donations plasma will be classified as Pertussis plasma (Green Control Number labels, plasma type P), until donor is removed from program by Suggested Action Report.
		c. Following removal from program, plasma from subsequent donations is classified as Normal plasma unless donor is enrolled in another hyperimmunization program (see Procedures 3.0.1 - 3.0.8).
Centrifuge Technician R	7.	Collect one plasma sample weekly after second injection is given and on Pertussis plasma, and store under refrigeration (2 to 8°C or 35 to 46°F) prior to mailing.
R	8.	Plasma samples must be collected in small vials. (Vials used for serum protein electrophoresis samples would be ideal).

GRO-C 4/21/81

GRO-C 5-27-81

GRO-C 5/29/81

109 6970

CSRW 07

Subject: Pertussis Vaccination and Pertussis Immune Plasma. Additional Requirements

Responsibility		Action
R	9.	Place vials and corresponding Form No. 81-9190 (Plasma Sample Packing List) in shipping container provided by Cutter Laboratories for SEP samples. Position vials as shown in Plate F (see Procedure 2.4.6), no more than 40 samples per box. On top of sealed shipping container apply yellow shipping label (Form MS-1142).
R	10.	Plasma samples on Pertussis plasma must be sent to Cutter Laboratories, Inc. weekly.
R	11.	Make sure shipping label on carton of frozen plasma is green.

GRO-C 4/21/81

GRO-C 5-27-81

GRO-C 5/29/81

PERTUSSIS IMMUNIZATION INFORMATION AND DONOR'S INFORMED CONSENT

Before participating in the Pertussis Immune Globulin program you should understand the significance of Pertussis Immune Globulin to the medical profession and the nature of the immunization program in which you will participate.

Under the Pertussis Immune Globulin program you will receive a series of injections of Pertussis Vaccine which has been specially prepared for immunization of infants to Pertussis (whooping cough). The amount and the concentration of the Pertussis Vaccine which you will receive under the program are the same as recommended for immunization of children 6 to 12 months of age. You will receive a primary series of three injections, at least one week apart. After you receive these injections, your body will probably produce antibodies in your blood plasma. During your participation in the Pertussis Immune Globulin program, you may receive no more than three booster injections per year to increase the quantity of antibodies in your plasma.

When your plasma is withdrawn by plasmapheresis, a portion of your antibodies becomes the source of the product, Pertussis Immune Globulin, which is used to protect non-immune children who have been exposed to Pertussis infection. The Pertussis Immune Globin produced from your plasma furnishes the medical profession a safe, effective product which provides protection to susceptible children. This product can be prepared only from human plasma. This is why the Pertussis Immune Globulin program is so important.

There are some risks in receiving an injection of Pertussis Vaccine under this program. There may be a stinging sensation immediately after the injection. In a few cases, a mild to moderate soreness, redness, or swelling at the injection site may occur. There may be a tenderness around the injection site for about a day. Occasionally, a small nodule may develop temporarily at the site of injection. It is rare, but it is possible to experience symptoms similar to the flu such as headache, aching muscles and a fever. In rare cases, a swelling of the lymph nodes may occur and may be noticed as a lump under the arm. While extremely uncommon, neurological disorders have been reported following the injection of almost all immunizing products. Even though it is rare, the possibility of such a disorder exists and must be appreciated.

We ask that you sign the statement below to indicate that you have read and understood this paper.

DONOR CONSENT

I have read and I understand the above information on immunization with Pertussis Vaccine.

To the best of my knowledge I have answered or will answer fully and honestly the questions asked me concerning my health as a donor.

I agree that I will not give blood or plasma donations or receive injections of any kind without advising the Medical Director in charge of this donor center when I next present myself for a donation or an injection. Furthermore, I agree to advise the Medical Director of any reaction during or following Pertussis immunization. I understand that I am free to withdraw my consent and not receive further injections of Pertussis Vaccine at any time.

READ THIS ENTIRE DOCUMENT AND DO NOT SIGN IT UNLESS YOU UNDERSTAND IT.

Signature _____ Date _____

Witness _____ Date _____

81-9747
(Rev. 4/81)

GRO-C 4/21/81

GRO-C 5-27-81

GRO-C 5/29/81

CSO W 09

109 6972

PROCEDURE 3.0.3.

Subject: Rabies Vaccination and Rabies Immune Plasma. Additional Requirements

Responsibility	Action
Medical Director	1. Selection of donors. a. Determine if donor is acceptable plasmapheresis donor (see procedures 2.2.1, 2.2.2, 4.0.4). b. Donor may be currently donating plasma of another hyperimmune type. c. Irrespective of time interval since last physical examination, donor must receive another physical examination. (1) Determine, in more detail than for donation of Normal plasma, that donor has absolutely no history of any allergic manifestations whatsoever, eg: hayfever, asthma for last 10 years, allergic rhinitis or any other atopic manifestation. (2) Determine that donor has absolutely no history of any allergic manifestation to <u>any</u> antibiotics. (3) Ask the donor "Do you now eat eggs without problems or reactions?" Donor must answer affirmatively. (4) Determine if donor meets these requirements. (a) Yes. Enroll donor in Rabies program (see procedure 2.2.1). (b) No. Do not enroll donor in Rabies program. 2. Reactions to Rabies Vaccination. a. Complete discussion of other adverse reactions may be found in literature accompanying vaccine. b. Reactions may be frequent and take several forms: (1) Local reactions (most frequent) include immediate pain, stinging or burning, local erythema and induration, pruritus and regional adenopathy.

GRO-C

CSOW 10

109 6973

Subject: Rabies Vaccination and Rabies Immune Plasma.
Additional Requirements.

Responsibility	Action
	(2) Non-specific systemic reactions (less frequent) include general malaise, neuralgia, fever and chills, generalized itching or rash. (3) Specific systemic reactions include: (a) Gastrointestinal (much less frequent) include nausea, vomiting, diarrhea and abdominal pain. (b) Central Nervous System (rare) include headache, dizziness, photophobia, paresthesia or increased fatigue; transverse myelitis and encephalitis have been reported. (c) Anaphylaxis may occur in about 0.5% of donors. c. Donors who are allergic to egg, chicken, chicken feathers or antibiotics may react unfavorably and more violently. d. If reaction does occur, write appropriate comments on Form No.81-9723 (Donor Card) in donor's chart for day injection given. e. Treat donors as necessary for reaction. f. If donor has significant reaction, take appropriate action to prevent donor from receiving further injections. 3. Donor Health Status. a. Annual Physical Examination (see Procedure 2.2.1) 12 months after beginning rabies program. (1) Review injection history of rabies vaccine to determine compliance with frequency and number of injections and history of reactions (see 2 above and 5 below). (2) Review increased frequency of upper respiratory infections (more than one every 2 months), lymph node enlargement, hepatosplenomegaly and review central nervous system more thoroughly than for donor of

GRO-C

CS0 W 11

109 6974

Subject: Rabies Vaccination and Rabies Immune Plasma
Additional Requirements

Responsibility	Action
	Normal plasma
	(3) If difficulties are found in any of these areas, take steps to ensure donor receives no further injections.
	b. Review Donor Chart (see procedure 2.2.2).
	(1) Review abnormality of serum electrophoresis with particular emphasis on difficulties in separation of alpha 2 and beta globulin.
	(2) If noted, take steps to ensure donor receives no further injections.
	4. On direction of Manager of Plasma Procurement, Cutter Laboratories, Inc. certain special donors may be assigned to Rabies program without receiving basic series of vaccination or regular booster injections.
Medical Director or Designated Trained Individual	5. Vaccination of Donor.
	a. Determine if donor has been approved for vaccination (see procedures 2.2.1, 4.0.4) and has consented to procedure (see Form No. 81-9749, Rabies Immunization Information and Donor's Informed Consent).
	b. Use only Rabies Duck Embryo Vaccine manufactured by Lilly, supplied by Cutter Laboratories, Inc.
	c. Maximum dose per injection is 1.0 ml.

GRO-C 1/10/80

GRO-C 12-20-79

GRO-C 12/7/79

CSO; M 12

109 6971

Subject: Rabies Vaccination and Rabies Immune Plasma
Additional Requirements

PROCEDURE TO BE USED AT SAN DIEGO CENTER ONLY:

Responsibility	Action
Medical Director or M.D. Designate	5. Vaccination of Donor. Give oral antihistamine (Chlortrimeton Repeerabs 4 mgs) 20 minutes before injection.

GRO-C

109 6976

Subject: Rabies Vaccination and Rabies Immune Plasma.
Additional Requirements.

Responsibility	Action

d. Inject subcutaneously following acceptable medical practices. DO NOT inject intramuscularly or intravenously. Medical Director must be present whenever donors are being vaccinated.

e. Provide injection information.

(1) Use blank sheet of paper 8 1/2x11" with Center name and address at top. Use a separate sheet from other types of injections.

(2) Next, write statement "On _____(enter date given), the donors listed below received Lilly Rabies Vaccine, Code L, dose 1.0 ml. Lot No. ____:"

AL 00003	AL 00040
AL 00401	AL 01036
AL 00010	etc.

(3) Include Center Code as part of Donor Number as shown. Be sure Donor Numbers are legible and accurate.

(4) Add information in Item (2) above on the sheet for each day's injections, noting date and Lot No.

(5) For each week, use one sheet (if sufficient) and mail weekly to Manager, Plasma Procurement, Cutter Laboratories.

(6) Record same information in comments section of Form No. 81-9723 (Donor Card). Also note date on which second, third and fourth injections are to be given.

f. Inject after but not before or during plasmapheresis.

g. Retain donor in Center for at least 30 minutes after injection to observe for anaphylaxis.

6. Number and frequency of Vaccination.

a. Give first injection on day donor is enrolled in program.

b. Give second injection 7 ± 2 days after first injection.

c. Give third injection 14 ± 2 days after first injection.

d. Give booster injection 42 ± 2 days after first injection, and every 26-32 days after donor is classified as a Rabies donor. Prior to booster injection, Medical Director examines donor to ascertain if donor's past history and present physical condition are acceptable. If so, Medical Director approves booster injection by signing Form No. 81-9723 (Donor Card). Booster injection is then given.

CSO W 14

109 6971

GRO-C

Subject: Rabies Vaccination and Rabies Immune Plasma.
Additional Requirements.

Responsibility	Action
	6. e. Removals from program are done on the basis of donor's titer results and suggestions to Medical Director by means of a weekly Suggested Action Report (see Procedure 3.0.7). Decision to cease further injection of a donor is the sole responsibility of Medical Director.
	f. Acceptable titer is 4 International Units (IU)/ml. or greater. If donor achieves that level, wait one month, give booster. Collect sample 2 weeks after booster. On day 100, automatically assign donor's plasma as plasma Type B. If donor titer less than 4 IU/ml. drop from immunization program. When donor's titer falls below 4 IU/ml. for 2 consecutive titer determinations drop from program.
Receptionist or Prep Technician	7. Convert Normal Tetanus or Pertussis Donors to Rabies Donors.
	a. Plasma collected from donors undergoing immunization will be classified as Normal, Tetanus, or Pertussis plasma (Black, Red or Green Control Number labels, plasma type N, T or P) until day 100 following start of Rabies immunization program.
	b. Plasma collected from Rabies donors will be classified Rabies Plasma (Pink Control Number labels, plasma type B).
	c. On subsequent donations plasma will be classified as Rabies plasma until donor is removed from program by weekly Suggested Action Report (see Procedure 3.0.7). Decisions to cease further injection of a donor are sole responsibility of Medical Director.
	d. Following removal from program, plasma from subsequent donations will be classified as Normal plasma unless donor is enrolled in another hyperimmune program (see Procedures 3.0.1 - 3.0.6).

GRO-C

CSD W 15

109 6978

Subject: Rabies Vaccination and Rabies Immune Plasma
Additional Requirements

Responsibility	Action
Centrifuge Technician	8. Plasma samples a. Collect samples 56 ± 2 days after first injection and once a week after donor assigned to Rabies program. b. Note that Form No. 81-9190 (Plasma Sample Packing List) will contain black, pink, and red Control Number labels since all donors are not yet classified as donors of Rabies plasma. (1) Therefore, write RABIES in large block letters in the space for Plasma Type. (2) If donor is currently classified as a donor of Tetanus plasma, no Tetanus sample is necessary at time of Rabies sample collection. c. Plasma samples must be collected on Rabies plasma and stored under refrigeration (2 to 8°C or 35 to 46°F) prior to mailing. d. Plasma samples on Rabies plasma must be sent to Cutter Laboratories weekly.
	9. Plasma samples must be collected in small vials. (Vials used for serum protein electrophoresis samples would be ideal).
	10. Position vials as shown on Plate F (see Procedure 2.4.6). Pack no more than 40 samples per box and make sure Control Numbers on samples in box correspond with Control Numbers on Plasma Sample Packing Lists accompanying samples.
	11. Make sure shipping label on carton of frozen plasma is pink.

GRO-C 4/21/57

GRO-C 5-27-5-1

GRO-C 5/29/61

109 6979

RABIES IMMUNIZATION INFORMATION AND DONOR'S INFORMED CONSENT

Before participating in the Rabies Immune Globulin program, you should understand the significance of Rabies Immune Globulin to the medical profession and the nature of the immunization program in which you will participate.

Under the Rabies Immune Globulin program you will receive a series of injections of rabies vaccine. The number of injections which you will receive under the program is greater than the number of injections which a person receives in pre-exposure immunization. You will receive one injection every week for a total of four injections. After you receive these injections your body will probably produce antibodies in your blood plasma. Through these antibodies you will become immunized against the disease of rabies. To maintain an adequate quantity of antibodies in your plasma, you will receive another injection every month you remain on the program. Only about 10% of donors vaccinated will develop an adequate amount of antibodies to be assigned to the rabies program.

When your plasma is withdrawn by plasmapheresis a portion becomes the source of the product Rabies Immune Globulin, which is used to protect people who have been exposed to rabies virus infection. This product can be prepared only from human plasma. This is why the Rabies Immune Globulin program is so important.

There are some risks involved in this program. The rabies vaccine is prepared using duck eggs and if you are allergic to eggs, poultry, feathers or antibiotics a serious reaction known as anaphylaxis coul occur. Persons allergic to egg protein, poultry or antibiotics will not be accepte for the program. In addition, there are risks in receiving an injection of rabies vaccine under this program. There may be stinging sensation immediately after the injection. A mild to moderate soreness, redness, or swelling at the injection site may occur immediately or within 10 days. There may be a tenderness around the injec tion site for about a day. Occasionally, small nodule may develop temporarily at th site of injection. It is possible to experience symptoms such as headache, aching muscles, malaise, chills and fever. It is possible to develop generalized rash or hives, difficulties in breathing or gastr intestinal problems. Swelling of the lymp nodes may occur and may be noticed as a lump under the arm. Rarely a condition known as anaphylaxis may occur. While extremely uncommon, neurological disorder have been reported following the injectio of almost all immunizing products. Even though this is rare, the possibility of such a disorder exists and must be appreciated.

We ask that you sign the statement bel to indicate that you have read and understand this paper and agree to participate Ask any questions that occur to you about this Rabies Immune Globulin immunization program.

CUTTER LABORATORIES, INC

DONOR CONSENT

I have read and I understand the above information on immunization with rabies vaccine. I give my consent and agree to participate in the Rabies Immune Globulin Program.

To the best of my knowledge I have answered or will answer fully and honestly the questions asked me concerning my health as a donor.

I agree to advise the Medical Director of any reaction during or following rabies immunization. I agree that I will not give blood or plasma donations or receive injections of any kind without advising the Medical Director in charge of this donor center when I next present myself for a donation or an injection. I understand that I am free to withdraw my consent and not receive further Rabies Vaccine at any time.

READ THIS ENTIRE DOCUMENT AND DO NOT SIGN IT UNLESS YOU UNDERSTAND IT.

Signature of Donor Date

Witness Date

81-9749 (4/16/76)

109 6980

CSO W 17

PROCEDURE 3.0.4

Subject: Reserved

PROCEDURE 3.0.5

Subject: Reserved

GRO-C

PROCEDURE 3.0.6

Subject: Immunization Procedures and Experimental Programs of Limited Application

These procedures will be limited to only a few Centers because of their limited application. Procedures will be supplied only to those Centers actually requiring them.

GRO-C

PROCEDURE 3.0.6.1.

Subject: Varicella-Zoster, Cytomegalovirus and Pseudomonas Antibody Plasma

Responsibility

Medical Director

1. Selection of donors
   a. Determine if donor is acceptable plasmapheresis donor(see Procedure 2.2.1, 2.2.2, 4.0.4).
   b. Donors whose plasma has been found to have an acceptable antibody titer.
      (1) Cutter Laboratories identifies to Center those donors that are to be classified as antibody donors, and their specific antibody.
2. Donor Health Status
   a. Must continue to meet requirements for an acceptable plasmapheresis donor (see Procedures 2.2.1, 2.2.2, 4.0.4).

Receptionist or Prep Technician

3. Convert Normal, Tetanus or Pertussis donor to Type H donor.
   a. Change the Plasma Type designation on Form No. 81-9723 (Donor Card) by placing a blue letter "H" in designated position (see Procedure 4.0.1). Immediately below the "H" enter donor's specific antibody type, i.e. "V-Z", "CMV" or "Ps 2" etc.
   b. On donor's next donation plasma will be classified as Type H (blue Control Number labels, Plasma Type H).
   c. On subsequent donations plasma will be classified as Type H plasma until donor is removed from program by notification to Center and Cutter Laboratories.
   d. On removal from Type H program, donor may be reinstated as a donor of Normal or hyperimmune plasma provided all requirements are met.

Centrifuge Technician

4. Labelling
   a. On Source Plasma (Human) label enter name of antibody on line designated "OTHER", i.e. "H-VZ", "H-CMV", "H-Ps2" etc. (There will be several pseudomonas antibody types).
   b. On Plasma Packing and Hepatitis Report forms enter Plasma Type H followed by antibody type, i.e. "H-VZ", "H-CMV", "H-Ps2" etc. Do not enter different antibody types on same form unless they are both pseudomonas antibody types; i.e. Ps2 and Ps3.

GRO-C 1/30/87

GRO-C

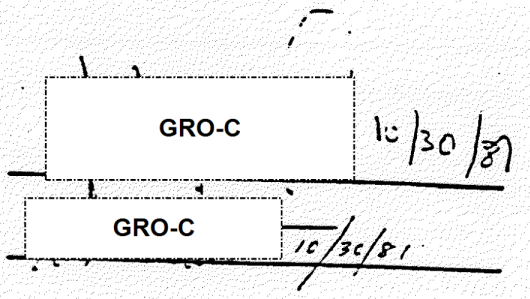
1 1 1 350 W 20

109 6983

Subject: Varicella-Zoster, Cytomegalovirus and Pseudomonas Antibody Plasma

Responsibility

5. Plasma Tubing Samples
   a. Pack RIA back-up sample with corresponding unit of plasma.
   b. Plasma tubing sample must be at least 5 inches long.
6. Shipping
   a. Pack all Type H plasma segregated by the three antibody types. Do not mix antibody types in same carton, except Ps types which can be packed together.
   b. Ship full cartons only. Plasma drawn during different weeks may be shipped in same carton.
   c. Make sure shipping labels on carton of frozen plasma are blue.
   d. Ship Type H plasma with regular shipment and clearly mark both labelled ends of carton in large red letters "TYPE H-VZ PLASMA", "TYPE H-CMV PLASMA", or "TYPE H-Ps2 and TYPE H-Ps3 PLASMA", etc.
7. Special Handling of Paperwork for Varicella Zoster and Cytomegalovirus Antibody Plasma only:
   a. Whenever a Plasma Packing and Hepatitis Report Form is copied prior to mailing samples for RIA testing, make an extra copy and send on a weekly basis to Plasma Procurement, Berkeley.



This procedure supplied to Plasma Centers owned and operated by Cutter Laboratories, Inc. ONLY.

PROCEDURE 3.0.7

Subject: Suggested Action Reports and Titer Labels - Handling of Donors on Hyper Immune Programs.

Responsibility: All Personnel

1. Description of Suggested Action Report.
   a. Gives name of hyperimmune program, Center location and list of Donor Numbers followed by a two digit code.
   b. Mailed to Center weekly.
2. Code definition.
   a. 01 - requests date of donors entry to program.
      11 - requests donor be given a booster, 1st request.
      12 - requests donor be given a booster, 2nd request (reminder).
      13 - requests donor be given a booster, 3rd request (reminder).
      21 - remove donor from program due to low titer.
      22 - remove donor from program because donor inactive.
      23 - remove donor from program, released; special case of code 22.
      24 - remove, other (miscellaneous). May be reinstated on direction from Manager of Plasma Procurement, Cutter Laboratories.
      25 - remove donor from program due to reaction.
      26 - remove donor from program due to excessive injections.
      31 - reinstate donor to program.
3. Description of Titer Labels.
   a. Gives titer value for each donor having a sample tested with date drawn and Control Number.
   b. Mailed to Center weekly.
   c. Apply titer label to a sheet of paper reserved for this purpose in each donor's chart.
4. Action to be taken by Center personnel on receipt of Suggested Action Report.
   a. Obtain donor's chart.
   b. Medical Director reviews donor's chart (ie: physical parameters, injection and donation history, serum protein electrophoresis, hyperimmune titer reports) in light of Suggested Action Report.
   c. Medical Director decides action to be taken and makes appropriate entry on Form No. 81-9723 (Donor Card) in next available space.
   d. When code 24 appears on Suggested Action Report, Medical Director must remove donor from program.
   e. Take indicated action at time of donor's next donation.

CSO W 22

GRO-C

109 6985

PROCEDURE 3.0.8

Subject: Anti-HB_s Plasma

Responsibility	Action
Medical Director	1. Selection of donors. a. Determine if donor is acceptable plasmapheresis donor (see Procedures 2.2.1, 2.2.2, 4.0.4). b. Donors whose plasma has been found to be HB Antibody positive. 2. Donor Health Status. a. Must continue to meet requirements for an acceptable plasmapheresis donor (see Procedures 2.2.1, 2.2.2, 4.0.4). b. Must remain HB Antigen negative.
Receptionist or Prep Technician	3. Convert Normal, Tetanus or Pertussis Donor to Anti-HB_s Donor. a. Prepare a new Form No. 81-9723 (Donor Card) and place a purple letter "A" on upper right hand corner of form. b. On donor's next donation plasma will be classified as Anti-HB_s (Purple Control Number labels, plasma Type A). c. On subsequent donations plasma will be classified as Anti-HB_s plasma until donor is removed from program by notification to the Center from Cutter Laboratories. 4. When donor's antibody titer drops below acceptable level the donor can be converted to Normal, Tetanus, Pertussis or Rabies donor PROVIDED donor has no history of either a positive HB_sAg test or having had viral or serum hepatitis.
Centrifuge Technician	5. Collect plasma tubing samples (see Procedure 2.4.4) at every donation after donor assigned to Anti-HB_s program. 6. Plasma tubing samples must be stored under refrigeration (2 to 8°C or 36 to 46°F) prior to mailing. 7. Plasma tubing samples on Anti-HB_s plasma must be sent to Cutter Laboratories weekly. (see Procedure 2.5.3). 8. Make sure shipping label on carton of frozen plasma is purple. 9. HB_sAg test will be done as usual on this plasma.

GRO-C 2/13/79

GRO-C 2/12/79

3/27/79

1 1 1 GSDW 2 3

109 9981

PROCEDURE 3.0.9

Subject: Institutionalized Donors

Responsibility: All Personnel

1. All rules and regulations of the institution are to be followed. If such rules prevent or hinder operation of Center according to these procedures, notify the Manager of Plasma Procurement, Cutter Laboratories immediately.
2. Procedure 1.0, General Procedure for Plasmapheresis, is written specifically for the operation of a Center not located in an institution. Deviations from this procedure with regard to movement of donors, paperwork, blood and plasma through the Center are encouraged, in Centers associated with an institution, provided the movement chosen is logical, orderly and the specific procedures of the remainder of the process are followed.
R 3. If the taking of donor's photograph for later donor identification as specified in procedure 2.0.1, Assemble and Prepare Donor Chart - New Donor is prohibited, substitute use of identification system employed by the institution with which the Center is associated.
4. The use of finger stain and ultraviolet lamp as specified in Procedures 2.0.1, 2.0.2, and 2.0.4 is unnecessary.
5. In addition to procedure 2.2.1, Medical History and Physical Examination, the Medical Director reviews medical records maintained by the institution on all new donors accepted into program as soon after that acceptance as possible but prior to donor's second donation.

This procedure supplied to correctional institutions only.

GRO-C 12/11/80

GRO-C 12/11/80

CSO W 24

PROCEDURE 3.0.10

Subject: Hemophilia Plasma

The purpose of this procedure is to list specific additional or alternate procedures to be followed in the collection of plasma from hemophilic donors. All Procedures will apply to hemophilic donors unless contraindicated in this Procedure.

Responsibility	Action
Medical Director	1. Selection of Donors - Donors must: a. meet criteria of acceptance for normal plasmapheresis donor <u>except</u> hemophilic plasma donor may have a history of hepatitis <u>if</u> donor has measurable anti-HB_s by RIA; b. be certified by laboratory test conducted not less than 10 days prior to first donation to have less than 1% of appropriate clotting factor activity; c. be certified by laboratory test to be free of inhibitor activity to appropriate deficient factor; d. not have received any blood or blood product infusion within 10 day period preceding donation; e. be HB_sAg "Negative" by RIA test conducted not less than 10 days prior to donation. f. Determine if donor meets these requirements Yes. Enroll donor in hemophilia program (See Procedure 2.2.1) No. Do not enroll donor in hemophilia program. g. Hemophilia plasmapheresis consent form must be signed by the donor and witnessed by the physician after a thorough explanation of hazards involved. The consent form must be accompanied by written permission from the donor's personal attending physicia authorizing participation in the program. Both the consent form and the private physician's written authorization must be updated at least every six months. 2. Donor Health Status a. Medical examination immediately prior to first donation and at 6 month intervals thereafter. b. Separate serum samples to be drawn during initial donation and after 6 consecutive donations (or 4 months from date of prior sample collection whichever occurs first) for laboratory testing of SGPT, SGOT, Inhibitor (Bethesda) units and SMA-12 Panel.

GRO-C 3/21/80

GRO-C

GRO-C 3/21/80

This Procedure is supplied to Plasma Centers owned and operated by Cutter Laboratories, Inc. ONLY.

CSO W 25

109 6988

Subject: Hemophilia Plasma

Responsibility	Action
	c. Must continue to meet requirements for an acceptable plasmapheresis donor. (see Procedures 2.2.1, 2.2.2 and 4.0.4).
Receptionist or Prep Technician	3. Enroll Donors to Hemophilia Program a. Plasma collected from hemophilic donors will be classified as Hemophilia plasma (plasma type K) b. Enter Plasma Type on form No. 81-9723 (Donor Card) by placing a blue letter "K" in designated position (see Procedure 4.0.1). c. Plasma will be designated as type K (blue Control Number labels). d. Outside of Donor Chart to be clearly marked in bold red letters "Hemophilic Donor" and to be filed separately from all other donor charts. All forms contained in the Donor Chart should be boldly marked "Hemophilic Donor". e. On subsequent donations, plasma will be classified as Type K plasma until donor is removed from program by notification to center by Cutter Laboratories, Inc. f. On removal from hemophilia program donor may not be enrolled as a donor of Normal or hyperimmune plasma
All Personnel	4. Plasmapheresis a. Frequency of Donation 1. Once per week. 2. At least six days between donations.
	b. Amount of Donation No more than 1,000ml of blood may be drawn per donation regardless of donor weight.
Medical Director	c. A licensed physician must be present at the center during the entire plasmapheresis procedure.
	d. Clotting Factors Koate® and Konyne® must be available at the center for administration to the hemophilic donor if medically indicated. Every effort should be made to consult with donor's private physician before administration.

GRO-C 3/2/81

GRO-C 3/18/80 D.A. Cutter Labs Director

GRO-C

This Procedure is supplied to Plasma Centers owned and operated by Cutter Laboratories, Inc. ONLY.

Subject: Hemophilia Plasma

Responsibility	Action
Prep Technician, Receptionist or Phlebotomist	5. Label Whole Blood Bags, Transfer Pack and Pooling Bags a. Apply blue Whole Blood Bag labels to Fenwal Double Plasmapheresis Bags 500ml Code 4R 3201. b. Apply blue Control Number labels to two Fenwal Transfer Packs, 300ml, Code 4R 2014. c. Apply blue Control Numbers to two Fenwal pooling bags, 800ml Code No. 4R 2053.
Phlebotomist	6. Set up plasmapheresis equipment per Fenwal Appendix and perform phlebotomy.
Centrifuge Technician	7. Express Plasma from first Bag Whole Blood. a. Aseptically connect blood bag and plasma transfer pack fittings. b. When plasma is fully expressed, seal tubing, taking an 8" tubing sample for RIA testing and a back-up sample, if desired. c. Recentrifuge plasma for same time and at same speed as whole blood is centrifuged.
	8. Express Plasma from Transfer Pack a. Aseptically connect plasma transfer pack and pooling bag fittings. b. Express plasma making sure absolutely no red cells, buffy coat or platelets are expressed into pooling bag. Be conservative, be alert, be careful.
	9. Express Plasma from Second Bag Whole Blood a. Follow procedure for expressing plasma from first bag whole blood, using second Transfer Pack and second Pooling Bag, but do not take sample for RIA testing.
	10. Weigh Plasma and Complete Plasma Packing and Hepatitis Report Form (form 81-9709) a. Weigh both units of pooled plasma. b. Convert to volume by referring to Conversion Chart for Fenwal pooling bags. c. Enter volume on each bag and on Plasma Packing and Hepatitis Report form (form 81-9709). d. Line out "Nonreactive for HB_sAg...." statement on Source Plasma (Human) label.

GRO-C 5/21/80

GRO-C 3/21/80

GRO-C 3/21/80

This Procedure is supplied to Plasma Centers owned and operated by Cutter Laboratories, Inc.

Subject: Hemophilia Plasma

Responsibility	Action
Centrifuge Technician	11. Disposition of Hemophilia Plasma a. Give both units of hemophilia plasma to Cutter Laboratories' coagulationist who will be present at the center.
Phlebotomist	Precaution After the phlebotomy is discontinued, place sterile gauze to site and apply direct pressure for 5 minutes. Then, without disturbing sterile gauze, secure to donor's arm with clear tape.
Medical Director	Donor center physician to observe bandaged phlebotomy site during the next 30 minutes and note results in Donor Chart prior to releasing donor. Donor may be released only if there is no sign of bleeding at the phlebotomy site.
Cutter Laboratories' Coagulation Lab	Will provide plasma center with results of enzyme studies for inclusion in Donor Chart.
Plasma Center Manager or Plasma Center Supervisor Only	Will call Cutter Laboratories' coagulationist (415)420-4000 Ext. 3095 immediately upon receiving notification that a hemophilia donor is RIA reactive. Will also notify coagulationist when said donor's confirmation test results are known.

GRO-C

GRO-C

GRO-C

This Procedure is supplied to Plasma Centers owned and operated by Cutter Laboratories, Inc. ONLY.

PLASMAPHERESIS INFORMATION AND HEMOPHILIAC DONOR'S INFORMED CONSENT

The plasmapheresis procedure is similar to the procedure used in whole blood donation. It involves initially inserting a hollow needle into a vein in your arm and withdrawing a quantity of blood. Your blood will then be specially processed and the plasma portion of it, a yellow or straw-colored liquid, will be separated and retained for Cutter Laboratories. Your red cells will be returned to you through the same hollow needle together with a sterile salt solution which will help to replace the volume of the fluid plasma which has been retained. Blood withdrawal is limited to 500ml (roughly one pint), and the process of withdrawal and cell return is performed twice during each visit to the center.

Because the red cells are returned to you each time you donate your plasma, it is no longer necessary to wait the long period between donations which is required when whole blood is donated. If you participate in the plasmapheresis program, you may donate your plasma as often as once per week.

Should you decide to participate in the plasmapheresis program, you will be performing a significant service in the preparation of some very important products.

There is an element of risk in participating in the plasmapheresis program. First of all, there is the risk that you would incur in a normal blood donation program. Although the majority of people experience no difficulty when donating blood, a few feel faint or weak during or following the blood donation.

Plasmapheresis poses five additional, but unlikely, risks. One is that during the processing of the blood which has been removed from you, contamination of your red cells could occur and they would not be returned to you. The chance of contamination is slight but it might happen. If it did occur, you might not even notice any ill effect. On the other hand, you might feel weak due to the blood loss.

The second risk, which is also remote, is that of having red cells which are not yours returned to you. If this happens and if the red cells are incompatible with your blood type, it is possible that you would suffer a reaction. Since the reaction can be serious in some instances, it is essential that you cooperate fully with the technicians and nurses in determining that only your own red cells are returned to you. Pay close attention to the attendant when you are asked questions. Recite clearly and accurately your number and name when you are requested to do so. Be sure to inspect the label on the blood bag which is to be returned to you to be sure it is your name and number that is on it. YOUR participation in this identifying procedure is a vital link in assuring that only YOUR blood cells are returned to YOU.

The third risk, which is unlikely if you eat properly, is that the overall protein content of your plasma, one of the specific proteins in your plasma, or the percentage of red cells in your blood might decrease. If this happens, you will not be permitted to donate again until normal levels have been reestablished. This is for your protection.

The fourth risk is a small one of thrombosis which is associated with any venipuncture. This is a clot which can form in an arm vein, and can cause inflammation and soreness. Usually this is treated with elevation and warm compresses.

The fifth risk is the increased risk of bleeding. This is not a major consideration if the proper technique for hemostasis is observed after the donation. The staff will insist on firm pressure for at least five minutes on the point of needle entry after the needle is removed. Later bleeding from this site must be immediately reported to the plasmapheresis staff or your private physician.

Please read the informed consent form below. Ask any questions that occur to you about the procedure of plasmapheresis. If you understand the nature of the plasmapheresis program and the informed consent, sign this form in the presence of the Medical Director.

DONOR'S INFORMED CONSENT

I have read, and the physician has explained, the above information on plasmapheresis. I give my consent and agree to participate in the plasmapheresis program.

To the best of my knowledge I have answered or will answer fully and honestly the questions asked me concerning my health as a donor.

I agree that I will not give blood or plasma donations or receive injections of any kind without advising the Medical Director in charge of this donor center when I next present myself for a donation or an injection. Furthermore, I agree to advise the Medical Director of any reaction during or following plasmapheresis. I understand that I am free to withdraw my consent to participate in the Plasmapheresis Program described above at any time. READ THIS ENTIRE DOCUMENT AND DO NOT SIGN IT UNLESS YOU UNDERSTAND IT.

Signature of Donor _____ Date _____

Medical Director _____ Date _____

GRO-C

GRO-C

GRO-C

3/24/80

8CE

P 1 1 CS0 W29

DONOR NAME	DONOR No.	PLASMA TYPE	
ADDRESS		CODE	CARD N
IDENTIFICATION		AGE	HT.

DATE	CONTROL No.	WT. lbs	B.P.	Pulse	Temp °F	Initials	Hct. %RBC	T.P. Gms%	Initials	COMMENTS

10/16/78

CS0 W 30

PROCEDURE 4.0.1

Subject: Form No. 81-9723, Donor Card, Instructions for Completing

Responsibility	Action

See facing page for Form No. 81-9723

Receptionist

1. Donor Name:
   Males - last, first, middle.
   Females - if single - last, first, middle.
   Females - if married - last, first, maiden last name.
   When a donor undergoes a name change, eg: due to a change in marital status, note change on all forms retained in donor chart.
2. Address: Permanent street address and town.
3. Identification: Number for identification purposes. Note source of number as well, eg: Driver's License (also note state), I.D. cards (military, student, State, Welfare), Social Security, etc.
4. Donor Number: Consists of a one or two letter alphabetic Center Code assigned by Cutter Laboratories and a five digit number. Use zeros in front of lower numbers to fill all spaces (eg: AT 00057). Must correspond to permanent Donor Number assigned to donor and recorded in Donor Log book. (See Procedure 2.0.1).
5. Plasma Type: N for normal (with black Control Number label), T for Tetanus (with red Control Number label), etc. Use space to left first. Use other spaces as Plasma Type changes.
6. Card No.: First Donor Card used will be 1, second Donor Card on same donor will be 2, etc.
7. Age: Consider both month and year. Example: If a donor was born on 11-14-25 and is applying to be a donor on 3-8-73 the age is 47 and NOT 48. This is particularly important on donors who are near minimum or maximum ages. Inattention in this area could result in taking a donor who is not yet of legal age or in terminating a donor before maximum age is reached.
8. Height: Feet and inches.
9. Date: Place date donor comes to Center in next available space. Date must be entered even if donor does not complete donation. In this event make appropriate comment in Comments space.

GRO-C PLD 11/30/17

GRO-C

12/27/77

88

P 1 : 1 1 [illegible] 0 W 3 1

109 6994

Subject: Form No. 81-9723, Donor Card, Instructions for Completing

Responsibility	Action
Receptionist or Prep Technician	10. Control No.: Place Control Number label in space provided adjacent to date.
	11. Weight: In pounds, from actually weighing donor without overcoats, jackets, galoshes, etc. Center personnel must read scale. Minimum 110 pounds. Record in space provided. Refer to Medical Director for evaluation in cases of recent marked weight loss, i.e.: greater than 10 pounds.
Prep Technician	12. Blood Pressure: Systolic 100-150, Diastolic 50-100. Donation can be given with blood pressure outside these limits if approved by Medical Director.
	13. Pulse: Determine for at least 30 seconds. Acceptable limits: 50-100. Medical Director must approve for donation if over 100 or under 50.
	14. Temperature: Lower limit is 97.6°F. Upper limit is 99.6°F. Record in space provided.
	15. Initials: Initials of person determining blood pressure, pulse and temperature.
	16. Hct: Hematocrit, minimum 38%. Record in space provided.
	17. T.P.: Total Protein, done on capillary blood only. Minimum 6.0 gm.%. Record in space provided.
	18. Initials: Initials of person determining hematocrit and total protein.
	19. Comments: Comments used for various purposes (see procedures 1.0, 2.0.1, 2.0.2, 2.0.3, 2.0.4, 2.3.8, 2.3.11, 2.3.12, 2.3.14, 2.4.4, 3.0.1, 3.0.2, 3.0.3, 3.0.7).
	a. Record DTH reactions: Donor transient hypotensi is to be graded by Medical Director according t degree of reaction.
	1+ Slight or mild degree of signs and symptoms of DTH (e.g.: pallor, restlessness, cold ski nausea, sweating, dizziness, slow pulse); systolic blood pressure tends to be in 90-10 range.
	2+ More marked degree of signs and symptoms as above; systolic blood pressure tends to be less than 90-100 range.
	3+ Actual unconsciousness (fainting or grand ma seizure).
	4+ Hospital observation carried out.
	5+ Hypotensive sequelae (coronary, CVA, etc.).
	b. Note failure to donate (and give reason), loss of red blood cells, incomplete donation, tempo-rary rejection due to bright finger staining indicating which finger was brightly stained. If appropriate, note also when donor may again be accepted for donation.
	20. Code: Either Non-O or X

GRO-C 10/5

GRO-C 10/2/78

CS0W32

PROCEDURE 4.0.2

Subject: Form No. 81-9711, PreDonation History, Instructions for Completing

Responsibility: Receptionist or Prep Technician and Medical Director

See facing page for Form No. 81-9711.

1. Complete Donor Name and Donor No. as on Donor Card (see procedure 4.0.1) on first donation.
2. Write date (month, day, year) donor is next due for a physical examination by Medical Director in space labeled MD Exam Due.
3. On day of each donation, except those on which donor has physical examination by Medical Director, write date in space provided and ask donor following questions, giving donor adequate time for response before marking each space yes (+) or no (0). A yes (+) answer to any medical history question may prevent donor from donating. Refer questionable donors to Medical Director for final determination.

   a. Identification: Can donor be positively identified as person described from information in chart? Involves visual recognition from photograph and comparison of donor's signature on photograph.
   b. Respiratory Disease: Does donor have presently an acute disease, eg: cold, sore throat, flu, influenza, bronchitis, tonsilitis, asthma, hayfever, tuberculosis? Donor must not be accepted until one week after complete recovery from upper respiratory problems and ten years following tuberculosis.
   c. Infectious Skin Disease: Does donor have any evidence of skin disease, eg: redness, swelling, flaking, scaling, eruptions, on arms, particularly in ante cubital fossa? Does donor have boils, furuncles, carbuncles, psoriasis, erysipelas any where on body?
   d. Disease Carried by Blood: Donors who have had brucellosis or undulant fever are not acceptable until two years after recovery. Donors who have had dental surgery or tooth extractions are not acceptable for 72 hours following procedure.
   e. Recent Illness: Has donor been hospitalized, had any treatment for illness, visited a doctor, had any inoculations or vaccinations or taken any medicine since last donation? May require evaluation by Medical Director.
   f. History of Viral Hepatitis: Has donor ever had hepatitis or jaundice? Has donor ever been told he was HBAg (Australia antigen, HAA) positive? If yes, permanent reject.
   g. Hepatitis Contact: Has donor had contact with any person who had hepatitis in last six months? Contact means cohabitation or using same eating and sanitary facilities. Has donor been tattooed or had ears pierced since last donation? If affirmative, donor is rejected until six months without evidence of hepatitis, has elapsed.

GRO-C

7/15/74

109 6996

CSC W3 3

Subject: Form No. 81-9711, PreDonation History, Instructions for Completing

Responsibility: Receptionist or Prep Technician and Medical Director

h. Blood-Plasma Received: Has donor received a blood transfusion [whole blood, packed red cells, platelet concentrate, fresh, frozen or single donor plasma cryoprecipitates, fibrinogen, blood coagulation factors (AHF, Factor IX)], since last donation? If so, donation must be deferred for six months without any signs or symptoms of hepatitis. Donation need not be deferred following administration of albumin, plasma protein fraction or immune serum globulin provided receipt of these items does not point to some underlying disease or recent contact with hepatitis.

i. Arms Skin Puncture Scars: Has donor given blood or plasma within past 48 hours? Examination of both exposed arms and hands must show absence of unexplained needle marks or scars possibly suggesting use of drugs. If donor has given whole blood or lost a unit of red cells during a plasmapheresis procedure, donor will not be permitted to participate in plasmapheresis for a period eight weeks from date of blood loss, unless donor is examined by medical director and certified by medical director, on Form No. 81-9723 (Donor Card) to be acceptable for further plasmapheresis prior to expiration of eight-week period. Examination must not be limited to return of hematocrit and total protein to acceptable levels.

j. Drug or Alcohol Influence: Donor must not be under influence of drugs or alcohol on day of donation. Refer to Medical Director for final determination if questionable.

k. Interviewer Initials: Initials of person conducting interview.

4. Comments Donor Acceptability:

a. Use for lack of donor acceptability for any reason not covered in the above questions.

b. On female donors only, use space for answering questions: 1) Are you menstruating today? 2) When did you stop your last menstrual period? 3) To the best of your knowledge, are you pregnant? Need not be done if donor is past-menopausal or if hysterectomy has been performed. Documentation of either of these situations must be clear on Form No. 81-9731 (Medical History and Physical Examination).

c. Medical Director uses for recording results of Review of Medical Chart (see procedure 2.2.2).

(1) During initial physical examination and each Review of Medical Chart, Medical Director writes date (Month and year) of next Review in spaces provided.

d. If donor is not acceptable, clearly document reason for lack of acceptability, whether permanent or temporary and, if temporary, date on which donor may again be considered.

GRO-C

109 6997

CSO W 34

PROCEDURE 4.0.3

Reserved

GRO-C

7/15/74

93-96

CSC W 35

PROCEDURE 4.0.4

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form

Responsibility: Medical Director

See facing page for Form No. 81-9731.

1. General.
   a. Donor name, Donor Number, sex, race and birthdate are completed by receptionist. All other entries are made by (or under the direct supervision of) Medical Director.
   b. Specific explanations given below are to be considered as guidelines. In many cases your own medical judgement must prevail.
   c. Note that many items are asked more than once allowing different approaches to be used in eliciting information. The form has been specifically designed to contain this feature at the request of several Medical Directors.
2. Donor Identification.
   a. Name: last name first, comma, first name and middle initial.
   b. Donor Number: consists of 7 figures, a one or two place alphabetic Center code and a 5 digit number. Use zeros in front of the lower numbers to fill the five spaces (e.g.: AT 00057).
   c. Ideally, donor name and number should be applied with imprinting card. If not possible, use clean, neat printing with block letters.
   d. Sex: circle M or F as appropriate.
   e. Race: circle appropriate symbol C - Caucasian, N - Negro, I - Indian, O - Oriental, L - Latin.
   f. Birthdate: month, day, year.
3. DONOR HISTORY - This section provides opportunity to elicit general information from donor which may be more fully covered later in examination.

   Date - write month, day, year in the appropriate column space.
   Each column is to be used for one examination only.
   a. Occupation - write in occupation. This may give clues to specific areas to be covered in greater detail, e.g.: coal miners - black lung disease; farmers - diseases associated with animals; chemical plant worker - liver damage from industrial solvents, etc. This is also an opportunity to warn those in hazardous occupations (e.g.: operators of power machinery, cranes, drivers of buses, trains, cabs, workers on ladders or scaffolding, airplane crews, etc.) not to engage in their occupation for 12 hours after donation and longer if a unit of red blood cells is not returned to them.
   b. Military Service - give dates, was person overseas and ever receive any medical treatment?
   c. Illnesses and Injuries (Past and Recent) - Is donor currently under a doctor's care? Some specific items are: no donation for 72 hours after dental surgery, two weeks if dental surgery involved infection;

GRO-C

9/5/75

109 6999

P 1 - 1 1 - CS0 W 36

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form

Responsibility: Medical Director

no donation for 2 years following recovery from brucellosis (undulant fever), relapsing fever; no donation for 1 year following recovery from infectious mononucleosis; no donation until complete recovery from flu, cold, sore throat, sinusitis or other upper respiratory infections for 1 week.

d. Hospitalization - No donation until at least 6 months after major surgery (may have been given transfusions with risk of hepatitis) or until wound from minor surgery has completely healed. Hospitalization for diagnostic procedures or minor treatment usually will not delay donation but may suggest other areas for investigation.

e. Medication, Drugs, Alcohol - Medication such as insulin, digitalis, quinidine, nitroglycerin, antihypertensives, anticoagulants, dilantin, thorazine or heavy doses of tranquilizers suggest a donor not be accepted or retained on the program. Recent narcotic addiction, usage of hallucinogens will prevent donor from being accepted. If donor has been six months without drug use and no evidence of hepatitis during that time, donor is acceptable. Recent participation in drug testing programs may suggest a donor not be bled for some period of time. Donation should be deferred until 30 days after cessation of antibiotic therapy. Alcohol habituation may suggest donor not be accepted. Use of drugs such as oral contraceptives, hormones, vitamins, occasional analgesics or low doses of tranquilizers usually will not prevent acceptance into the program. In short, any use of a drug by a potential donor at the time of being examined is reason of non acceptance of donor for plasmapheresis for that visit.

f. Transfusions or Blood Fractions - Following transfusion of whole blood, packed red cells, platelet concentrates, fresh, frozen or single donor plasma, cryoprecipitates, fibrinogen, blood coagulation factors (AHF, Factor IX), donation must be deferred for 6 months without any signs or symptoms of hepatitis. Donation need not be deferred following administration of albumin, plasma protein fraction or immune serum globulin provided use of these items does not point to some underlying chronic disease or recent contact with hepatitis.

g. Hepatitis (Disease or Contact) - Any history of hepatitis will prevent donor from entering program. Clinical Jaundice from an unproven cause is to be considered as indicative of a positive history of hepatitis. Contact with person who has hepatitis will cause donation to be deferred for 6 months without symptoms of hepatitis. Contact means cohabitation, routine use of the same eating and sanitary facilities.

109 7000

GRO-C 09-28

GRO-C 10/2/28

FILE — CSO-W 37

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form

Responsibility: Medical Director

h. Malaria - Donor must be symptom free and not under current drug therapy for the disease. Donor may be accepted with a past history of malaria (at least 6 months must have elapsed since last drug therapy has been taken) or malaria suppressive therapy or travel in an endemic malaria area.

i. Convulsions, Coma, Fainting, Epilepsy - All may be causes for non-entrance into program if occurring past infancy. Convulsions in infancy are no barrier to donation.

j. Immunizations - Any donor with a history of immunization with red blood cells or blood group specific substances will not be accepted on the program. Donations are to be deferred until 2 weeks following smallpox or yellow fever immunizations, 24 hours or until any local reaction subsides following immunizations with Salk polio, plague, flu, typhoid, measles, typhus, Rocky Mountain Spotted Fever, cholera, diphtheria or administration of therapeutic animal serums (e.g.: horse tetanus antitoxin).

k. Tattoos and ears pierced - Donation deferred until 6 months after tattooing and ear piercing with no symptoms of hepatitis.

l. Blood, Plasma donor (difficulties) - Any adverse reaction (e.g.: DTH or other) may be reason for non-acceptance into the program.

Comments, Pertinent Family History - This space is provided for explanation of any of above items and for comments on such items as recent direct contact with family member who has a communicable disease, any family history of inheritable disease such as bleeding tendencies (hemophilia), etc.

4. REVIEW OF SYSTEMS - This section is a continuation of donor history and provides an opportunity to explore further any areas uncovered in the more general review above. It also provides for an orderly review of donor's past health status.

a. Allergies - Chronic asthma under current drug therapy is a cause for rejection. Seasonal hayfever, food allergies, drug sensitivities are acceptable if not active at present time and donor is not currently taking antihistamines plus if recovery has been of at least 1 week's duration.

b. Skin - Unexplained jaundice provides another clue to hepatitis. Chronic eczema, chronic dermatitis, recurring boils may be cause for rejection.

c. EENT - Dental surgery, chronic tonsillitis or other underlying infections may be cause for deferring donation for a short period. Difficulty with eyes or ears may signify partial sight or hearing.

d. Cardiovascular - Rheumatic fever in last year, heart disease, chest pain, shortness of breath, hypertension, hypotension, chronic phlebitis, palpitation, irregular pulse, shifting of apex beat,

GRO-C

CSO W 38

109 7001

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form

Responsibility: Medical Director

syncope, may be causes for rejection. Past short episodes of rheumatic fever, pericarditis, heart murmur or thrill, repair of congenital heart defect usually are not causes for rejection.

e. Pulmonary - Active tuberculosis within past 10 years, shortness of breath especially on exertion may be reasons for rejection. Recovery from any upper respiratory disease should be of at least one week's duration prior to donation.

f. Gastrointestinal: Jaundice, liver trouble, cirrhosis, ulcers, ulcerative colitis, especially accompanied by recent episodes of gastrointestinal bleeding or black stool, may be cause for rejection.

g. Genitourinary - Chronic Kidney diseases, red blood cells, pus cells or protein in urine may be cause for rejection.

(1) Menstrual cycle - should be regular and uncomplicated, frequent excessive bleeding may be cause for rejection.

(2) Last menstrual period - month, day, year. Abnormal or excessive bleeds may be reason for rejection. Provides beginning point for question of pregnancy.

(3) Pregnancy GPAM - G - gravida, P - para, A - abortion, M - miscarriage. Insert numbers where appropriate. Prospective donor must not be pregnant now and must be 6 months after pregnancy no matter how terminated.

h. Neuromuscular - Seizures, fainting, epilepsy, collagen diseases, myasthenia gravis, arthritis if associated with anemia may be cause for rejection.

i. Skeletal - Recent fractures particularly with open reduction and/or complications, osteomyelitis may be cause for rejection.

j. Blood diseases - Bleeding tendencies, slow clotting, easy bruising, frequent nose bleeds, chronic anemia, polycythemia, leukemia are cause for rejection.

Comments: This space is provided for explanation of or further comment on any of above items.

5. LABORATORY - Results of these tests are available on Donation Record which should accompany donor to examination area.

a. Hematocrit (%) - minimum 38%.

b. Total Protein (gm%) - Minimum 6.0 gm%.

c. Urine - Negative for protein and sugar.
(Note: traces of sugar and protein such as from dietary or hydration variability are acceptable).

d. Other - Results of any other tests done should be entered here.

Comments: This space is provided for explanation of or further comment on any of above items.

GRO-C 3-20-79

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form.

Responsibility: Medical Director

6. PHYSICAL EXAMINATION - This section is provided for results of actual observation of donor.
Date - Write month, day, year in appropriate column space.
Each column is to be used for one examination only.
   a. Vital signs - Results of these observations are available on Donation Record which should accompany donor to examination area. Medical Director should determine blood pressure. However, if Medical Director repeats the other observations it will provide an excellent opportunity to maintain a continuous check on capabilities of Prep Technicians by comparing Medical Director's findings to those on Donation Record.
      (1) Temperature - Minimum 97.6°F., maximum 99.6°F.
      (2) Pulse - Must be regular, Minimum 50, Maximum 100.
      (3) Respiration - Must be regular, not labored.
      (4) Blood Pressure - Systolic 100-150, Diastolic 50-100. Donation can be given with systolic blood pressure up to 200 if approved by Medical Director.
      (5) Weight - Minimum 110 lbs. No maximum has been established. Donors of excessive weight should be carefully evaluated for other medical problems and for difficulties in performing venipuncture. Medical Director should also evaluate recent marked weight loss. If unexplained (e.g.: dieting), may be indicative of some inapparent disease state.
      (6) Height - If recorded here does provide a way to examine the height to weight ratio.
   b. General Appearance and Nutrition - In addition to the usual meaning of this section, Medical Director should be aware of mental or emotional difficulties presented by donor. Does donor present adequate mental capabilities to understand and to participate in identification of red blood cells? Does donor have sufficient emotional stability to not present a problem in the donor room?
   c. Skin - Note: Jaundice, chronic eczema, chronic dermatitis, boils. Look for unexplained needle marks on both arms or other areas where narcotic administration might be practiced.
   d. Head and Neck - Scars indicative of severe head injury.
      (1) Eyes - Jaundice; narcotic influence; does donor have sufficient vision to participate in identification of red blood cells? If not, Donor Card (form 81-9723) must be conspicuously marked that assistance must be provided. Similar notation should be made in "Comment" section of form 81-9731. Should donor be required to wear glasses (contact lenses) while participating in identification of red blood cells?
      (2) ENT - Note: current infections. Does donor have sufficient hearing to be able to participate in identification of red blood cells?
      (3) Teeth - Infections or abscesses; does donor have sufficient teeth to be able to obtain a normal bite?

GRO-C 2/9/79

GRO-C 2-6-79

2/20/79

103

CSO W 40

109 100

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form.

Responsibility: Medical Director

e. Cardiovascular System - Note: irregular pulse, engorged neck veins, presence, absence or diminution peripheral arterial pulse: deformities of chest, visible cardiac impulses, apex beat and thrill: precordial bulging, ausculation of heart sounds; rhythm, force and quality of sounds: any friction rub or gallop; heart murmur, rate, location, position in cycle, intensity, pitch, effect of change of position and transmission.

f. Pulmonary System - Note: Any deformities of chest, type of breathing, dyspnea, prolongation of expiration, unequal or diminished movement of either or both sides of chest; cough, stridors or wheezes: vocal fremitus, any dullness to percussion: ausculation of breath sounds, rhonchi, rales, crepitation, friction rub, wheezing or diminished air entry.

g. Abdomen - Note: size and contour, visible peristalsis, respiratory movement, distended veins, tenderness and rigidity, shifting dullness, tympany, rebound tenderness and fluid waves; palpable organs (should be performed with donor lying down), liver, spleen, kidneys or masses, abdominal bruit, bowel sounds.

h. Genitourinary - Exclude chronic kidney disease or kidney enlargement detected by abdominal palpation. Female donors: Examine for engorged or lactating breast, change of color of areola, uterus enlargement etc., which may point to pregnancy or recent period of post-partum.

i. Neuromuscular - Note: Cerebral function, general behavior, level of consciousness, emotional status, orientation, ability to understand and follow instructions: cranial nerve function; motor system function, reflexes. Some test for neuromuscular function other than eye responses to light must be performed.

j. Skeletal - Note: casts, scars due to open reduction of fractures.

Comments: This space is provided for explanation of or further comment on any of above items.

7. ACCEPTANCE.

a. Plasmapheresis Donor - Write yes or no. DO NOT use checks, pluses, dashes, minuses or other symbols. Symbol O.K. is acceptable.

b. Reason if rejected - If the answer is no, a short simple statement of the reason should be given here.

c. For Hyperimmunization - List the types of toxoids or vaccines which the donor is eligible to receive. This can be done most easily by giving the plasma type, e.g.: T. P. etc.

d. Rejected for Hyperimmunization - List the types of toxoids or vaccines which the donor is NOT eligible to receive. This can be done most easily by giving the plasma type, e.g.: T, P, etc.

GRO-C

9/5/75

109 7004

GSC W

Subject: Form No. 81-9731, Medical History and Physical Examination, Explanation of Form.

Responsibility: Medical Director

Comments: This space is provided for explanation of or further comment on any of above items.

M.D. This space is provided for the signature of the physician performing the Medical History and Physical Examination. No rubber stamps are permissible.

GRO-C

CENTER CODE	WEEK NUMBER	DATE	CENTER NAME AND ADDRESS	FOR CUTTER USE ONLY
				Number of samples received _____
PAGE ____ OF ____ PAGES				Received by/date _____
				Membrane number(s) _____

SERUM SAMPLE PACKING LIST

DONOR NUMBER	CONTROL NUMBER	TOTAL PROTEIN gm %	MEMBRANE POSITION	CODED

DONOR NUMBER	CONTROL NUMBER	TOTAL PROTEIN gm %	MEMBRANE POSITION	CODED

81-0751 Rev 1/78

2/13/78

CS0 W43

109 7006

The plasmapheresis procedure is similar to the procedure used in whole blood donation. It involves initially inserting a hollow needle into a vein in your arm and withdrawing a quantity of blood. Your blood will then be specially processed and the plasma portion of it, a yellow or straw-colored liquid, will be separated and retained for use in the manufacture of medically valuable products. Your red cells will be returned to you through the same hollow needle together with a sterile salt solution which will replace the volume of the fluid plasma which has been retained. Blood withdrawal is limited to 600ml. and the process of withdrawal and cell return is performed twice during each visit to the center.

Because the red cells are returned to you each time you donate your plasma, it is no longer necessary to wait the long period between donations which is required when whole blood is donated. If you participate in the plasmapheresis program, you may donate your plasma as often as twice a week but you must wait at least 48 hours between donations.

Should you decide to participate in the plasmapheresis program, you will be performing a significant service in the preparation of some very important drugs. Some of the drugs which will be manufactured from the plasma you donate are truly lifesaving products used in emergency situations. Others go into products which help prevent such diseases as tetanus, measles, whooping cough, rabies and hepatitis.

There is an element of risk in participating in the Plasmapheresis Program. First of all, there is the risk that you would incur in a normal blood donation program. Although the majority of people experience no difficulty when donating, a few feel faint or weak during or following the donation.

Plasmapheresis poses some additional but unlikely risks. One is that during the processing of the blood which has been removed from you, contamination of your red cells could occur and they would not be returned to you. If this occurs, you may not donate again for at least 8 weeks. The chance of contamination is slight but it might happen. If it did occur, you might not even notice any ill effect. On the other hand, you might feel weak due to the blood loss.

A second risk, which is also remote, is that of having red cells which are not yours returned to you. If this happens and if the red cells are incompatible with your blood type, it is possible that you would suffer a reaction. Since the reaction can be serious in some instances, it is essential that you cooperate fully with the technicians and nurses in determining that only your own red cells are returned to you. Pay close attention to the attendant when you are asked questions. Recite clearly and accurately your number and name when you are requested to do so. Be sure to inspect the label on the blood bag which is to be returned to you to be sure it is your name and number that is on it. YOUR participation in this identifying procedure is a vital link in making sure that only YOUR blood cells are returned to YOU.

A third risk, which is unlikely if you eat properly, is that the overall protein content of your plasma, one of the specific proteins in your plasma, or the percentage of red cells in your blood might decrease. If this happens, you will not be permitted to donate again until normal levels have been reestablished. This is for your protection.

A fourth risk, also a small one, is of thrombophlebitis, which is associated with any venipuncture. This is caused by a clot which can form in an arm vein and result in inflammation and soreness. Usually this is treated with elevation and warm compresses.

Another risk, usually caused by movement of the arm during plasmapheresis, is hematoma (bruising) caused by infiltration. If the needle comes out of the vein, but remains in the arm, saline or red cells will flow into the surrounding tissue instead of the vein, causing discoloration, swelling and soreness that could last for a few days.

Please read the informed consent form below. Ask any questions that occur to you about the procedure of plasmapheresis. If you understand the nature of the plasmapheresis program, the informed consent and wish to participate, sign the paper at the bottom line in the presence of the Medical Director.

DONOR'S INFORMED CONSENT

I have read, and the physician has explained, the above information on plasmapheresis. I give my consent and agree to participate in the plasmapheresis program.

To the best of my knowledge I have answered and/or will answer fully and honestly the questions asked me concerning my health as a donor.

I agree that I will not give blood or plasma donations or receive injections of any kind without advising the Medical Director in charge of this donor center when I next present myself for a donation or an injection. Furthermore, I agree to advise the Medical Director of any reaction during or following plasmapheresis. I understand that I am free to withdraw my consent to participate in the Plasmapheresis Program described above at any time. READ THIS ENTIRE DOCUMENT AND DO NOT SIGN IT UNLESS YOU UNDERSTAND IT AND WISH TO DONATE.

Signature of Donor _____ Date _____

Medical Director _____ Date _____

GRO-C

GRO-C

GRO-C 7/2/79

81-9744 (9/79)

050 W 44

9/24/79

PROCEDURE 4.0.6

Subject: Form No. 81-9751, Serum Sample Packing List, Instructions for Completing

Responsibility: Prep Technician, Receptionist and Centrifuge Technician.

See facing page for Form No. 81-9751.

1. Write Center name and address in space provided. Rubber stamp satisfactory if imprint clear and readable.
2. Complete Center Code. This is a one or two letter code assigned your Center for identification purposes by Cutter Laboratories.
3. Write date on which samples collected in space provided using month, day, year, eg. 5/1/78. In the event date of sample collection changes before form is filled, insert new date above Control Number of first sample collected on new date.
4. Write Donor Number in space provided. Write LEGIBLY and NEATLY in ink.
5. Affix Control Number label in space provided.
   a. Make sure Control Number affixed corresponds to Control Number assigned to Donor Number listed.
6. Write total protein value in space provided, (see Procedure 2.4.6). Write LEGIBLY and NEATLY in ink.
7. Make sure Control Number labels affixed correspond exactly to Control Number labels on vials shipped.
8. Use donor's name in place of Control Number to label serum sample vial and on Serum Sample Packing List when a serum sample is taken but there is no donation.

GRO-C

GRO-C 10/2/78

CSOW 45

Date ____________

Type ____________

Page ______ of ____

Date Test ____________

Set up by ____________

Read by ____________

Checked by ____________

To Computer on ____________

Donor Number	Bottle Number	
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
		0 1 2 3 4 5 6 7 8 9
11/19/73	108	0 1 2 3 4 5 6 7 8 9

8-5150

CS W

PROCEDURE 4.0.7

Subject: Form No. 81-9190, Plasma Sample Packing List, Instructions for Completing

Responsibility: Prep Technician or Receptionist, Centrifuge Technician

See Form No. 81-9190 facing page.

1. Write Center name and address under form title. Rubber stamp satisfactory if imprint clear and readable.
2. Complete Center Code. This is a one or two letter code assigned your Center for identification purposes by Cutter Laboratories.
3. Complete date by inserting month, day and year, eg: 1/1/73.
4. Complete type information. This is a Plasma Type designation, eg: T for tetanus, P for Pertussis, etc. Only one Plasma Type per page, please.
5. Write Donor Number in space provided. Write LEGIBLY and NEATLY in ink.
6. Affix Control Number in space labeled Bottle Number.
   a. Make sure Control Number affixed corresponds to Control Number assigned to Donor Number listed.
   b. Control Number labels should be in sequence.
7. Make sure Control Number labels affixed correspond exactly to Control Number labels on plasma tubing samples shipped.
8. If necessary to mark out an entry, do so with a single horizontal line through both Donor Number and Control Number with a black ink pen. Make sure corresponding sample is removed from shipment.
9. Write Week Number below Center Code for Plasma Types B, H, P.

GRO-C

WEEK NUMBER

CENTER CODE

CENTER NAME AND ADDRESS

Cutter Laboratories, Inc.
PLASMA PACKING AND HEPATITIS REPORT FORM

Plasma Type _____ Donor Code _____

CUTTER USE ONLY

CONTAINERS _____ RR No _____

LITERS _____ DATE REC'D _____

CARTONS _____ TYPE _____

Case No _____ Bleeding Date _____

CONTROL NUMBER	Donor Number	Volume	Initials	Test No	HBs Ag RESULT
10/26/81					
110					

Total Volume _____ Total No Bags/Case _____

Case No. _____ Testing Laboratory Control Number _____

TESTED BY SCRIPPS-MILES, INC. DATE _____ R.T. # _____

THESE RESULTS FOR MANUFACTURING PURPOSES ONLY!

CONTROL NUMBER	Donor Number	Volume	Initials	Test No	HBs Ag RESULT

Total Volume _____ Total No Bags/Case _____

Subject: Form No. 81-9709, Plasma Packing and Hepatitis Report Form, Instructions for Completing.

Responsibility: Centrifuge Technician and Center Manager

See Facing page for Form No. 81-9709

1. Write Week Number in space provided clearly and legibly.
   a. Defines a working week. Week Numbers assigned to weeks of year by Manager of Plasma Procurement, Cutter Laboratories.
   b. Do not ship split Week Numbers.
2. Write Center Code in space provided clearly and legibly using block letters. This is a one or two letter code assigned your center for identification purposes by Cutter Laboratories. Rubber stamp satisfactory.
3. Write Center name and address in space provided. Rubber stamp satisfactory if imprint clear and readable.
4. Write plasma type, eg: N for normal, T for tetanus, etc., in space provided. Only one type of plasma per page.
5. For Normal and Tetanus plasma only: write Donor Code in space provided. Only one Donor Code category per page.
6. Write case number in space provided. Each new Week Number should begin with Case No. 1 for each Plasma Type and each Donor Code. There is a space for two cases on the form. (Cases that contained 12 x 500 ml Sodium Chloride for Injection USP will hold 12 units of plasma.)
7. Write date on which plasma collected in space provided, using month, day, and year. In the event date of plasma collection changes before form is filled, insert new date above first Control Number collected on new date.
8. In space provided under case number, affix a Control Number label for each bag of plasma placed in that case.
   a. If Control Numbers are not used in your Center, clearly and legibly write the bleeding number for each bag of plasma placed in that case.
9. In space provided, write legibly and clearly the Donor Number corresponding to the affixed Control Number.
10. In the space provided, write legibly and clearly volume of plasma in that plasma pooling bag milliliters. No fractions or decimal points, please. Round off to nearest milliliter.
11. Person entering volume of plasma should write initials in space provided.

GRO-C 10/12/81

GRO-C 10/13/81

109 7012

Subject: Form No. 81-9709, Plasma Packing and Hepatitis Report Form, Instructions for Completing.

Responsibility: Centrifuge Technician and Center Manager

12. After Form No. 81-9709 is this far completed, use form for submitting plasma samples for HB_sAg testing (see Procedure 2.5.1).
    a. Any form not completely filled in, ie containing <24 Control Numbers, should be retained in the center, together with the HB_sAg test plasma samples listed thereon, until the form can be completely filled in on the next working day of the same Week Number.
    b. At the end of the working week submit all forms, completely filled in or otherwise, and the corresponding plasma samples. Do not submit partial forms to the testing laboratory at any other time than on the last day of the working week.
13. After checking Form No. 81-9709 received from HB_sAg testing laboratory (see Procedure 2.5.1.1) proceed to mark out any plasma not to be shipped for any reasons, eg: broken bag, etc., by drawing a line through all entries for that bag, initial and date line. State reason for marking out.
14. Add up total volume in milliliters of plasma in each case and write figure in space marked Total Volume.
15. Write number of bags of plasma in the case in the space marked Total No. Bags/Case.
16. Prepare a legible photocopy for back-up to be kept on file together with the trucker's Bill of Lading for that shipment.
17. Send original of form to Cutter Laboratories (see Procedures 2.4.8 and 2.4.9.)

GRO-C 7/18/79

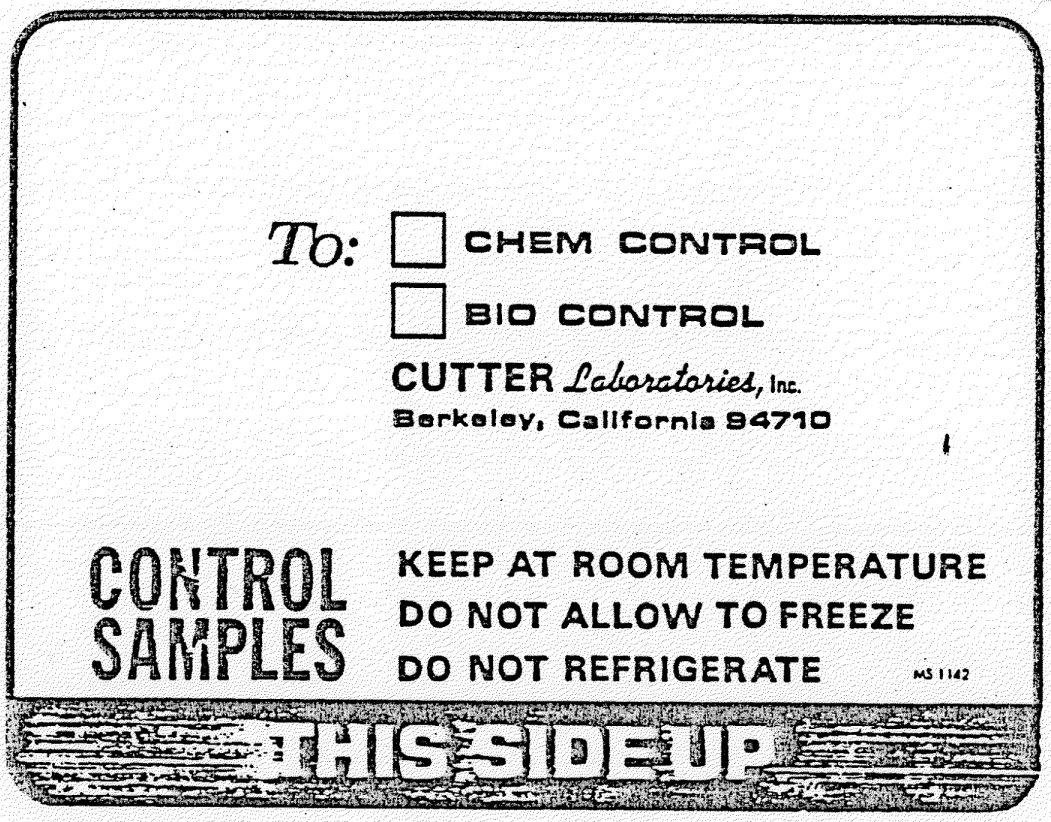
GRO-C 7/19/79

109 7013

PROCEDURE 4.0.9

Subject: Label No. MS-1142, Address Label for Hyperimmune Plasma Samples.

Responsibility: Centrifuge Technician and Laboratory Technician
See Procedure 2.5.3 for use.



Place an X in box opposite Bio Control for hyperimmune samples (plastic tubing).

GRO-C

8 1 0 1 1 2 CSO W 5 1

PROCEDURE 4.0.10

Subject: Label Nos. 81-9706 and 81-9707, Source Plasma (Human) Label for Plasma Pooling Bags.

Responsibility: Centrifuge Technician
See Procedures 2.4.2, 2.4.4 for use.

1. Non-Cutter owned Centers:

SOURCE PLASMA (HUMAN)

CAUTION: FOR MANUFACTURING USE ONLY
STORE AT -20°C. OR COLDER

DONOR NUMBER

COLLECTION DATE OF THE PLASMA

CENTER CODE

PLASMA COLLECTED FROM NORMAL ☐
TETANUS ☐ TETANUS TOXOID
PERTUSSIS ☐ PERTUSSIS VACCINE

OTHER _____ ☐ _____

Contains _____ ml. plasma separated from
☐ 1000 ☐ 1200 ml. whole blood collected in ☐ 100 ☐ 120 ml. Anticoagulant 4% Sodium Citrate Solution.

Nonreactive for HB_sAg when tested by the RIA or RPHA method.

81-9706 (Rev. 5/76)

2. Cutter owned Centers:

SOURCE PLASMA (HUMAN)

CAUTION: FOR MANUFACTURING USE ONLY
STORE AT -20°C. OR COLDER

CUTTER Laboratories, Inc.
Berkeley, Calif. 94710

DONOR NUMBER

U.S License No. 8 _____

COLLECTION DATE OF THE PLASMA

CENTER CODE

PLASMA COLLECTED FROM NORMAL ☐
TETANUS ☐ TETANUS TOXOID
PERTUSSIS ☐ PERTUSSIS VACCINE
RABIES ☐ RABIES VACCINE

OTHER _____ ☐ _____

Contains _____ ml. plasma separated from
☐ 1000 ☐ 1200 ml. whole blood collected in ☐ 100 ☐ 120 ml. Anticoagulant 4% Sodium Citrate Solution.

Nonreactive for HB_sAg when tested by the RIA or RPHA method.

81-9707 (Rev. 5/76)

GRO-C

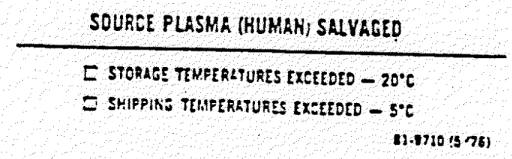
9/27/76

8 10112 CS0 W 52

PROCEDURE 4.0.10.1

Subject: Label No. 81-9710, Source Plasma (Human) Salvaged Label for Plasma Pooling Bags.

Responsibility: Centrifuge Technician and Manager
See Procedure 2.4.9 for use.



GRO-C

114A

9/27/76

109 7016

810112 CSO W 53

PLASMAPHERESIS CUSTOMER SERVICE REPORT

Ship to: Cutter Laboratories, Inc.
Fourth and Parker Sts.
Berkeley, California 94710
Attn: Customer Service Report Coordinator

Q.A. Reference No. _____

Date _____

Plasmapheresis Center _____

_____

Product _____

Code _____

Serial No. _____

Number of Samples Submitted _____

Nature of Report:

(Describe in detail - the more information provided concerning the particular situation the easier it will be to solve the problem.)

109 7017

Submitted by _____

Position _____

PROCEDURE 4.0.11

Subject: Plasmapheresis Customer Service Report

Responsibility: All Personnel

See facing page for form.

1. Inevitably every user of the type of equipment employed in plasmapheresis finds some few items that do not function properly. This may be due to a variety of causes including damage in transit.
2. Every manufacturer wishes to be kept informed of all difficulties found with his equipment. Only in this way can defects or problems in manufacture or transit be eliminated.
3. In order to serve you better, Cutter Laboratories has instituted use of the Plasmapheresis Customer Service Report. Whenever a problem occurs with Cutter Laboratories manufactured equipment, solutions or supplies, please complete this form and send it together with the item to address indicated.
   a. Please pack item so that further damage does not occur during transit between your Center and Cutter Laboratories.
   b. If the item is a blood bag, pooling bag, or Saftifilter® Admin. Set, please drain blood or plasma from item (cutting bag film if necessary), wash interior and exterior, circle area of problem with a black permanent ink marking pen and ship.
4. Please remember Cutter Laboratories should not be held responsible for damage to any item that occurs due to misuse, improper use or accidents occurring at your Center.

GRO-C

109 7018

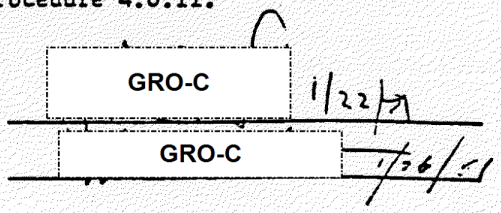
8 10112 CSO W 55

Subject: Plasmapheresis Equipment

Manufacturer: Cutter Laboratories, Inc.

Code No.	Name	Description
400-27	Sodium Chloride For Injection USP.	500ml
732-72	Plasma Pooling Bag	Plastic Bag
732-73	Plasma Pooling Bag	Plastic Bag
798-11	Attached Double Bleeding Plasmapheresis Unit	50ml 4% Sodium Citrate
798-12	Attached Double Bleeding Plasmapheresis Unit	60ml 4% Sodium Citrate
798-13	Attached Double Bleeding Plasmapheresis Unit	50ml 4% Sodium Citrate
798-14	Attached Double Bleeding Plasmapheresis Unit	60ml 4% Sodium Citrate
865-99	Saftifilter® Administration Set	Blood Filter and inletting spike with 1 male luer fitting and 2 trocar fittings

1. Maintain on permanent file within center a record of all supplies received to include name of manufacturer, code number, batch number, if any, lot number, expiration date, if any, and date of receipt. Note: It is important that the Code Number on each case of equipment or solution be checked against this list and the lists accompanying any current alternate procedures before the case is opened. If a Code Number is not listed in any current Procedure the case must be quarantined and the Manager, Plasma Procurement, Cutter Laboratories notified immediately.
2. Maintain on permanent file within center a record of disposition of all rejected supplies and/or defective equipment. Disposition of latter should be according to Procedure 4.0.11.



PROCEDURE 5.0.2

Subject: Fluorescent Finger Stain and Ultra Violet Lamp

Manufacturer: Shannon Luminous Materials Corporation
7356 Santa Monica
Los Angeles, California 90046
213-876-2660

1. CS-20 Blood Donor Stain supplied in pint bottles.
2. Ultraviolet Lamp, 6 watt, Model 317A with handle.
   a. Center should maintain an extra bulb at all times.

11/19/73

118

GRO-C

109 7020

8 1 0 1 1 2 CS0 W 57

PROCEDURE 5.0.3

Subject: Microhematocrit Centrifuge and Capillary Tubes

1. Any model of any standard brand microhematocrit centrifuge is acceptable.
2. Centrifuge must be maintained in good working condition and be safe for use.
3. Rotating centrifuge head must be shielded.
4. Centrifuge must be equipped with an automatic cut-off timer in operable condition.
5. Centrifuge must be operated according to manufacturer's instructions.
6. Rubber gaskets and centrifuge head must be kept clean and undamaged.
7. Scale for measuring hematocrit percentage may be integral in centrifuge head or may be separate from centrifuge.
8. Type and size of capillary tube specified by the centrifuge manufacturer must be used; it must be heparinized.

GRO-C

PROCEDURE 5.0.4

Subject: Refractometer for Total Plasma Protein Determination

1. Only acceptable instrument is American Optical TS Meter and T/C Refractometer model 10400 (Armed Forces version model 10414). Instrument is temperature compensated between 60-100°F.
   a. May have either of two reticules, both have two scales.
      (1) One reticule has a Protein scale with values from 0.0 to 15.0 and a Refractive Index scale with values from 1.3330 to 1.3730.
      (2) The other reticule has a Protein scale with values from 2.5 to 15.0 and a Urine Specific Gravity scale with values from 1.000 to 1.035.
      (3) Protein scale of either reticule must be labeled PR/N Ratio 6.54.

GRO-C

PROCEDURE 5.0.5

Subject: Blood Collection and Measuring Devices

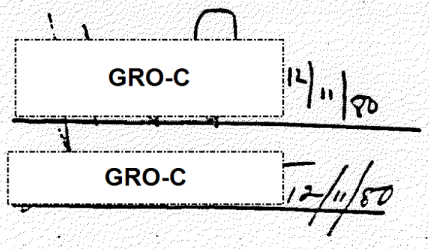
1. Two types of devices are recommended with either being equally satisfactory.
   a. Hemomatic vacuum device which agitates bag during blood collection to continuously mix anticoagulant and blood. A vacuum is also provided to assist withdrawal of blood. Measuring of blood drawn is by means of occluding vacuum outlet.
      (1) Manufactured by:
          Dewberry Dye and Stamping Company
          3201 Fourth Ave. South
          Birmingham, Alabama
      (2) Plastic chamber must rock evenly around a central shaft so that blood bag does not shift within chamber during agitation.
      (3) Equipment must be kept clean and free of blood at all times.
      (4) Maintain equipment in good working order.
      (5) Each day of use, standardize each Hemomatic with a container of known mass or volume and record the calibration in the whole blood log book or some other suitable log book. Restandardize a particular Hemomatic with a container of known mass or volume after every overbleeding on that particular Hemomatic. Note such restandardization in the whole blood log (see Procedure 2.4.1).
   b. Plasmapheresis cut-off scale is a precalibrated counterbalanced scale equipped with device to pinch tubing and stop flow of blood when preset weight is reached.
      (1) Manufactured by:
          Cutter Laboratories
          Code 844-10
          Similar devices by other manufacturers may be safisfactory.
      (2) Scale must be mounted securely in such a manner that scale may be accurately leveled.
      (3) Scale must be tared for weight of blood bag and anticoagulant.
      (4) Cut-off portion of scale must be used.
      (5) Blood bag must be manually agitated frequently during blood collection to mix anticoagulant and blood.
      (6) Each day of use, standardize each scale with a container of known weight and record the calibration in the whole blood log or some other suitable log. Restandardize a particular scale with a container of known weight after every overbleeding experienced on that particular scale. Note such restandardization in the whole blood log (see Procedure 2.4.1).

Subject: Test Tubes, Vials for Preparation and Shipping of Serum Samples

1. Test tubes must be of sufficient size to allow adequate blood collection to consistently provide a minimum of two milliliters of serum. Test tubes must be chemically clean and dry prior to use.
2. Plastic vial for shipping serum sample must be between 2 and 2-1/2 inches high with screw cap and liner. A glass vial with screw cap and liner is satisfactory if of comparable size. Plastic vials are preferred.
   a. Vials and caps must be clean and completely free of extraneous matter before use. Inspect vials carefully.
   b. Suggested Sources for Plastic Vials:

	Description
E & K Scientific Products, Inc. P.O. Box 822 Saratoga, CA 95070 Phone: (408) 867-1157	Vial No. 606016
R General Bottle Supply Co. 1501 S. Figueroa Los Angeles, CA 90015 Phone: (213) 741-0198	Short Style 2-dram vial with screw cap and liner

Screw-cap vials from other manufacturers may be satisfactory if of comparable size.



PROCEDURE 5.0.7

Subject: Refrigerated Centrifuge

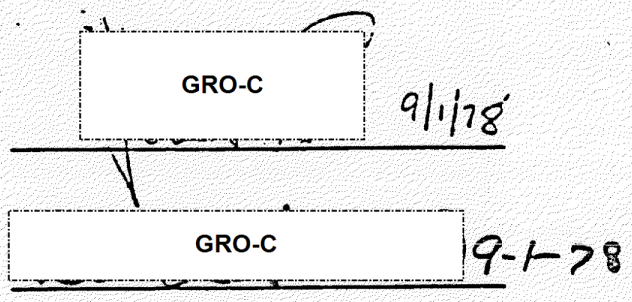
At least four types of refrigerated centrifuges are in general use, e.g. Sorval RC3, MSE LR6 or 6L, IEC-FR6000 and Beckman J6 or J6B. As each machine has its own characteristics only rotors and up to maximum speeds recommended by the manufacturer should be used. Acceptable chamber temperature for maintaining proper whole blood temperature during centrifugation may range between 0°C and +15°C. Centrifugation time may range between 5 and 20 minutes. Adequate separation of blood cells and plasma may be obtained at speeds ranging from manufacturer's recommended maximum to as little as 50% of this maximum. In general, greater rotor speeds will require lower temperatures and shorter centrifugation times for separation of clear, cellular-free plasma in high yield.

1. Keep cups, rotor, shield and chamber clean (free of blood or plasma) and dry at all times.

2. Maintain centrifuges in good working order.

3. To prevent build-up of adhesive from blood bag label in cups, interior of cups may be lubricated with Dow Corning 200 Silicone Oil (360 Medical Fluid, Dow Corning Corporation) if desired. Since composition of other silicone oils or sprays are not known and hence their effect on plastic film of the bag or the bag contents are not known, their use is not recommended.

4. Some centrifuges are equipped with adjustable braking circuits. Adjust control to give maximum braking while maintaining production of clear, red cell free plasma. Readjust as necessary.



Subject: Control of Scales for Weighing Whole Blood and Plasma; Conversion Tables

1. Control Procedure
   a. Daily
      (1) The scales used to weigh whole blood and plasma are in daily use and must be checked daily to determine their accuracy.
         (a) Scales are mounted on a firm level surface.
         (b) Make sure scale is level.
         (c) Make sure scale shows zero reading when pan is empty.
         (d) Obtain a weight of accurately known gram or ounce mass. Most scale companies carry these as stock items in the 453.6 gm. (1 lb.) range. Each working day place weight on pan and check reading. Adjust scale if necessary to obtain correct reading.
         (e) In a bound log book, record each daily check of scale. Include date of check, initials of person performing check, results obtained, and any adjustment required.
   b. As necessary - defined as whenever scale requires repair by a commercial firm due to lack of adequate performance.
      (1) Have scales calibrated by State Bureau of Weights and Measures or commercial firm competent for certification of scales.
2. Conversion Tables
   a. Conversion tables from gram weight of whole blood bag or plasma pooling bag to milliliters of whole blood or milliliters of plasma are available from Plasma Procurement Administrator, Cutter Laboratories. R
      (1) If Cutter whole blood bags and/or plasma pooling bags are used, these conversion tables must be used.
      (2) Match conversion tables showing bag code number to code numbers on bag envelope.
      (3) If other plasmapheresis equipment is used, conversion tables must be prepared using these formulas:

$$\text{ml. whole blood} = \frac{\text{Gross weight of bag whole blood in grams} - \text{Tare weight of blood bag and anticoagulant in grams}}{1.050 \text{ gm. / ml.}}$$

$$\text{ml. plasma} = \frac{\text{Gross weight of bag plasma in grams} - \text{Tare weight of plasma pooling bag in grams}}{1.030 \text{ gm. / ml.}}$$

GRO-C 12/11/80

GRO-C 12/11/80

109 7026

8 1 0 1 1 2 0 5 W 8 3

PROCEDURE 5.0.9

Subject: Methods of Obtaining Sterility

1. The best method of obtaining sterility is autoclaving with live steam under pressure at 121.5°C, 15 psi, for 30 minutes to 1 hour depending on size of load. Refer to the operating manual supplied for the sterilizer in use.
2. HB_sAg positive and other unacceptable units of plasma must be autoclaved at 121.5°C, 15 psi, for not less than two hours after stated temperature and pressure is reached. (See Procedure 2.5.2).
3. An alternate method of obtaining sterility, not applicable to solutions or any wet objects, is dry heat at 170°C (338°F) for 2 hours.
4. Each load sterilized is adequately controlled with sterilizer tape and/or other suitable controls, eg: Diak sterilizer controls, and dated as to date of sterilization. Objects sterilized will not stay sterile indefinitely. Unless container is adequately sealed, contents should not be considered sterile for more than one month following sterilization.
5. An adequate record of each sterilizer run is maintained and includes quantity and type and time sterilized, date of sterilization, sufficient information to determine adequate function of sterilizer and appearance of any sterilizer controls, eg: sterilizer tape of Diak sterilizer controls, following sterilization.
6. Label each container of sterilized supplies with date of sterilization.

GRO-C 3/17/81

GRO-C 3/17/81

PROCEDURE 5.0.10

Subject: Freezers and Refrigerators; Records of Temperature

1. A record is kept of the temperature maintained on each freezer used to store Source Plasma (Human) and any refrigerator used to store vaccines, toxoids, medicines (where low temperature storage is required) or laboratory reagents used in connection with immunization, treatment or testing of donors.
2. Refrigerators:
   a. Variety of devices may be used, e.g.: maximum-minimum thermometer, mercury thermometer, etc.
   b. Read twice each working day, once immediately after opening refrigerator door at the beginning of the working day and again at the end of the working day.
   c. Record in refrigerator temperature log book which contains, as a minimum; identification of refrigerator, date and time of reading temperature, temperature reading observed including whether degrees Fahrenheit or Centigrade, initials of person reading and recording temperature.
   d. Document in log book reason for any temperature readings out of applicable temperature range including steps taken to correct problem and bring refrigerator temperature into applicable temperature range.
3. Freezers for storing Source Plasma (Human).
   a. Recording thermometer is mandatory on each freezer.
      (1) Be sure chart is dated properly so that temperature at any hour of any day may be accurately determined.
      (2) When chart is changed, sign back of chart.
      (3) When chart is changed compare day and time on chart with actual day and time. Take whatever action is required to maintain accuracy within $\pm$ 2 hours.
      (4) Keep charts on file permanently in chronological order.
   b. Mercury or alcohol thermometer whose range is at least -20°C. to +25°C. is mandatory in each freezer.
      (1) Read thermometer at least twice each working day, at the beginning of the working day and again at the end of the working day.
      (2) Record in freezer temperature log book which contains as a minimum, identification of freezer, date and time of reading temperature, temperature reading observed including whether degrees Fahrenheit or Centigrade, initials of person reading and recording temperature.
   c. Place recorder probe and thermometer bulb in a solution of 50% glycerol in separate large containers (empty Sodium Chloride for Injection bottles with labels removed are excellent) so that probe or bulb does not touch glass walls and so that scale divisions on the thermometer may be easily observed. Recorder charts that show regularly spaced temperature increases above -20°C., at time of freezer defrost cycle, indicate either improper placement of recorder probe (probably against container wall) or insufficient volume of glycerol solution.

GRO-C

9/27/76

Subject: Freezers and Refrigerators; Records of Temperature

d. Recorder probe and thermometer must be placed in freezer such that they reflect, as nearly as possible, temperature of Source Plasma (Human) being stored.

R e. Daily compare temperature shown on recorder chart with that observed on the thermometer. If temperatures do not agree within 2°C, action should be taken to determine which reading is accurate and correct the device giving inaccurate temperature.

R f. Document on the record, eg: recorder chart and thermometer log book, reason for any temperature rises above -20°C, eg: "Freezer door open 1/2 hour during shipping of plasma". Initial and date statement.

g. Document in freezer temperature log book any repair of freezer necessary to permit freezer to constantly maintain -20°C.

h. Consideration should be given to installation of alarm system which has characteristics:

(1) Signaling device is located in an area in which responsible individuals are constantly on duty;

(2) Device does not depend solely on community electrical power;

(3) Device is checked at least monthly for accuracy and reliability.

4. Vaccines, toxoids, medication or any material given to a donor by ingestion or injection must be stored in a separate refrigerator from that used for storing HB_sAg test samples, RPR testing reagents and supplies of foodstuff.

R 5. Documentation of shipping temperatures need not be maintained at the plasma center.

GRO-C 12/11/80

GRO-C 12/10/80

1 1 2 CSO W 6 6

109 1025

PROCEDURE 5.0.11

Subject: Equipment and Reagents for RPR Test

Manufacturer: Hynson, Wescott & Dunning, Inc.
Charles & Chase Streets
Baltimore, Maryland 21201
Inquire about availability from
Manager of Plasma Procurement
Cutter Laboratories

1. Card Test Rotator, 100 rpm, 3/4 inch radius auto timer controlled, Model 300 (cat. No. 8780-30).
2. RPR Card Test Kit No. 110 (cat. No. 8750-05).
   a. Three 3 ml. size ampule antigen, 20 g. needle, dispensing bottle.
   b. Fifty cards with ten 18 mm. circle spots each.
   c. Five hundred Dispenstirs.
3. RPR Card Test Control (Cat. No. 8767-09), test card with strongly positive, weakly positive, and negative serum samples dried in circle spots.

GRO-C

PROCEDURE 5.0.12

Subject: Equipment for Obtaining Blood Samples

Manufacturer - Becton Dickinson & Company
Rutherford, New Jersey 07070

1. B-D Vacutainer Evacuated Blood Collection Tube
2. Evacuated blood collection systems made by other manufacturers may be equally satisfactory.

GRO-C 6/24/78

GRO-C 6/28/78

7/17/78

CSC W 68