Date: March 10, 1995

From: Director, Center for Biologics Evaluation and Research

Subject: Revision of FDA Memorandum of August 27, 1982: Requirements for Infrequent Plasmapheresis Donors

To: All Registered Blood and Source Plasma Establishments

I. INTRODUCTION

The Center for Biologics Evaluation and Research (CBER) is updating its existing guidance relating to plasma collection by automated apheresis. CBER believes that the donor suitability and protection procedures should take into consideration the frequency of donation as well as the total volume of plasma collected over a period of time, namely one year. In its August 27, 1982, memorandum "Requirements for Infrequent Plasmapheresis Donors", FDA notified manufacturers that it would review supplements to Source Plasma license applications requesting Source Plasma collections every 8 weeks, or less frequently, without a physical examination or plasma or serum protein tests. FDA's approval of the supplement requesting a variance to 21 CFR 640.63 and 640.65 was made in accordance with FDA regulations provided in 21 CFR 640.120 (formerly 21 CFR 640.75). In a public meeting on June 21,1994, the FDA Blood Products Advisory Committee agreed that the maximum permissable volume limits addressed below and collected at four week intervals would not compromise donor safety. These volumes are consistent with those currently allowed for plateletpheresis donors.

The recommendations in this memorandum apply to all Blood and Source Plasma Establishments engaged in the collection of plasma by apheresis both for transfusion (i.e. Fresh Frozen Plasma) and for further manufacturing (i.e. Source Plasma), as well as plasma included in a plateletpheresis product. These plasma products are the only ones permitted by automated collection. This memorandum supersedes the recommendations of the August 27, 1982, memorandum "Requirements for Infrequent Plasmapheresis Donors", which defined infrequent plasmapheresis as every 8 weeks or less frequently. This memorandum defines infrequent plasmapheresis as every 4 weeks or less frequently.

II. RECOMMENDATIONS

A. Plasmapheresis Donors

1. Plasma (Source Plasma, Fresh Frozen Plasma) may be collected from healthy, non-immunized individuals who donate every four weeks, or less frequently, i.e. infrequent donors, provided that such donors meet all physical and history requirements/recommendations for donors of Whole Blood, other than donation frequency, and have a minimum weight of 110 pounds.

2. The maximum allowable plasma volume (excluding anticoagulant) collected annually would be 12.0 liters (14.4 liters for donors weighing more than 175 pounds). Volumes per donation should not exceed those outlined in the November 4, 1992 memorandum " Volume Limits for Automated Collection of Source Plasma" unless a variation has been approved by CBER in a license application or supplement.

3. The Standard Operating Procedures should include procedures to ensure that the donor is not participating simultaneously in other blood or plasma collection programs, or has not been a frequent (more often than every 4 weeks) apheresis donor.

4. Collection from a plasmapheresis donor who returns in less than 4 weeks or who donates more than the maximum annual volumes, described in II.A.2, whichever comes first, should follow all Source Plasma regulations in 21 CFR 640.61 through 21 CFR

640.65; the donor should have a medical examination and plasma or serum protein tests before being accepted for another donation. If Fresh Frozen Plasma is collected, the infectious disease test requirements and recommendations for Whole Blood would also apply.

B. Plateletpheresis Donors

1. Plateletpheresis collections may currently be performed every 48 hours (two procedures within a 7 day period) with a maximum of 24 collections per year, as stated in the October 7, 1988, memorandum "Revised Guideline for the Collection of Platelets, Pheresis", provided that all such donors meet all physical and history requirements/recommendations for donors of Whole Blood, other than donation frequency, and, in addition, have a platelet count greater than 150,000/ul.

2. The total volume (excluding anticoagulant) of all blood products retained per plateletpheresis procedure should not exceed 500 ml (600 ml for donors weighing more than 175 pounds) except as specifically approved by CBER in a license application or supplement. The maximum volume collected annually should be 12.0 liters (14.4 liters for donors weighing more than 175 pounds).

3. Any plateletpheresis donor who donates more than these maximum annual volumes (including plasma "by-products") should have a medical examination and plasma or serum protein tests consistent with 21 CFR 640.63 and 640.65 before being accepted for another donation.

III. LICENSING

A licensed establishment desiring to include an infrequent (every 4 weeks or less frequently) plasmapheresis collection program at its facility must submit a supplement to the applicable product license application, requesting a variance under 21 CFR 640.120. The supplement should include a copy of the Standard Operating Procedures (SOPs) that will be used for the infrequent plasmaphesis collection program. Before

implementing these recommendations, licensed establishments must obtain CBER approval of the supplement. A registered, non-licensed establishment should request a variance under the provisions of 21 CFR 640.120, and submit a copy of the SOPs that will be used.

Questions concerning plasma collection may be directed in writing to Director, Division of Blood Applications (HFM-370), Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Blood Research and Review, 1401 Rockville Pike, Rockville, MD 20852-1448; FAX: (301) 594-6431. Questions regarding platelet collection may be directed in writing to Director, Division of Hematology (HFM-330) at the above address; FAX: (301) 402-2780.

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11/05/93 topic initiated at Senior Management Meeting

11/08/93 discussion with Office of Compliance counterpart

11/09/93 discussion at CBER Blood Meeting; first draft distributed

11/15/93 discussion with Acting Office Director (OBRR)--E-mail

11/23/93 discussion at CBER Blood Meeting; PLASMAME.2 draft distributed

11/24/93 comments received by E-mail from HFM-330 (Hematology)
incorporated into PLASMAME.3

12/06/93 comments received from HFM-350 (Acting Division Director, DBCP) incorporated into PLASMAME.4

12/14/93 discussion at CBER Blood Meeting; PLASMAME.4 draft distributed

12/17/93 comments incorporated into PLASMAME.5

01/03/94 comments received from Office of Compliance

01/23/94 comments incorporated into PLASMAME.6

02/18/94 comments received from Office of General Counsel

03/06/94 comments incorporated into PLASMAME.7

03/15/94 comments incorporated from HFM-370 (Acting Division Director, DBA) and OGC into PLASMAME.8

04/11/94 additional comments received from Office of General Counsel

05/14/94 comments incorporated from OGC into PLASMAME.9

05/23/94 comments from OGC incorporated into PLASMAME.10

06/29/94 revised to incorporate BPAC, June 21, suggestions into into PLASMAME.11

07/20/94 revised after discussion with J.Epstein into

PLASMAME.12; to J. Wilczek of OBRR Policy Group

07/21/94 further revisions into PLASMAME.13; to J. Wilczek for distribution

08/01/94 revised after further discussion with J. Epstein into PLASME.14

08/03/94 revised to incorporate comments from J.Epstein and B. Poindexter into PLASMAME.15; faxed to J. Wilczek

10/27/94 received additional comments from M. Gustafson

11/09/94 received response from S. Falter to M. Gustafson's comment

01/05/95 received response from OGC (D. Maloney) by telephone to M. Gustafson's comment on 21 CFR 640.120

01/22/95 revised into PLASMAME.16, sent to M. Gustafson and J. Wilczek

02/13/95 comment received from M. Gustafson; revised into PLASMAME.17; given to J. Wilczek on 2/14/95