GUIDELINES FOR IMMUNIZATION OF SOURCE PLASMA (HUMAN) DONORS WITH BLOOD SUBSTANCES

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Bureau of Biologics
Division of Blood and Blood Products

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BLOOD GROUP SUBSTANCES

1. Must be a licensed product
2. May be administered only to healthy males or else to females in good health who are either physiologically or surgically incapable of childbearing.
   a) Primary - no more than 1.0 mL subcutaneous or intramuscular. An initial "skin test" injection may be 0.1 mL intradermal, followed later the same day by up to 0.9 mL either subcutaneous or intramuscular.
   b) Booster - no more than 1.0 mL by the same routes as the primary, to be administered only if both the following criteria are met:
      i) The serum hemagglutination titer is less than 1:256 and
      ii) More than one year has passed since the previous immunization.

RED BLOOD CELLS

1. Cell Donor - Meets whole blood donor criteria as specified in 640.3; also:
   1. No history of hepatitis or past reactive test for HBsAG.

2. No history within the past 6 months of ear piercing, acupuncture, or tattooing.

3. No history of previous transfusions.

4. Previously used as red cells donor for transfusion or immunization of at least three recipients, who have been followed for at least six months without having developed hepatitis, jaundice, or reactive HBsAG tests: or

   If a new previously unused red cells donor, the cells should be used to immunize no more than three recipients in an initial six month period, during which time recipients shall have monthly HBsAG tests and SGOT or SGPT determinations.

   If at the end of 6 months, there is no clinical or laboratory evidence of hepatitis or other blood transmissible diseases in the recipients, the donor may be considered acceptable for providing red blood cells for stimulation purposes.

5. In special instances, selected donors with properly documented histories of voluntary blood donations which resulted in transfusions without subsequent hepatitis may be found acceptable.

2. Volume and frequency of red blood cells collections:

Total of no more than 450 mL of whole blood drawn in any

8 week period, and no more than 2,250 mL whole blood drawn per year.

3. Laboratory Tests

   a. Each Donation:

      serological test for syphilis must be nonreactive; third generation HBsAg tes must be nonreactive; SGOT or SGPT within normal limits established by testing laboratory; and ABO and Rh_0(D) typing.

   b. Initially - before use as donor:

      Red Blood Cells phenotyping done - for C, D, E, $\bar{c}$, $\bar{e}$, Kell and Fy^a; although not required, phenotyping for other specificities is often desirable and is rocommended.

4. Preparation of Antigen

   a. Collection

      1. Collected under aseptic conditions, into sterile, pyrogen-free containers in an appropriate ratio of an approved anticoagulant.

      2. May be aseptically aliquoted into sterile, pyrogen-free, single-dose vials or tubes for storages.*

*BD red stoppered vacutainers are not prepared as sterile containers.

BD/yellow stoppered vacutainers are sterile, but are not pyrogen-free nor intended for injection. Manufacturers of

sterile, pyrogen-free vials suitable for injection:

Elkins-Sinn, Inc.
Cherry Hill, NJ 08002
Product Code: 452700

New England Nuclear
Atomlight Place
Radiopharmaceutical Division
North Billerica, MA 01862

Neither of these vials contain anticoagulant.

b. Storage

1. Stored at 1 - 6° C, or

2. Frozen

If stored frozen, should be washed prior to use, and used within 2 hours after entry for washing. After washing - store at 1 - 6° C.

c. Dating Period

1. If stored at 1 - 6° C and unfrozen, storage must not exceed 45 days.

a. Must submit sterility data to support requested dating.

2. On all blood aliquoted in an open system, a bacterial culture performed according to the specifications set forth in Section 640.2(b), except that the test shall be performed on at least one single-dose vial from each bleed lot which is stored unfrozen for more than seven days. One culture shall be performed on day 8 for at

least one single-dose vial from each lot and an additional culture shall be performed on the last date of the dating period.

d. Washing of Red Blood Cells

1. Washing is desirable, but not required, for RBC stored liquid.

2. If washing is done, sterile, Sodium Chloride Injection USP must be used.

3. If Red Blood Cells are washed, must be used within 2 hours after entry for washing.

4. If washing is not performed, single-dose vial of cells should be stored upside down, and only packed red blood cells should be aspirated for immunization purposes.

5. Record Keeping - As required in GMP and Source Plasma Regulations.

6. Additional Testing of Red Blood Cell Recipients.

a. Must be ABO, Rh, Kell and Duffy phenotyped prior to immunization. Kell negative, $Fy^{(a-)}$ or persons who are both Kell negative and $Fy^{(a-)}$ must not receive Kell positive or $Fy^{(a+)}$ cells except for specific purpose of producing Anti-Kell or Anti-Fy^a. Only ABO compatible red cells may be transfused.

b. Screening for unexpected antibodies by methods that

demonstrated hemolyzing, agglutinating, and coating antibodies should also be performed.

1. Whenever antibody screening tests demonstrate the presence of unexpected antibodies, other than those deliberately stimulated through immunization by the licensee, the prospective red blood cell recipient shall be interrogated as to whether they have ever been pregnant, transfused or a tissue graft recipient, or whether they have received past injections of red blood cells for any reason. This history shall be made part of the permanent record and shall identify as clearly as possible the cause of immunization.
2. Recipient should be notified in writing of any antibody specificity he develops.
3. The Director, Bureau of Biologics, shall be notified in a written report on an annual basis of any unintended specificity antibodies elicited by red blood cell immunization.

c. Women shall not be immunized unless physiologically or surgically incapable of childbearing.

7. Immunization schedule

a. Immunization procedures

1. <u>De novo</u> immunization for anti-Rh_0(D): The

maximum volume of packed red cells to be used for de novo $Rh_0(D)$ immunization shall not exceed 50 mL within any 4 month period. Subjects not responding after receiving a total of 150 mL of injected packed red cells shall be dropped from the program.

2. De novo immunization for atypical antibodies other than anti-$Rh_0(D)$: Any de novo immunization with red blood cells for elicitation of antibodies other than anti-$Rh_0(D)$ shall be performed under IND according to a Bureau of Biologics approved protocol. All such immunization protocol will be considered on an individual basis.

b. Immunization of donors with positive antibody screening tests (donors with pre-existing Rh antibody titers): The maximum volume of packed red blood cells to be given to donors with pre-existing antibody (regardless of titer) shall be 4.0 mL in a single injection. This volume may be administered up to 5 times in a single month, but shall not exceed 40 mL of packed red blood cells within any six month period.

c. Red cells for immunization shall not be administered as part of any plasmapheresis procedure. Red cell immunization may be performed on the same day as

plasmapheresis, but only following plasmapheresis and only as a totally separate procedure.