DRAFT
REVIEWERS' GUIDE
INFORMED CONSENT FOR PLASMAPHERESIS/IMMUNIZATION

I. INTRODUCTION

This reviewers' guide on informed consent for plasmapheresis/immunization procedures serves to elaborate on the requirements of 21 CFR 640.61. It is designed to assist the reviewer in determining whether a license application/supplement includes this information, and does not change any current statutory or regulatory requirements and recommendations.

II. RECOMMENDATIONS

Plasmapheresis

The informed consent for donors participating in plasmapheresis programs should include the following information:

1. Donor acceptability will be determined by a medical interview, physical examination and laboratory testing. Certain procedures will be performed at each visit; others will be performed every 4 months. The donor will be examined by a qualified licensed physician or his/her trained substitute initially and annually thereafter. If these evaluations so indicate, the donor will be temporarily or permanently deferred from donating plasma.

2. The explanation of the procedure should be in language that the donor can understand and include the approximate length and the frequency of the procedure.

3. Although rare, the following adverse reactions may occur:

    a. blood loss from the inability to return red blood cells which may result in
        i. the procedure being terminated
        ii. deferral for 8 weeks

    b. complications at the venipuncture site
        i. hematoma formation
        ii. local infection

    c. tingling of fingers or lips or tremor due to the anticoagulant (automated plasmapheresis)

    d. allergic reactions such as flushing, itching, hives,

abdominal cramps, difficulty breathing, chest pain, or bronchospasm which may be life-threatening

e. nausea, vomiting, light-headedness, fainting, or convulsions related to change in blood volume

f. return of the wrong red blood cells to the donor (manual plasmapheresis) which could result in life-threatening complications. The donor will be asked to participate in identifying his/her own red blood cells.

4. Total plasma or serum protein, including immunoglobulin levels, may decrease and that these will be monitored every 4 months. Abnormal test results may result in temporary deferral.

5. Information regarding all required and recommended laboratory tests that will be performed and the consequences of an unacceptable or positive test, including possible detection of infectious agents such as Human Immunodeficiency Virus (HIV), temporary or permanent deferral, listing of names in deferral registries, reporting of results to public health officials, and inspection of test records and registries by governmental agencies, will be provided. In addition, there is a time interval early in infection during which tests for HIV may be negative although infection may still be transmitted.

6. The opportunity to ask questions will be provided.

7. Participation is voluntary and the donor may withdraw at any time.

8. If there is not a separate Acquired Immunodeficiency Syndrome (AIDS) Informed Consent Form, the general consent process should also include signing of a statement that the donor has read and understands the material on high risk groups/AIDS and believes he/she is not at risk for transmitting HIV infection to others through this donation.

9. The donor should participate in only one plasmapheresis program at a time, and should not donate blood while participating in the program. Blood donation would serve as a basis for an 8-week deferral.

Immunization

There should be a separate informed consent form for a donor who is participating in an immunization program including one which involves an Investigational New Drug (IND). The informed consent

should include the following information, in addition to the information in Section II:

1. The participant's acceptability will be determined by a medical interview, physical examination by a qualified licensed physician or trained substitute [except as stated in 640.63(b)(2)(ii)] and laboratory testing.

2. The explanation of the procedure should be in language that the participant can understand and should include the expected rate of success of the immunization procedure, the volume and the route of administration of the injection, the interval between the initial injection and subsequent boosters, and the criteria for discontinuation in the program, e.g., unacceptable level of antibody.

3. The participant may participate in only one immunization program at a time. Moreover, the participant may not be eligible for other programs, including regular plasmapheresis programs and/or blood donation.

4. The following adverse reactions may occur:

a. local reactions at the site of injection which may include redness, induration, tenderness, pain, swelling, itching and nodule formation;

b. mild, generalized reactions which may include fever, malaise, fatigue, headache, nausea, vomiting, dizziness, myalgia, arthralgia and lymphadenopathy;

c. severe, generalized reactions including specific reactions which have occurred for each vaccine or antigen that may be administered. For licensed products, these complications are found in the package inserts. Such complications may result in severe disability and/or permanent neurologic sequelae. Information on possible severe allergic reactions (anaphylactoid) and/or life-threatening reactions for which immediate medical care should be provided.

d. Female participants

i. For some vaccines, neither animal nor human studies have been conducted to determine harmful effects on the fetus or on the infant exposed to human milk. For these vaccines, females should be advised that if they are currently nursing or pregnant or if they may become pregnant during the time frame of the immunization program, they should not participate.

ii. For red blood cell immunization, females

should not participate unless permanently incapable of bearing children, and this should be documented.

e. For red blood cell immunization, the development of additional antibodies may cause the participant's plasma to be unsuitable for future use or may result in transfusion or transplantation delays. Although the donor of the red blood cells has been tested initially and 12 months later for all required/recommended infectious disease tests prior to the use of the red blood cells, there remains the possibility of infectious disease transmission by these immunizing cells.

f. Appropriate information about any other potential problems associated with the specific antigen to be used will be given.

5. For red blood cell immunization, required and recommended tests will be performed on his/her blood initially and at periodic intervals.

The consent process for both plasma donation and immunization should be documented in writing using consent forms that communicate all necessary information. These consent forms should be signed and dated by both the donor and the physician or trained substitute overseeing the consent process. The signed forms should be incorporated into the permanent records of the donor.