Guidance for Industry

Implementing a Collection Program for Source Plasma Containing Disease-Associated and Other Immunoglobulin G (IgG) Antibodies

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact the Office of Blood Research and Review at 301-827-3524.

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Contains Nonbinding Recommendations

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

Source Plasma manufacturers might want to implement a collection program to collect Source Plasma from donors who have detectable levels of disease-associated Immunoglobulin G (IgG) antibodies and other existing IgG antibodies (see section IV). Such disease-associated IgG antibodies are antibodies that have occurred in response to exposure to disease agents or other antigens. This guidance is intended to assist you, a Source Plasma manufacturer, in submitting the appropriate information to FDA when implementing an IgG antibody collection program or when adding a new IgG antibody collection to your existing program. This guidance finalizes the draft guidance entitled "Guidance for Industry: Recommendations for Implementing a Collection Program for Source Plasma Containing Disease-Associated and Other Immunoglobulin (IgG) Antibodies" dated October 2005 (70 FR 61135; October 20, 2005), and replaces the draft Reviewers' Guide, "Disease Associated Antibody Collection Program," issued October 1, 1995.

FDA's guidance documents, in general, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required. Insofar as this guidance adjusts reporting categories for manufacturing changes pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 Code of Federal Regulations (CFR) 601.12, it does have binding effect. If you have any questions about the effect of any portion of this guidance, contact the Office of Blood Research and Review, Division of Blood Applications, at 301-827-3524.

II. DISCUSSION

Source Plasma donors participating in a disease-associated IgG antibody collection program must meet all donor suitability requirements under § 640.63 (21 CFR 640.63). Donors who have

disease-associated IgG antibodies are individuals who are in good health at the time of donation and either have recovered from their illness or were exposed to the disease agent but remained asymptomatic. Donors participating in a disease-associated IgG antibody collection program possess specific IgG antibodies as a result of their exposure to the disease agent.

Source Plasma collected from donors participating in disease-associated IgG antibody collection programs and in other IgG antibody collection programs (see section IV) may be used in the manufacture of injectable products and for noninjectable products, such as controls for in vitro diagnostic assays.

This guidance does not include recommendations for the implementation of Immunoglobulin M (IgM) antibody collection programs; nor does it include recommendations for donors who do not meet all donor suitability requirements under § 640.63. The review and approval of collection programs for plasma containing IgM antibodies and for plasma from donors who do not meet all donor suitability requirements under § 640.63 will continue through the submission of a prior approval supplement (PAS) to the biologics license application (BLA) for Source Plasma.

III. RECOMMENDATIONS

Donors of Source Plasma, including Source Plasma collected under a disease associated IgG antibody collection program, must meet donor suitability requirements under § 640.63.

We, FDA, believe that, for establishments licensed to collect Source Plasma, the implementation or expansion, consistent with the recommendations in this section, of a program involving collection from eligible donors of Source Plasma containing the disease-associated IgG antibodies to the following disease agents or antigens, represents a change in the product that has a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as it relates to the safety or effectiveness of the product:

1. C-Reactive Protein
2. Mononucleosis (Epstein Barr)
3. Cytomegalovirus (CMV)
4. Herpes Type I
5. Herpes Type II
6. Varicella Zoster
7. Coccidioidomycosis
8. Histoplasmosis
9. Pseudomonas
10. Rubella
11. Mumps
12. Hepatitis A (Anti-HAV)
13. Hepatitis B surface (Anti-HBs)
14. Hepatitis B core (Anti-HBc)*

*Anti-HBc reactive donations, otherwise nonreactive when tested for HBsAg, have a low risk of infectivity for Hepatitis B virus (HBV) and must not be shipped or

used under 21 CFR 610.40(h)(1). However, 21 CFR 610.40(h)(2)(v) permits the use of these donations for further manufacturing into plasma derivatives (e.g., hepatitis B immune globulin), since the derivative manufacturing process will inactivate the HBV. In addition, when labeled under 21 CFR 610.42(a), these donations may be used for reagents in in vitro diagnostic products (e.g., positive controls for Anti-HBc test kits).

15. Toxoplasmosis
16. Rubeola
17. Respiratory Syncytial Virus (RSV)
18. Chlamydia
19. Hemophilus influenza
20. Parvovirus B19

Upon implementing or expanding such a program at your establishment, you must document this change in an annual report to the approved BLA and submit the report to FDA under § 601.12(d) (21 CFR 601.12(d)). Your annual report notification should confirm that donors meet all required donor suitability criteria for Source Plasma under § 640.63, and that the plasma is collected from donors who have been exposed to the disease agent but are in good health at the time of collection.

Changes to the labeling to describe the products must be submitted as a "Supplement – Changes Being Effected" (21 CFR 601.12(f)(2)(i)(E)).

IV. OTHER NATURALLY OCCURRING OR PRE-EXISTING IgG ANTIBODIES

For establishments licensed to collect Source Plasma, the implementation or expansion of a program involving collection of other naturally occurring IgG antibodies from donors meeting all donor suitability requirements under § 640.63, represents a change in the product that has a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as it relates to the safety or effectiveness of the product. As described in Section III, report the manufacturing change in an annual report (21 CFR 601.12(d)) and changes to the labeling as a "Supplement – Changes Being Effected" (21 CFR 601.12(f)(2)(i)(E)).

In addition, for collections of Source Plasma containing pre-existing red blood cell antibodies, we recommend that at the time of donation, donors not be in any immunization program, and not have been immunized, either deliberately or by transfusion, within the past twelve months. Your annual report should describe the procedures you have implemented to address this issue.

V. EXCEPTIONS

Source Plasma may only be collected and shipped following FDA's review and approval of a BLA for the product. If you make manufacturing changes to an existing Source Plasma BLA to collect Source Plasma containing IgG antibodies as described below, we believe that, because of the substantial potential for adverse effect of the change on the identity, strength, quality, purity, or potency of the product, changes involving the following collections require supplement submission and approval (PAS) prior to distribution of the products made using the change (major change) (21 CFR 601.12(b)). In some circumstances, such collections may be made only if FDA grants a variance under 21 CFR 640.120 to permit the collections. This paragraph applies to the following collections:

- Plasma collected from donors tested and found to be positive for evidence of infection due to communicable diseases as required under 21 CFR 610.40;
- Plasma collected as a by-product of therapeutic procedures;
- Plasma collected from donors participating in an immunization program (e.g., smallpox, anthrax); and

Plasma collected from donors who do not meet all required donor suitability criteria for Source Plasma under § 640.63.