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FOOD AND DRUG ADMINISTRATION WORKSHOP ON PLASMA STANDARDS

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The starting plasma material for the further manufacture of Immune Globulin, Intravenous (IGIV) for the treatment of individuals with primary immune deficiency diseases may be obtained from Source or Recovered plasma. There are potential differences between these two plasma resources that could impact efficacy and/or safety of the final product. A summary of potential areas that merit further investigation is shown in Figure 1.

Figure 1
SOURCE VS. RECOVERED PLASMA: CHARACTERISTICS WITH IMPLICATIONS FOR IGIV
<ul style="list-style-type: none">• EFFICACY
--Antibody titers and biologic potency
<ul style="list-style-type: none">• SAFETY
<ul style="list-style-type: none">– Record keeping, feasibility and speed of look back, sample/specimen retention– Adverse Event Rates– Impact of repeat donors receiving repeat testing and education– Impact of donation processing parameters– Supply limitations

Prior to concluding that Source and Recovered Plasma are identical materials regarding efficacy of IGIV manufactured from each of the resources, additional testing of the manufacturing plasma pools and final products may be useful to

affirm the equivalence of antibody titers to selected pathogens such as encapsulated microorganisms and the biologic potency of the chosen antibodies. To accomplish this evaluation, tests of biologic potency may need to be developed and validated. Currently employed antigenic, rather than functional, assays may not be predictive of *in vivo* activity.

There are also safety issues that need to be clarified prior to concluding that Source and Recovered Plasma are identical materials for the manufacture of IGIV.

1. An assessment should be performed to determine characteristics and accessibility of record keeping and corporate policies on sample/specimen retention in the event of a recall or look back.
2. What are the mild, moderate, severe and serious adverse event rates for IGIV products manufactured from the two starting materials? More recently described events such as TRALI and hypercoagulability should be specifically addressed.
3. Is there an impact on the wholesomeness of the final IGIV products when the starting material is derived from repeat donors who receive reinforced testing and education in comparison to the whole blood donor who is interviewed less than twice annually on the average?
4. Does a delay in the separation of plasma from the cellular components of blood affect the IGIV that is manufactured? Are antibody affinities reduced or lost?
5. The number of blood and blood component donations limits the total volume of recovered plasma annually. If recovered plasma becomes the most important or potentially sole source of starting material for the manufacture of IGIV, even if yields per liter are higher than with source plasma, would there be sufficient raw material to produce the IGIV needed by patients with primary immune deficiency?

We suggest that these important efficacy and safety questions be addressed as part of the Agency's review of Source and Recovered Plasmas.