PPTA Statement on
Current Considerations on Plasma Obtained from Whole Blood Donors for Further Manufacturing Use

FDA Blood Products Advisory Committee
April 2, 2009

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide comments to the Blood Products Advisory Committee (BPAC) on the issue of plasma obtained from whole blood donors for further manufacturing use.

PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies. Our members provide 60 percent of the world's needs for Source Plasma and plasma protein therapies. These include clotting therapies for individuals with bleeding disorders, immunoglobulins to treat a complex of diseases in persons with immune deficiencies, therapies for individuals who have alpha-1 anti-trypsin deficiency which typically manifests as adult onset emphysema and substantially limits life expectancy, and albumin which is used in emergency room settings to treat individuals with shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed life-sustaining therapies.

PPTA agrees with FDA's stated overall concept to recognize a plasma component for manufacturing use manufactured by apheresis under regulatory criteria for whole blood donors. PPTA has worked with the blood organizations as a member of AABB's Plasma Task Force for the past several years with this as the task force's goal.

While PPTA agrees with FDA's overall concept, PPTA wishes to address several points in FDA's Issue Summary.

- FDA is proposing two product names, Concurrent and Component Plasma, differentiated by whether the component is collected as a by-product of other component manufacture or whether collected as a free-standing component. PPTA sees no reason to differentiate these plasma components by labeling. In fact, something as simple as Plasma for Manufacture would suffice.
- FDA is proposing a complex regulatory stratification for labeling based on separation, freezing, storage and shipping conditions. PPTA has the same position it voiced at the 2004 FDA workshop, Development of Plasma Standards. FDA should set minimum regulatory requirements in these areas. Anything beyond minimum requirements is a yield issue, not a regulatory issue, and is currently addressed in contracts between the fractionators and their suppliers. The regulatory process can be slow and encumbered creating complex regulatory requirements that lead to obsolete and inflexible requirements. Minimum requirements allow for flexibility and evolution as needed and specific regulations should only be set when presented with a specific problem which is best addressed through the regulatory policymaking process.
- FDA expresses concerns that whole blood donors have "the perception that their blood will be transfused to help save patient lives." PPTA does not want to diminish the importance of having life-saving blood components locally for transfusion but wishes to remind the FDA those plasma protein therapies, albeit on a global level, also save lives.

As stated in our introductory paragraph, PPTA represents member companies that manufacture life-sustaining and life-saving therapies for end users who depend on them. Having a regulatory option for blood centers to provide plasma for manufacture obtained from whole blood donors on automated apheresis platforms will allow collection of plasma concurrently with the collection of transfusible cellular components and also as a free-standing component. For the latter, FDA mentions the benefit of inventory management in TRALI mitigation strategies. There are also instances in which the whole blood donor would not be eligible to donate transfusible cellular components, e.g., travel to an area identified as a malaria risk or having had a reactive test for anti-HBc, but can contribute by donating plasma for manufacturing use. This is established practice outside the United States and recognized internationally by standard setting documents, e.g. the Council of Europe's Guide

FDA states that creating the new component(s) "likely would involve changes to current regulations and considerations for potential licensure of the new products." However, in the Issue Summary, FDA does not discuss potential regulatory pathways. PPTA recommends:

- Redefine Source Plasma by amending the definition at 21 CFR 640.60 to state that "Source Plasma is plasma collected by plasmapheresis 'under the provisions of this subchapter' intended for manufacturing use."
- Provide an alternative definition of Plasma at 21 CFR 640.30(a) (2) to include "for intravenous or further manufacturing use."
- Add processing requirements for the further manufacturing component under 21 CFR 640.34
- Until regulatory changes can be effected, use the exception provision at 21 CFR 610.53(d) to the Dating Table at 21 CFR 610.53(a) to allow the outdate of Fresh Frozen Plasma (FFP) at any time after preparation. The "oudated' FFP could then be shipped as recovered plasma.

FDA's Issue Summary references the short supply provisions (21 CFR 601.22) in several instances. PPTA suggests that as FDA makes regulatory changes needed to facilitate plasma for manufacture obtained from whole blood donors that it also update the regulations by removing the short supply provisions. The short supply provision for "initial manufacturing at other than licensed location" is outdated, confusing and, at best, duplicative of current contract manufacturing arrangements as outlined in FDA's "Guidance for Industry: Cooperative Manufacturing Arrangements for Licensed Biologics." At the time the licensing regulations were amended (61 FR 24232, May 14, 1996) to expand the definition of "manufacturer" to include "any legal person or entity who is an applicant for a license where the applicant assumes responsibility for compliance with the applicable product and establishment standards," the need for a regulatory mechanism to allow manufacture of the biologic component by anyone other than the license holder became moot. Licensed fractionators procure plasma from outside sources under contractual arrangements. The contracts include regulatory and quality oversight that meet or exceed the requirements of 21 CFR 601.22. To require a short supply agreement in addition to the contract is duplicative, burdensome to both parties and adds no value to the contractual arrangement.