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July 5, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852-1448

Re: Docket No. 2004N-0539, Public Workshop, "Development of Plasma Standards"

Dear Sir or Madam:

Talecris Biotherapeutics, Inc. (Talecris) is pleased to provide the following comments to the above referenced docket established to receive comments on the August 31 and September 1, 2004, public Workshop entitled "Development of Plasma Standards" (the workshop). Talecris is a newly formed company that acquired the assets of the Biological Products Division of Bayer HealthCare LLC and is backed by financial investors Cerberus Capital Management, L.P., New York, and Ampersand Ventures, Wellesley, Massachusetts. We appreciate both having the opportunity to provide you with these comments and your consideration of these comments when discussing standards for plasma for further manufacture/fractionation.

Talecris supports efforts to harmonize requirements and standards for source materials and the final plasma-derived products manufactured from plasma. Amendments to regulations in pursuit of harmonization should be based upon scientific data supporting the amendment in order to establish the most effective requirements leading to safe effective products for the patients who depend upon the live saving therapies produced by the plasma-fractionation industry. Harmonization for the sake of having the same language across global regulatory requirements does not provide any added value to either the industry or the patients we serve.

In the July 2003 proposed rule published in the Federal Register¹ harmonization was listed as the primary reason for changing the US Source Plasma storage temperature requirements from the existing -20°C to -30°C. Specifically, harmonization with the current requirements in the EP Monograph 0853, *Human Plasma for Fractionation*. Subsequent discussions between industry and regulators appear to have resulted in the acceptance of -20°C storage temperature requirements by FDA as -20°C is the real requirement for storage of plasma for fractionation in Europe whether the proteins being produced are labile or non-labile. Talecris appreciates this discussion subsequent to the proposed rule and the recognition on the part of FDA that the storage temperatures for plasma are already harmonized.

Following the discussions and review of the comments submitted on the proposed rule, the focus shifted to the freezing temperature after collection of plasma which is where the difference really lies between the United States and European requirements and even within the European

¹ Revisions to Labeling and Storage Requirements for Blood and Blood Components, Including Source Plasma [Docket No. 2003N-0211].

requirements depending on whether the proteins being manufactured are labile or non-labile. Concerning this topic, it is important to refer to the presentation at the workshop made by Dr. Johannes Dodt of the Paul-Ehrlich-Institut (PEI) and a member of the Group of Experts 6B. During his presentation, Dr. Dodt mentioned Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components (also known as the Blood Directive). This European legislation sets the standards both for plasma for transfusion or for fractionation. Dr. Dodt went on to say in his presentation that the Group of Experts 6B decided to have the freezing temperature requirements for plasma for fractionation similar to the requirements for plasma for transfusion. Therefore, one could argue that the European requirements for plasma for fractionation are not based on any scientific data that would support a higher quality, safety, or effectiveness of plasma-derivatives produced from plasma frozen at -30°C following collection than those produced from plasma frozen at -20°C following collection. Indeed a scientific basis for the European requirements for freezing and storage of plasma for fractionation appears to be lacking.

Talecris strongly supports harmonization **between** requirements mandated by Health Authorities rather than harmonization **with** existing regulatory requirements in a different geographic region. This is important given that the regulatory requirements in the European Union for freezing temperature of plasma for fractionation are based upon the standards established for transfusion products which were most likely derived from the published analytical data only. Again, to the point above, no clinical safety and/or efficacy data are available supporting a need for the lower freezing requirement in the European Union for plasma used to produce labile components.

As for a review of the available analytical data that has been published, some of the data demonstrate a greater yield of Factor VIII from plasma frozen at -30°C after collection. The plasma products industry does not feel that yield should be considered a regulatory issue. Jan Bult of the Plasma Protein Therapeutics Association has made a number of presentations in which he has mentioned the improvements in plasma-derivative manufacturing technologies that have an impact on yield. Indeed some new plasma-derived products have been shown to produce a higher yield than existing products. Manufacturers, in an effort to provide a sufficient quantity of therapies to patients, continue to pursue advancements in technology to produce greater quantities of these much-needed therapeutic products. With that said, new plasma-derived products are subject to strict regulatory requirements for licensure including clinical studies to demonstrate safety and efficacy. At Talecris, the clinical trial material must be produced from plasma collected, qualified and handled according to established FDA specifications for Source Plasma as a licensed biological product. Therefore, when investigating and licensing new plasma-derived products manufactured from FDA licensed Source Plasma (frozen at -20°C after collection) clinical data is generated supporting the safety and efficacy of the final plasma-derived product produced from the current long standing FDA requirements that have served and continue to serve both the industry and consumers well.

As for plasma products on the market today that were licensed prior to the strict clinical trial requirements in place today, these products have been manufactured in the United States for

a number of years and in some cases decades in accordance with current Good Manufacturing Practices under the oversight of the FDA. Indeed this significant historical experience may very well be the foundation for harmonization of the European plasma requirements to the regulations established by FDA. Decades of historical data (including post marketing surveillance) and the current FDA requirements for licensure of new products demonstrate the safety and efficacy of U.S. produced plasma-derivatives. In fact, so overwhelming is the historical data that one should not consider revising the European requirements to the existing FDA regulations as harmonizing to a lesser standard as discussed during the workshop. Further, Dr. Dodt stated at the workshop that the Group of Experts 6B would be willing to look into revising the European requirements should data be presented supporting such a revision. Talecris believes such supporting data is already available in the form of the aforementioned historical experience in the United States. In the end, complete harmonization of plasma freezing requirements may never be achieved and that would not necessarily be an unacceptable conclusion on this topic. Industry has adapted well and continues to adapt to evolving and ever changing regulatory requirements such that small areas of disharmonization e.g., freezing to -30°C after collection, are not a barrier to providing safe and effective products to patients in different regions while maintaining compliance with the applicable regulations established in those regions.

As for recovered plasma, which of course is not a licensed biological product as is the case with Source Plasma, manufacturers must establish specifications to ensure an acceptable starting material is obtained from which to manufacture products. The manufacturer must then generate and analyze validation data for the manufacturing process to verify the product can be consistently produced to meet the established specifications. In the case of Talecris, such validation studies provide assurance that the final products made from recovered plasma are comparable to and meet the specifications required by the license approved by FDA for the products made from Source Plasma. The current situation in the U.S. where recovered plasma is obtained through short supply agreements provides the flexibility for a manufacturer to qualify suppliers of recovered plasma who are capable of meeting the requirements established by the manufacturer. All these things considered, Talecris supports the position of AABB in their letter² to this docket demonstrating support of FDA setting standards for the licensure of recovered plasma as a starting material for the manufacture of plasma-derived products. Standards provide basic minimum requirements that establish the basis for assurance of starting material consistency. This in turn could further the availability of final plasma-derived products as the plasma could be used by any manufacturer distributing final products in the United States. A proposal for such requirements has been made by the AABB in past BPAC meetings and is worthy of consideration by FDA as a basis for recovered plasma licensing requirements. The standards proposed by the AABB should be given consideration when further discussing regulatory requirements for recovered plasma to ensure that enough starting material remains available to meet the needs of manufacturer's and patients.

In conclusion, we believe that the existing and long standing Source Plasma handling requirements in the United States do not need to be modified. There are more significant areas of disharmonization that warrant attention by industry, regulators, and patient groups

² Recovered Plasma (Task Force Comments) – June 23, 2005.

such as updating the generation of viral marker screening test kits available in the U.S. compared to other regions, and harmonization of lookback and post donation information. Talecris supports the establishment of standards for FDA licensure of recovered plasma and believes FDA should consider the AABB proposal to establish those standards.

We wish to thank the FDA for the opportunity to comment on this topic.

Sincerely,

A handwritten signature in cursive script, appearing to read "Mary Ann Lamb".

Mary Ann Lamb, Ph.D.
Vice President, Regulatory Affairs

MAL/mn