

PPTA Statement on Review of Donor Weight Loss Monitoring

FDA Blood Products Advisory Committee October 21-22, 2004

The Plasma Protein Therapeutics Association (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 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 welcomes the efforts made by the Food and Drug Administration (FDA) in reviewing the necessity to monitor at each plasma donation records of the donor's weight measurements over a two-month period of time for the purpose of detecting an unexplained ten-pound weight loss. The recommendation to monitor donor weight using measurements obtained to determine the amount of plasma that can be donated by the donor was instituted prior to the development of tests able to detect HIV infection. We agree with FDA that such monitoring today does not add a margin of safety with respect to HIV/AIDS. For Source Plasma collection centers, the repeated review of these weight-loss records over a two month period, rather than adding to the protection of public health, has instead become an onerous and difficult task that frequently results in auditing pitfalls rather than protecting the plasma donor or plasma supply.

PPTA agrees with the FDA assessment of the utility of new and improved testing technology, such as NAT. We also agree with FDA that unexplained weight loss could be an indication of poor health, but we would add that it could indicate a change in physical activity, dietary habits, employment, or season. FDA has focused on the usage of the word "unexplained" as being the operative term in its analysis, but this presupposes that any weight loss has one cause, and it is either explained or not. This binary approach may be suitable for determinations of objective testing criteria and standards, but a distal, surrogate marker such as the weight loss tracking, which never was truly determinative of a disease state, is not subject to such an interpretation, due to its inherent subjectivity.

We also agree, in large part, with FDA's historical review of the blood memoranda issued over the past twenty years, and the recommendations contained therein. The weight-loss tracking criterion is contained only in the Current Guide to Inspections,

which is categorized as a Level 2 Guidance, which is not subject to comment before implementation. Our reading of these past memoranda is that while the 4/23/92 memorandum “did not specifically state whether the 2/5/90 memorandum was to be superseded[,]” [FDA BPAC Issue Brief, p. 1] we would like to point out that the 4/23/92 memorandum states that it “*replaces*” the 2/5/90 memorandum [Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products, p. 2]. Since the 2/5/90 memorandum is replaced by the later memorandum, the earlier memorandum should be considered to be superseded. We also note that the 1984 and 1990 memoranda are not generally available to the public on the FDA website, which indicates that they are, in fact, considered by the Agency to be obsolete.

PPTA appreciates the efforts of the Agency in this regard. PPTA also encourages the FDA to continue review of regulatory requirements and recommendations that do not add to the safety profile of product manufacture, plasma donation, or public health. While PPTA supports requirements and recommendations that can add measurable improvements to donor health and final product safety, outdated or valueless requirements add burdens without benefit. PPTA supports the FDA’s review of requirements that have become obsolete and FDA’s efforts to examine regulations and guidance criteria that limit efficiency and do not generate enhanced safety.

**Update Summary
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Topic: FDA's current thinking regarding data tracking by Source Plasma establishments to identify a 10-lb donor weight loss in a 2 month period

Background:

Tracking donors to permit identification of a 10-lb weight loss in a two month period commenced following CBER's revised memorandum "Revised Recommendations to Decrease the Risk of Transmitting Acquired Immunodeficiency Syndrome (AIDS) from Blood and Plasma Donors" dated 12/14/84. These recommendations, issued prior to the development of laboratory tests for markers of HIV infection described interim procedures to minimize the risk of transmitting AIDS through blood products or plasma derivatives. These procedures included specific donor questions concerning unexpected weight loss as a criterion of donor suitability. In addition, as stated in the memorandum, "The existing cumulative records of each source plasma donor's weight should be examined to assure that any weight loss of 10 pounds or more in less than two months is detected."

The 12/14/84 memorandum was superseded by a memorandum dated 2/5/90, entitled "Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products," which also included the recommendation to defer donors on the basis of an unexplained weight loss of 10 lbs in a two month period. An addendum to this memorandum, Section I B, Additional Procedure for Source Plasma, states "The existing cumulative records of each Source Plasma donor's weight should be examined on the day of collection to assure that any weight loss of 10 pounds or more in less than two months is detected."

A subsequent 4/23/92 memorandum entitled, "Revised Recommendations for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products" addressed the additional possibility of HIV-2 exposure, but no longer made mention of the 10-lb weight loss tracking obligation for Source Plasma donors. The memorandum did not specifically state whether the 2/5/90 memorandum was to be superseded.

The current "Guide to Inspections of Source Plasma Establishments" revised April 2001 still requires (Section II, Page 11, Item 6, Weight) that the "Source Plasma donor's weight should be examined to assure that any weight loss of 10 pounds or more in less than two months is detected."

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Discussion:

Since the early 1980's, sensitive tests for HIV antibodies, improved testing technology, and licensed NAT for HIV-1 have reduced or eliminated the predictive value of weight loss tracking. FDA's current thinking is that unexplained weight loss remains a general indicator of possible ill health, but does not add a margin of safety with respect to HIV/AIDS.

All whole blood and Source Plasma collection establishments currently list unexplained weight loss as a sign or symptom of HIV/AIDS in donor informational materials. In addition, this information is presented to each Source Plasma donor in the form of a High-Risk Poster at which time the donor is questioned as to whether he/she has any of the signs or symptoms listed.

Source Plasma donors are weighed at each donation in order to determine how much plasma to obtain. These weights are recorded in the plasma donor's records and are available for review as deemed appropriate by the center's medical staff. Current practice includes active review of weight records for the previous two months to rule out unexplained weight loss. Industry has expressed concern that this active process is out of date and burdensome in the current Source Plasma collection environment.

Current requirements pertinent to Source Plasma donor eligibility include: *21 CFR 640.63, Suitability of donor, (a), "The suitability of a donor for Source Plasma shall be determined by a qualified licensed physician or by persons under his supervisions and trained in determining donor suitability. Such determination shall be made on the day of collection from the donor by means of a medical history, tests, and such physical examination as appears necessary to the qualified licensed physician." And, as per 21 CFR 640.63 (b) (1) "Each donor shall be examined by a qualified licensed physician on the day of the first donation or no more than 1 week before the first donation and at subsequent intervals of no longer than 1 year."*

FDA's Current Thinking:

FDA's current thinking is that our recommendation for active review of weight records to determine a 10-lb weight loss among Source Plasma donors can be satisfied by a review of such records at the time of the annual physical examination. Additionally, we believe that other donor informational materials should be harmonized with those in place for whole blood donor eligibility (i.e. that the donor information should contain wording analogous to the "FDA-accepted" Uniform Donor History Questionnaire in regard to unexplained weight loss.)