

Date: July 6, 2006
Reference No.: FDAA06013

VIA E-MAIL & USPS

Dockets Management Branch, HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

SUBJECT: Draft Guidance entitled, "Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments" (August 2001) [Docket No. 01 D-0220]

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these additional comments to append comments on the Draft Guidance entitled, "Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments," [hereinafter, "Draft Guidance"] submitted on November 14, 2001, by the American Blood Resources Association (ABRA). ABRA became the Source Division of PPTA in 2002. 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 not only adhere to FDA's strict regulatory requirements but also adopt industry-specific voluntary standards. PPTA members are committed to assuring the safety and availability of medically needed life-sustaining therapies.

In ABRA's comment letter dated November 14, 2001 (copy enclosed) several items were discussed. One area of concern by the industry was the inclusion in the draft of the following example in Section IV. A. (1):

"Other similar situations that would be reportable as an unforeseen or unexpected event that may affect the safety, purity, or potency of previously distributed products include: Donor tested negative and products were distributed, the donor returns and subsequently tested positive for any viral marker."

ABRA objected to including this situation as reportable based on it being neither “unforeseen” nor “unexpected,” with any risk being mitigated by safeguards implemented by the industry. PPTA’s argument that the situation is neither “unforeseen” nor “unexpected” remains valid. When an infectious disease is prevalent in the general population, it is known that there will be both a prevalence of disease in a donor population and an incidence of new infections in occasional donors. While both the prevalence and incidence of infections are below that in the general population, the acknowledgement of incident occurrence is addressed by “lookback,” a series of steps taken to identify, quarantine, and retrieve previous donations from the donor and notify consignees of donations shipped for manufacturing use. As required by regulation for HIV and recommendations for other viral markers, plasma establishments have developed and follow Standard Operating Procedures (SOPs) to address “lookback.” PPTA’s position that the event is neither “unforeseen” nor “unexpected” remains as stated in 2001.

PPTA is writing this additional comment letter to provide supplementary information on why the “safety, purity, and potency of previously distributed products” is not an issue. With the implementation of nucleic acid testing (NAT) for HIV and HCV [as required by regulation at 21 CFR 610.40(b) with issuance of the October 2004, Guidance for Industry: Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components (including Source Plasma and Source Leukocytes) to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV] and for HBV as a PPTA voluntary standard, the viral load of any previous donation that tested NAT negative is known to be below the detection limit of the test employed. This knowledge is in sharp contrast to concerns that donations drawn in the “window period” before antibody detection tests are positive are highly viremic.

It must be remembered that Source Plasma is a product for further manufacturing, not transfusion. The manufacturing processes for plasma therapies include robust viral clearance processes. In fact, FDA’s own lookback recommendations do not include “retrieval” once the donation is pooled for manufacturing, attesting to the efficiency of industry’s viral clearance processes. It should be noted that there has not been a hepatitis B, hepatitis C or HIV transmission by a plasma-derived Factor VIII product since 1987 (FDA’s Talk Paper, “New Recombinant Antihemophilic Factor Licensed,” July 25, 2003) or an immune globulin product in over ten years (Epidemiologic Notes and Reports: Outbreak of Hepatitis C Associated with Intravenous Immunoglobulin Administration—United States, October 1993 – June 1994, MMWR, July 22, 1994). Therefore, the “safety, purity or potency” of the “previously distributed products” and the final plasma-derived therapeutic are not in question.

As the event is neither “unexpected” nor “unforeseen” and further does not affect the “safety, purity or potency,” the discovery that a donor of a previously distributed donation of Source Plasma tests positive for a required viral marker test fails to meet the regulatory definition of a reportable event in 21 CFR 606.171 and should not be included in the list of examples in this guidance document.

It is known that several PPTA members have initiated actions to report these events after being pressured to do so during and after facility inspections. It should be noted that the initiation of reporting these events is not because the member agreed that the event is reportable. PPTA requests that FDA not only remove this example from the guidance when published but also advise the plasma companies that have commenced reporting that they can discontinue such reporting.

Should you have any questions regarding these comments or would like more information, please contact PPTA.

Respectfully submitted,



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CC: Diane Maloney, Associate Director for Policy, CBER
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5630 Fishers Lane, Room 1061
Rockville, MD 20852

SUBJECT: Draft Guidance entitled, "Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments (August 2001)," Docket No. 01 D-0220

Dear Sir or Madam:

ABRA is pleased to provide these comments on the Food and Drug Administration's (FDA's) Draft Guidance entitled, "Guidance for Industry: Biological Product Deviation Reporting for Blood and Plasma Establishments (August 2001)." ABRA is the trade association and standards-setting organization for the Source Plasma collection industry. ABRA represents the interests of approximately 400 plasma collection centers nationwide. These centers are responsible for the collection of nearly 11 million liters of Source Plasma annually. This plasma makes up roughly 60% of the world's plasma supply and is manufactured into life-supporting and life-sustaining therapies.

The Source Plasma industry recognizes the importance of Biological Product Deviation Reports (BPDR) and appreciates the Agency's assistance in defining the types of reports and the timeframe for reporting. Industry is requesting clarification on the submission of BPDRs for donors that subsequently test positive for viral markers and deferrals resulting from new donor history questions.

Section IV.A.(1) [page li] of the Draft Guidance includes the following language for describing unforeseen or unexpected events:

"Other similar situations that would be reportable as an unforeseen or unexpected event that may affect the safety, purity or potency of previously distributed

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products include: . . . Donor tested negative and products were distributed, the donor returns and subsequently tested positive for any viral marker.”

Given the baseline prevalence of the viruses tested in the population, the situation referenced above, in which a donor with a negative history subsequently tests positive for a viral marker, is not considered to be an “unexpected” or unforeseeable” event. Industry currently uses safety nets such as donor screening, the viral marker standard, PCR testing and inventory hold to reduce the potential risk associated with this type of event. Procedures, such as “lookback” in which units are retrieved and destroyed, protect public health. Therefore, industry is requesting that FDA re-consider the requirement for the submission of BPDRs for this type of event and consider an alternative data collection mechanism. Industry would be pleased to meet with FDA to discuss an alternate mechanism.

Industry is also requesting clarification on the BPDR requirements for the addition of a new question to the donor history questionnaire as part of the donor screening process. The Draft Guidance entitled, “Revised Preventative Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products (August 29, 2001)” recommends that Source Plasma centers include additional travel questions during the screening process- The guidance language implies that BPDRs will be required for donors that become deferred as a result of the new donor screening questions. This reporting mechanism is not an efficient means for reporting the impact of new screening questions. Industry is interested in meeting with FDA to discuss an alternate mechanism for the collection of these data.

ABRA appreciates the opportunity to comment on this Draft Guidance. Should you have any questions regarding these comments or would like additional information, please contact me. Thank you for your consideration.

Respectfully submitted,

Trish Landry
Director, Regulatory Affairs