



Formerly International Plasma Products Industry Association

0328 00 APR -6 P1.27

Reference No. CBER00004  
March 31, 2000

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

Re: Docket No. 99D-4577  
(Draft) Guidance for Industry  
Application of Current Statutory Authority to Nucleic Acid Testing of Pooled  
Plasma

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments to the Food and Drug Administration (FDA) on the Draft Guidance for Industry, Application of Current Statutory Authority to Nucleic Acid Testing of Pooled Plasma. PPTA is the trade association representing the major commercial producers of plasma derivatives including Alpha Therapeutic Corp., Aventis Berhing, LLC, Baxter Healthcare, Bayer, and ZLB. We believe that stakeholder participation in the regulatory process is important in achieving rational regulations, and we appreciate the extension granted by the FDA to allow additional comments on this draft guidance.

**General Comments:**

As the document scope encompasses the testing of both blood and plasma, it is suggested that the title be changed to "... Testing of Blood and Source Plasma" instead of "... Testing of Pooled Plasma".

There appears to be some inconsistency with respect to the name of the material being tested; in some cases it is referred to as "blood" and in others it is referred to as "plasma". It is suggested that the term "blood and/or source plasma" always be used.

FDA makes no distinction in this guidance to NAT used for in process controls (IPC) versus NAT used for donor screening. However, at recent public meetings (BPAC September, 16, 1999, and NAT Meeting, December 14, 1999) the agency discussed its current thinking that NAT for viruses that do not have a licensed serology test and produce a self limiting disease (i.e., Parvovirus B-19), could be implemented as an IPC and not as a donor screening test. We therefore request that this guidance be revised to reflect this policy.

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PPTA recommends that all NAT supplements to product files be submitted as CBE 30. Currently, the data supporting the validity of NAT for donor screening has already been reviewed by the FDA under an IND, and many products manufactured from plasma screened by NAT are already on the market. The addition of a *licensed* NAT for donor screening (as opposed to the donor screening currently conducted under IND) will not change the manufacturing process for final products and therefore will have minimal potential to adversely impact the identity, strength, quality, purity, or potency of the final product.

Similarly, for tests to be implemented as in-process Quality Control tests (e.g. Parvo, HAV), submission as CBE immediate should be adequate. While these tests have not been implemented under INDs as the donor screening tests have been, the FDA has recognized that IPCs are intended to improve the quality of the starting plasma. The implementation of an IPC will have little chance to affect the manufacturing process for final products and therefore will have minimal potential to adversely impact the identity, strength, quality, purity, or potency of the final product. Since NAT is intended to increase the quality of the plasma, and ultimately the product, we believe that it is preferable to make these changes as quickly as possible, which can be accomplished through the CBE immediate filing.

The FDA draft guidance focuses on the identification of an individual positive unit with subsequent identification and notification of the donor, and thus requires an IND. The guidance document is not harmonized with the European guideline and the Japanese draft guideline. Testing of production pools, not under consideration in the U.S., is mandatory in Europe, and anticipated in Japan. We therefore propose that these regulatory authorities make additional efforts to harmonize the requirements on implementation of NAT.

### **Section III. BACKGROUND**

Re: Last paragraph – donor notification/counseling and product retrieval for positive units

It is implied that whenever any unit is determined to be positive by NAT, donor deferral, notification and counseling, plus product retrieval should occur. As discussed above, the FDA's current thinking does not indicate that this is required for IPCs. We suggested that the relevant portions of the last paragraph be clarified/modified.

### **Section IV.B**

Re: Four different regulatory approaches.

The use of four different approaches seems to make the regulatory requirements unnecessarily complicated. It is recommended that there be two sets of

requirements/conditions. One would cover the manufacturer of the test/test kit, and the other would cover the user of the test/test kit.

- A. The manufacturer would file an IND followed by a BLA (and perform tests on reference panels provided by FDA).
- B. The user (who may either purchase test/test kit and perform testing in-house, or who may send samples for testing to the test/test kit manufacturer) would file a CBE 30 for each plasma/blood product tested and provide details of the system used to manage the information generated by the testing.

A combined manufacturer and user (develops own test/test kit and uses it for its own products) would have to meet the requirements for both A and B.

Re: Reference panels of infectious agents provided by FDA to test/test kit manufacturers

It is recommended that the appropriate sections be reworded to clarify/confirm that it is the lot release of the tests/test kits that is dependent on the reference panel testing results (not the material produced from tested plasma).

In addition to the test/test kit's ability to accurately identify the reference panel agents, is the sensitivity of test/test kits also to be evaluated? If so, it is recommended that FDA adopt international unit nomenclature so that detection limits between different laboratories can be accurately compared.

Following a review of the Section IV.B it seems that the reader would ask the following questions. It is therefore recommended that the answers be included in the final version of the guidance document.

- Would panel testing be done for every test/test kit lot?
- Assuming that panel testing is not performed for every lot, how often would panel testing be performed?
- How would a panel test failure impact tests/test kits manufactured?
- Could panel testing frequency be reduced after a specific number of successful tests?
- Would all test results have to be submitted to CBER?
- Would manufacturers have to wait for CBER authorization to release lots?

The last sentence in last paragraph of Section B (fourth approach) states "Performance would be subject to lot-release testing by CBER" which implies CBER would perform the testing, whereas in three previous paragraphs it states/implies that the manufacturer would perform the testing using panels provided by CBER. It is suggested that the document be revised to clearly define who will do testing and monitoring.

We appreciate the opportunity to provide these comments to the agency on this topic and would be happy to answer any questions regarding this issue.

Sincerely,



Jason Bablak  
Director, Regulatory Affairs



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