



Plasma Protein Therapeutics Association

01D-0584

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VIA HAND DELIVERY

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

SUBJECT: Draft Guidance entitled, "Guidance for Industry: Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors to Adequately Reduce the Risk of Transmission of HIV-1 and HCV," dated December 2001, Docket No. 01D-0584

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) is pleased to provide these comments on the Food and Drug Administration's (FDA's) draft guidance entitled, "Guidance for Industry: Use of Nucleic Acid Tests on Pooled Samples from Source Plasma Donors to Adequately Reduce the Risk of Transmission of HIV-1 and HCV," dated December 2001 (hereinafter "Draft Guidance"). 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, and burns among other things. PPTA members are committed to assuring the safety and availability of these medically needed life-sustaining therapies for the people who depend on them.

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PPTA recognizes the importance of the use of state-of-the-art licensed Nucleic Acid Amplification Technology (NAT) testing for hepatitis C (HCV) and Human Immunodeficiency Virus-1 (HIV-1). PPTA also recognizes the importance of the availability of test results prior to pooling. However, industry would benefit by improved clarity of several issues addressed in the Draft Guidance. The implementation of the Draft Guidance recommendations, as written, has the potential to severely impact the supply and availability of these important plasma therapies to consumers and patients. Therefore, the Draft Guidance should be revised to reflect the current industry management scenarios (explained in section 1 of this document) to assure the ultimate goal of the use of licensed NAT testing prior to pooling.

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The current industry paradigm for NAT testing is described in section 1 of this document. PPTA's recommendations for revisions to the Draft Guidance reflect the industry paradigm. These recommendations are aimed at maintaining industry operations from a logistical standpoint and are aimed at providing the highest quality plasma therapeutics. Specifically, recommendations for the reporting requirements, implementation timeframe, and labeling are discussed in sections 2, 3, and 4, respectively.

1. Current Industry Paradigm for NAT Testing

At present, all plasma collection establishments and producers of plasma therapeutics have systems in place to conduct and manage HIV-1 and HCV NAT testing. There are several scenarios by which NAT testing is managed in the plasma therapeutics industry. Accommodation of these different scenarios by FDA will further the Agency's goal of assuring that all plasma donations are tested by licensed NAT.

While it is not possible to discuss every testing paradigm, PPTA would like to highlight the two general representative management scenarios:

A. In-House Testing

In one approach the plasma therapeutics fractionation facility assumes primary responsibility for testing and sample management. Collection establishments ship Source Plasma, along with samples to be tested by NAT for HIV-1 and HCV, that has undergone serology testing and found to be acceptable for shipment to the fractionation facility. The fractionation facilities have Standard Operating Procedures (SOPs) in place to allow Source Plasma pooling to take place only after the results for NAT testing have been obtained. Similarly, the collection establishments have systems in place to work in parallel with the fractionation facilities so that proper donor notification, counseling, lookback, and product retrieval occurs.

B. Contract Testing Laboratory

In another scenario, the collection establishment or plasma therapeutics fractionation facility sends test samples to a contract testing laboratory. In this scenario, collection establishments employ one of two management paradigms. In one common management approach, the Source Plasma is shipped to the fractionation facility pending completion of the NAT testing. The collection facilities using this approach are often smaller entities and rely on the fractionation facility's logistics and storage capacity to fully manage the Source Plasma inventory pending NAT testing. In another less frequently employed

management approach, Source Plasma is stored by the collection establishment pending NAT testing. In both of these approaches, the collection establishments and fractionation facilities have SOPs in place to allow Source Plasma pooling to take place only after the NAT test results have been obtained. As mentioned above, the collection establishments and fractionation facilities also have systems in place so that proper donor notification, counseling, lookback, and product retrieval occurs.

Regardless as to which scenario is followed, establishments have adequate systems to assure that Source Plasma pooling is not performed prior to obtaining NAT test results. In addition, there are systems in place to assure proper donor deferral and product management.

Most if not all collection facilities would be unable to manage the inventory storage if they were required to hold Source Plasma pending NAT test results. The inability to maintain increased inventory could force the collection facilities to significantly reduce their current collection capacity. This reduction in capacity could also have the potential to lead to significant plasma therapy shortages. Due to the complex nature of NAT testing for pooled samples, test resolution can require a considerable amount of time. Such a requirement would cripple the current mechanism, thereby forcing many collectors to drastically reduce collections for the foreseeable future. Moreover, as demonstrated by the above scenarios, the current management scenarios operate efficiently and effectively and will allow for industry to appropriately use licensed NAT testing. Therefore, PPTA recommends that the Final Guidance Document should be revised to reflect the current industry management scenarios for NAT testing for HIV-1 and HCV. Specifically, the implementation section of the Draft Guidance should be revised to reflect the current management scenarios described above.

2. Reporting Requirements

PPTA recommends that the Draft Guidance be revised to include provisions for reporting requirements depending on the scenario. The current Draft Guidance only provides for the use of prior approval supplements (PAS) to implement HIV-1 and HCV NAT in establishments (21 C.F.R. §601.12(b)). The Final Guidance should provide for the use of alternative reporting requirements depending upon the scenario. For example, if a licensed fractionation establishment begins using a licensed NAT according to the manufacturer's test insert at their facility, the establishment should be allowed to notify FDA of a testing change in their annual report. In the event that an establishment begins using a new contract laboratory to perform NAT, and the laboratory already performs infectious disease testing for plasma products, then the establishment should be allowed to report this change using the CBE-30 mechanism (21 C.F.R. §601.12(c)). Similarly, if a contract

laboratory that has been performing under an investigational new drug application (IND) and then receives FDA approval they should be authorized to submit the change using the CBE-30 mechanism. If the contract laboratory has not previously performed infectious disease testing, the establishment should report the change as a PAS.

3. Implementation Timeframe

PPTA recommends that the Final Guidance should permit adequate time to prepare for a change in testing or for the submission of data to support a Biologics License Application (BLA) for licensing a test for NAT for HIV-1 and/or HCV. Currently, the implementation date in the Draft Guidance is June 1, 2002. A minimum of six months following the publication of the Final Guidance is reasonable to implement the licensed NAT test provided that the CBE-30 mechanism is included in the Final Guidance, as discussed in section 2 of this document (Reporting Requirements). If all changes have to be reported as a PAS, as included in the current Draft Guidance, a considerably longer period of time would be needed for establishments to implement the necessary changes.

PPTA also recommends that an establishment that is currently conducting NAT testing under an IND should be authorized to continue NAT testing under the IND. The establishment should not be required to submit for approval to FDA to use a licensed NAT test for an additional six months beyond the implementation deadline proposed in this document provided that the establishment submits for licensure of its in-house NAT test by the implementation deadline. The additional six months would also allow establishments to avoid the problems associated with duplicate testing (*e.g.*, conflicting test results). This extension of time would not pose a public health risk as all Source Plasma would continue to be NAT tested.

Performing two different NAT tests systems in parallel (one approved and one under IND) carries the risk of having conflicting test results and the need to implement systems to resolve such issues. Each single donation would need two instead of one NAT test samples that must be shipped, pooled and tested in different pathways, in parallel. In addition, the results of the tests would need to be matched before release of the donation. To create such a system would be overly burdensome, without adding value to the process.

In a duplicate testing scenario as recommended in the Draft Guidance there would be a substantial burden imposed on both industry and the Agency. For industry, this would result in submission of documents pertaining to the change of the testing site to the contract testing laboratory and again back to the in-house laboratory, once licensure is approved. This would also involve numerous changes in SOPs as well as requiring a significant amount of resources to be employed in staff training. For the Agency, the duplicate testing scenario would result in the use of a substantial

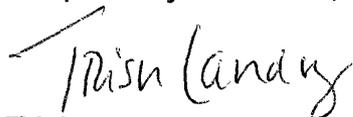
amount of resources to review and approve the submissions. Therefore, PPTA recommends that the Final Guidance should grant an additional six months for implementation for an establishment that is currently conducting NAT testing under an IND, provided that the establishment submits for licensure of its in-house NAT test by the implementation deadline.

4. Labeling

PPTA recommends that the Final Guidance provide that upon implementation of a licensed NAT test for HIV-1 and HCV, establishments that have obtained NAT test results prior to shipment, should be authorized to include appropriate Source Plasma labeling language that reflects that NAT testing has been completed. For example, the FDA Draft Guidance entitled, "Use of Nucleic Acid Tests on Pooled and Individual Samples from Donors of Whole Blood and Blood Components for Transfusion to Adequately and Appropriately Reduce the Risk of Transmission of HIV-1 and HCV," includes labeling language that would be acceptable for use and submitted for use as a change being effected immediately (CBE). The Draft Guidance should similarly include labeling language that, if used by a Source Plasma establishment, would enable the establishment to make the labeling change using a CBE.

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

Respectfully submitted,



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