Plasma Protein Therapeutics Association

Date: December 20, 2018 **VIA WEB**

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

SUBJECT: Further Testing of Donations That Are Reactive on a Licensed Donor Screening Test for Antibodies to Hepatitis C Virus; Draft Guidance for Industry
Docket No. FDA-2018-D-3197

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) appreciates the opportunity to participate in the guidance development process and is pleased to provide these comments on the draft guidance for industry "Further Testing of Donations That Are Reactive on a Licensed Donor Screening Test for Antibodies to Hepatitis C Virus;" September 2018 (hereinafter "Draft Guidance"). We will describe in this letter why we believe what is described in the Draft Guidance would create a need for an additional test that is not required by 21 CFR 610.40 and does not advance the goals of donor health shared by PPTA and the FDA.

PPTA is the standards-setting and global advocacy organization that represents the private sector manufacturers of plasma-derived and recombinant analog therapies, collectively known as plasma protein therapies, and the collectors of Source Plasma used for fractionation. Plasma protein therapies are primarily used in the treatment of a particular set of rare diseases. These diseases are often genetic, chronic, life-threatening conditions that require patients to receive regular infusions or injections of plasma protein therapies for the duration of their lives. These therapies include blood clotting factors for individuals with bleeding disorders, immunoglobulins (IG) to treat a complex of diseases in persons with antibody deficiencies and severe autoimmune disorders, 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 to treat individuals with severe liver diseases and, in emergency-room settings, shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

The Draft Guidance provides blood establishments, including Source Plasma establishments (SPE), with recommendations for further testing of donations that are reactive on a licensed donor screening test for antibodies to hepatitis C virus (anti-HCV), as required under 21 CFR 610.40(e). The interpretation guide in the Draft Guidance (Section III. Recommendations for further testing of donations that are repeatedly reactive on a licensed screening test for anti-HCV) requires that when there is a repeat reactive anti-HCV screening result and HCV RNA is not detected, further testing is necessary. The guidance defines further testing as a second, different licensed donor screening test for anti-HCV. The guidance also gives recommendations for the actions to be taken based on the further testing result. In both cases (negative and repeat reactive) the recommendations are to appropriately counsel the donor.

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PPTA would like clarification on a few items found in the Draft Guidance:

- The second sentence in the first paragraph of page 2 states, "This guidance also does not provide recommendations for product disposition, donor deferral or re-entry." This statement appears to be a conflict with the instructions found in Section III under 2a and 2b regarding what steps to take when referencing CFR 610.47. Could you please clarify in the final guidance?

- Item 2 on page 4 states, "You should perform a second, different licensed donor screening test."
  Questions: Is there a time frame for the completion of this test? Should a different sample be used?

- Item 2 b. on page 4 states, "If the result is repeatedly-reactive for anti-HCV, …"
  Question: Should it be presumed that no additional HCV NAT is necessary? Clarification would be needed to indicate that additional HCV NAT testing is not required when following this protocol. Corresponding recommendations are needed to address the issue in an establishment's SOPs.

The regulation that is the subject of the Draft Guidance, 21 CFR 610.40, requires that all Source Plasma donations are tested for evidence of HCV. If that test is found to be reactive, 21 CFR 610.40(e), requires an additional test to be performed to provide additional information concerning the donor's infection status. The Draft Guidance indicates a need for third test (second anti-HCV) depending on the result of the second test. This would appear to be beyond the scope of the regulation without furthering the regulatory goal of obtaining additional information concerning the donor's infection status.

The Draft Guidance suggests that the donor be counseled on the result of the third test. The counseling provided after the third test is the same as would be provided after the second test, which is the NAT test. The donor is counseled to seek medical attention as soon as possible. The donor is also counseled to be aware that they may be infectious and could pose a risk to others and to take appropriate caution in personal hygiene. After this counseling, it is hoped that the donor will visit a medical provider. Those providers would perform a diagnostic test for HCV. Therefore, a fourth test.

The requirement of a third test has some problems. First, the guidance requires using another licensed donor screening test for anti-HCV. This is challenging because there are only two test systems licensed by the FDA for anti-HCV donor screening. These are the Ortho HCV Version 3.0 ELISA Test System (Ortho Clinical Diagnostics) and Abbott PRISM HCV (Abbott Laboratories). Both systems are qualitative and differ by recombinant HCV antigens for detection of anti HCV antibodies and the chemistry of the test systems, one being chromogenic assay (Ortho) and another being chemiluminescent assay (Abbott).

Additionally, the third test would increase the cost of manufacturing plasma protein therapies since each SPE will be obligated to make arrangements with third party laboratories (which would also need to be an approved supplier which requires a contract, quality agreement and on-site inspection) to perform this testing. Although there are many clinical reference laboratories that perform infectious disease testing, including for anti-HCV, most do not use test systems licensed for donor screening. Those few who do perform donor screening testing may not use the alternative platform needed to complete further testing. The anticipated burden would exceed $500,000 without improving donor health or protecting public health.

Furthermore, a problem caused by the third test is the unnecessary delay in donor advisement. The third test would lengthen the time needed to complete testing and will add unnecessary complexity due to the additional shipping of samples and arrangement of an appropriate secure communications process for result reporting. The requirement of a third test would delay the counseling of a donor if an SPE waited for all the required tests to be completed before counseling a donor. This certainly would not be in the best interest of public health.

Conclusion

The third test found in the Draft Guidance would not benefit Source Plasma donors and would create additional cost and delay in the manufacturing plasma protein therapies. Therefore, PPTA is requesting the FDA exempt SPE's from the additional testing requirements in the final guidance.

Should the FDA decide to include SPE's in the final guidance, we would ask the FDA to include an alternative algorithm choice of using FDA-cleared moderate or high-complexity serology assays (anti-HCV or NAT) to provide additional information concerning the reactive donor's HCV infection status in addition to assays licensed for donor screening. This would allow the additional testing to be performed in a reasonable time frame and would not in any way harm or reduce the value of information required to protect, in the case of plasma collected for manufacturing use, the plasma supply, patients and the plasma donors.

PPTA appreciates your consideration of our concerns and welcomes the opportunity to discuss them further. Should you have any questions or require additional information please do not hesitate to contact me at: bspeir@pptaglobal.org or (443) 433-1110.

Thank You,

Bill Speir
Senior Director, State Affairs