

## **Blood Products Advisory Committee Meeting, March 15, 2001**

### **Comparative Sensitivity of HBsAg and HBV NAT Tests**

**Data presented by the American Red Cross (ARC) at the March 16, 2000 Blood Products Advisory Committee meeting, indicated that HBV NAT testing of Source Plasma donations, using the format of testing pools containing 512 plasma samples, i.e., representing 512 donors, currently being performed under IND, might offer little improvement in sensitivity compared to HBsAg testing of individual donations using some currently licensed tests. Furthermore, the ARC data indicated the possibility that testing individual units using some newer, more sensitive, HBsAg tests, might be--marginally--more sensitive than pooled HBV NAT. The ARC data was based on studies performed on seroconversion samples.**

**As a response to the ARC data, FDA and industry, in consultation with NIH, are performing studies that directly compare the sensitivity of HBsAg individual donor sample testing with HBV NAT pooled donor sample testing, using 10 seroconversion panels and 28 well characterized controls.**

**The study specifically involves a comparison of testing of individual samples from the seroconversion panels using various HBsAg screening assays to the following:**

- (1) HBV NAT testing using the 1200 and 512 donor sample pool formats that are presently being used for testing Source Plasma under IND.**
- (2) HBV NAT testing in the 16 and 24 donor sample pool formats, which are currently used for testing Whole Blood and components for HCV and HIV under IND. (Note: In the United States, at the present time Whole Blood and components for transfusion are not tested by HBV NAT assays. HBV NAT testing of all blood donations has been implemented in Japan, and is being discussed in Europe.)**
- (3) Single sample HBV NAT. This part of the study is being performed only by those organizations that use the Whole Blood and components testing format described in (2) above. Single unit NAT testing has not yet been fully developed for high-volume blood screening.**

**The results of the study, which is being analysed, will be used to estimate the increase in the yield of detecting potentially HBV infectious units by using (a) newer, more sensitive, HBsAg assays, (b) current HBV NAT pool testing methods and (c) single unit HBV NAT testing as compared to currently licensed HBsAg assays.**

**The sensitivities of newer tests for HBsAg on individual donations range from about 0.10 to about 0.20 ng HBsAg/mL; the sensitivity ranges from about 0.4 to 1.0 ng HBsAg/mL in some of the older tests. In the case of Source Plasma donor sample**

**pool testing under IND (1200 and 512 donor sample pools), the lower limit of detectability in the individual donation varies from about 5,000 to about 10,000 gEq/mL.**

**In donor sample pool testing, the sensitivity of NAT in the individual donation varies according to the size of the donor sample pool, i.e., as to whether the pool is composed of 1200, 512, 24, or 16 donor samples, and to the lower limit of detection of the particular HBV DNA NAT assay used. Currently, this ranges from about 10 to 50 gEq/mL. During manufacture of injectable products from human plasma, effective, validated, viral inactivation and/or removal steps are in place.<sup>1</sup> No such viral inactivation or removal steps currently constitute a part of processing Whole Blood and components for transfusion. (Also, as a practical matter, in current pool NAT testing procedures--as has already been described above--donor pool sample sizes for Source Plasma are much larger than those used for Whole Blood and components, 1200 and 512 donor samples versus 24 and 16. Thus, the lower limit of detection of nucleic acid that can be attained in the individual donation, is much lower in Whole Blood and component testing than in Source Plasma testing.)**

**The two policy issues that will be specifically addressed at the meeting are as follows:**

- 1. In light of the fact that sensitive HBsAg tests are available and that more sensitive tests are under development, FDA is considering changing the lot-release requirements of licensed HBsAg tests to lower the required limit of detection.**
- 2. FDA is considering establishing two separate standards for the lower limits of detection for HBV DNA in individual donations, i.e., one for plasma for further manufacture into injectable products and a different one for Whole Blood and components.**

**FDA will ask the Committee to vote on the following two questions:**

- 1. As tests for HBsAg continue to increase in sensitivity, should FDA change the lot-release specifications for licensed HBsAg tests in regard to lower limits of detection?**
- 2. Inasmuch as products derived from pooled plasma undergo validated viral inactivation/removal steps during their manufacture, whereas Whole Blood and components are not subjected to such steps, should FDA set two separate standards for the lower limits of detectability of HBV DNA in individual donations: one standard for plasma for further manufacture and a different standard for Whole Blood and components?**

## Reference

1. **Tabor E. The epidemiology of virus transmission by plasma derivatives: clinical studies verifying the lack of transmission of hepatitis B and C viruses and HIV type 1. Transfusion 1999;39:1160-1168**