
Transplantation Safety & Hepatitis B virus Nucleic Acid Testing (NAT)

Lori Lai, M.B.A., D.H.S., Sr. Scientific Affairs Manager, Novartis Vaccines and Diagnostics, Inc.

Overview

This paper examines the current movement toward adoption of hepatitis B virus (HBV) nucleic acid testing (NAT), as well as highlights the benefits of using the Procleix® Ultrio® Assay to screen for HIV-1, HCV, and HBV on the fully automated Procleix® TIGRIS® System.

HBV, A CONTINUING THREAT

HBV infection is the leading cause of hepatocellular carcinoma¹ (the most common cancer of the liver in the world), liver failure, and liver transplantation. There are over 350,000,000 chronic carriers of hepatitis B virus worldwide with over 2 billion infected.² Expected outcomes of infections are as follows: 90% recover, 7–9% become chronic carriers, and 1–3% die.

In the U.S. in 2010, overall prevalence was 4.7% (anti-HBc) and 0.27% (HBsAg), and 0.5% - 8.2% (HBsAg) in the native Alaskan population³ (though vaccinations have resulted in a decrease in infections in the last two decades)⁴. There were 2,003 HBV related deaths in 2006⁵, and an estimated 1.25 million Americans with chronic HBV infection⁶. Foreign-born residents can have HBV prevalence rates exceeding 15%⁵. HBV infection is more common in men than in women⁶ and intravenous drug use remains a significant mode of HBV transmission (23% of all cases)⁶.

Although HBV seroprevalence in the general U.S. population has been lower than other global regions, this very common, infectious viral disease continues to be a worldwide health concern. As a result of several factors such as immigration patterns, the number of unvaccinated people, and higher risk lifestyle practices, HBV is expected to remain a public health risk in the U.S. for the next 20 to 30 years⁶.

HBV TTIS – POTENTIALLY FATAL

The risk of HBV transfusion- or transplantation-transmitted infection (TTI) is greatest for recipients who are immunosuppressed or have sepsis or autoimmune hepatitis. A number of cases of HBV transfusion-transmitted infections have been documented, with resulting deaths due to HBV infection complications in some cases, where recipients received blood or blood products from donors with low HBV DNA copy numbers with no detectable anti-HBs⁷. Several cases, including one fatality, have also been documented for HBV transplantation-transmitted infections^{8,9,10} despite vaccinations and prophylactic treatments.

NAT SCREENING INCREASING SAFETY OF BLOOD

NAT technology has led to improvements in the efficiency of viral sequence amplification, the clinical sensitivity of molecular screening compared to serology, and a marked decrease in the window period of infection¹¹. Scientific models estimate that NAT reduces the infectious window period by 35–91% for HIV-1 (9 days), HCV (53 days), and HBV (14 days) with individual donor nucleic acid testing (ID-NAT).^{12,13}

SCREENING TEST ADOPTION TRENDS

Screening adoption patterns over the last 70 years have shown faster adoption of test methods that detect pathogens impacting the safety of blood (e.g., HBV was recognized as a transfusion risk in 1940 and the first screening assay was developed in 1970, 30 years later; for HIV, the adoption of a new screening method took just three years (1982–1985); and WNV was one year (2002–2003).¹⁴ Adoption of HBV NAT worldwide has also been increasing rapidly (~5 countries in 2005 to ~30 in 2010).¹⁵

FAQ

➤ What prompted the change from the Procleix HIV-1/HCV Assay (“duplex”) to the Procleix Ultrio Assay (Ultrio)?

An increasing trend toward, and need for, HBV screening worldwide, along with continued industry-wide adoption of next-generation multiplex NAT screening assays, has diminished the demand for the HIV-1/HCV assay. As HBV transfusion risk continues to be a concern, the introduction of NAT assays has reduced the residual risk of infection¹⁶, modifying the assay to detect additional viruses such as HBV has proven to be beneficial for many customers.

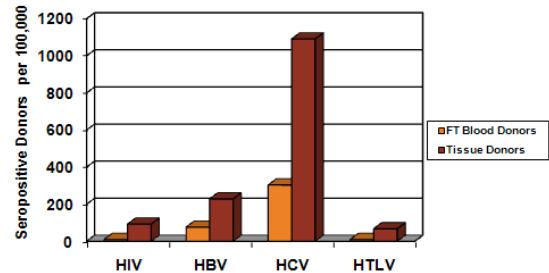
Please note that like the Procleix HIV-1/HCV Assay, the Procleix Ultrio Assay also uses NAT assay technology with specific target capture of only viral DNA and RNA, magnetic-based micro-particle wash, patented transcription-mediated amplification (TMA) testing methodology, and detection via light emissions of captured sequences in the Dual Kinetic Assay (DKA).^{18,19}

➤ **What else sets the Procleix Ultrio Assay apart from the HIV-1/HCV assay?**

The Procleix Ultrio Assay can run on the Procleix TIGRIS System, a fully-automated sample handling and assay processing instrument. TIGRIS has a similar TAT as the Procleix System, with 24/7 standby for urgent sample testing via bracketing; can perform discriminatory tests on the same platform, handle Positive ID tracking, and the built-in Reagent Dispense Verification (RDV) system monitors critical reagent addition steps.

➤ **Why is testing for HBV important for tissue/organ donors?**

The prevalence of viral infections in tissue donors is higher than in first-time blood donors¹⁶ (see image on right), which leads to the conclusion that the introduction of HBV NAT would potentially reduce the residual risk from HBV infection.



➤ **What kind of results can I expect if I test for HBV?**

Seronegative cadaveric blood specificity is consistent with whole blood specimens. The next-generation Ultrio Assay has shown 99.9977% specificity (n = 1.9 million blood donor samples P16).

Dr. Susan Stramer, Scientific Support Office, American Red Cross (ARC), showed test specificity data for Ultrio using the TIGRIS instrument at the 2009 AABB conference. Minipools of 16 were tested across three ARC National Testing Labs, and of the 1,992,160 donations screened, specificity was 99.9977% with a 95% confidence interval of 99.9970% to 99.9984%.¹⁷

Also, in an e-published article, where ARC documented the use of the Procleix TIGRIS System with the Procleix Ultrio Assay in MP16 format to screen blood donors, a total of 699 confirmed HBV infected donors were detected (n = 6.5 million).¹⁸

➤ **Will I need to increase my sample size with the Procleix Ultrio Assay?**

Both the Ultrio and HIV-1/HCV Assays have comparable volume requirements for non-reactive donor samples. For reactive samples on the Ultrio assay, 0.5 mL more is needed for the additional discriminatory HBV test.

➤ **Can I freeze my samples using the Procleix Ultrio Assay, and if so, for how long?**

Yes. Plasma or serum from cadaveric donors can be stored for up to 14 days @ ≤ -70° C using the Ultrio Assay.^{19,21}

➤ **How long can I use the Procleix HIV-1/HCV Assay? Which part numbers are affected by the obsolescence?**

The last assay lot for the Procleix HIV-1/HCV Assay will expire on March 15, 2012. The part numbers that will be discontinued are: 301118 and 301117, Procleix HIV-1/HCV Assay, 1K and 5K Test Kits; 301115, Procleix HIV-1 and HCV Discriminatory Probe Reagents; and 301119, Procleix HIV-1/HCV Assay Calibrators.

¹ Nishioka, K. *Viral Hepatitis and Liver Diseases*, 1994, pg 12-15

² <http://www.who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/index1.html> (accessed Aug. 2011)

³ McMahon BJ, Schoenberg S, Bulkow L, Wainwright RB, Fitzgerald MA, Parkinson AJ, Coker E, Ritter D. Seroprevalence of hepatitis B viral markers in 52,000 Alaska Natives. *Am J Epidemiol* 1993;138: 544-9.

⁴ Wasley, A. et al. (2010) *J. Infec. Dis.* 202(2):192

⁵ Kim, W.R. (2009) *Hepatology* 49:S28

⁶ <http://www.cdc.gov/hepatitis/HBV/HBVFaq.htm> (accessed Aug. 2011)

⁷ Gerlich, W. et al. (2007) *J Med Virol* 79:S32

⁸ Avelino-Silva et al. *Clin. Transplant* 2010; 24: 785-746

⁹ Ko WJ et al. *J Heart Lung Transplant* 2001; 20(8): 865-75

¹⁰ Razonable RR & Eid AJ. *Minerva Med* 2009; 100(8): 479-501

¹¹ Hollinger B. F. *Transfusion* (2008) 48:1001

¹² Busch, MP, *Evolving Approaches to Estimate Risks of Transfusion-Transmitted Viral Infections: Incidence-Window Period Model After Ten Years*. Dax EM, Farrugia A, Vyas GN (editors): *Advances in Transfusion Safety – Volume IV, Development in Biologicals* (Basel), Basel, Karger, 2007, vol 127, pp. 87-112.

¹³ Kleinmann SH, Busch MP, *Assessing the Impact of HBV NAT on Window Period Reduction and Residual Risk*, *J Clin Virol* 36 Suppl. 1 (2006) S23-S29.

¹⁴ Alter H. *Transfusion Medicine Reviews* 2008;22(2): 97-102

¹⁵ Roth et al. *Vox Sanguinis* (2011) e-publication

¹⁶ Zou S. et al *N Eng. J Med* 2004, 352, 751.

¹⁷ Stramer, S. et al (2009) Seminar content from *Transfusion* 49 Supplement:1A

¹⁸ Stramer SL et al. *Transfusion* 2011 (e-published)

¹⁹ Procleix Ultrio Assay Package Insert, P/N 502165 Rev. A / QCS 501633 (effective date 2011-03)

²⁰ Procleix HIV-1/HCV Assay Package Insert, P/N 501847 Rev. A / QCS 501036 (effective date 2010-06)

²¹ The 2°-25° C period indicated above may occur at any time.