

AABB 2005: new products, techniques and automation on the agenda

Tools for safer blood products, emerging technologies and automation were among the key themes at the annual AABB exhibition and meeting on October 14-18 2005, in Seattle, Washington, which attracted 3% more attendees (7,049), 17% of them hailing from outside the US. HBV NAT and bacterial contamination testing were major topics of discussion from a clinical issues standpoint, and there was much new product approval and launch news during what was an exciting show, writes Kerri Weinert and Carrie Cresenzi, of Boston Biomedical Consultants Inc

Current US blood donation/supply

Based on preliminary estimates, the US blood supply in 2005 has remained relatively stable, at approximately 15 million units of whole blood, and there have been no major changes in factors encouraging or limiting blood donation.

According to the American Red Cross (ARC), as of late November 2005, their red cell collections reflected a 2.5% increase versus the same period in the prior year, with September very strong due to the response for Hurricane Katrina.

The ARC's collection increase was also positively impacted by the timing of holidays and extra collection days in the reporting period. The ARC, America's Blood Centers (ABC), and the AABB nationwide blood donation awareness campaign is ongoing.

In order to improve compliance and cost containment, four ARC National Testing Laboratories (NTL) were closed by March 31 2005, leaving five remaining. This increased consolidation heightens the need for automation of NAT (especially for individual donor testing) and IAT-based testing (see below).

Automation/NAT-based testing

HBV NAT was a major clinical issue highlighted at AABB 2005, with 11 abstracts read. In October 2004, the Blood Products Advisory Committee (BPAC) approved a proposed algorithm to re-enter donors deferred for repeatedly reactive (RR) anti-HBc test results on more than one occasion if the following criteria were met:

- after a minimum of eight weeks from the last RR anti-HBc test, a new (non-donation) sample tests non-reactive (NR) for HBsAg, anti-HBc, and negative for HBV NAT (95% LOD at = 10 copies/mL) with an FDA licensed assay; and
- when the donor presents to donate, he/she must also be NR to these three tests.

Core re-entry is now feasible because there is a licensed NAT, and Abbott's Prism HBcore is licensed, which provides a more specific core assay as well. Roche received an FDA licence for its Cobas AmpliScreen HBV test in April 2005 for testing whole blood, blood components, and source plasma from living donors and an expanded claim in August 2005 for screening of individual cadaveric organ and tissue donations.

However, adoption of HBV NAT has not been immediate because of the controversy surrounding whether the clinical significance of the yield of seronegative/NAT reactive donors seen in clinical trials justifies the addition of HBV NAT to current testing.

While a low number of HBV infections will be prevented, most of these infections will resolve with no clinical sequelae, unlike HIV and HCV. Given this data, HBV NAT is not mandated by the FDA at this time. This may change in the future as multiplex NAT testing, including HCV, HIV, and HBV,

becomes available and automation allows testing of individual donations rather than pools of samples, which will increase yield.

As a result of these factors, HBV NAT testing may not be feasible at some testing sites. Automation, especially for higher-volume testing sites, enhances feasibility of smaller mini-pools or IDT; however, demonstration of clinical utility compared to current serological tests in light of increased costs is key to facilitating adoption.

Chiron/Roche high-profile HBV NAT activity

In order to promote increased blood safety through HBV NAT, Chiron and Roche continued to invest in market development activities, such as the AABB 2005. Chiron continued to discuss the potential of the Procleix Ultrio Assay on the Procleix Tigris system (not commercially available in the US). The Procleix Tigris system would provide enhanced automation that would allow for improved workflow and smaller pool sizes or IDT.

In addition, the company believes that HBV NAT will provide added safety in low-prevalence areas where HBsAg testing may miss positive samples. As part of its educational efforts, Chiron provided an unrestricted educational grant to support a companion day programme, "HBV NAT Testing: A Global Perspective" at AABB 2005.

As mentioned previously, IDT NAT may be valuable for re-entry of anti-HBc false-positive donors. Several testing sites in the US, along with Roche, have been evaluating an algorithm that uses the Cobas AmpliScreen HBV test in triplicate PCR reactions (to achieve a LOD 95% of the time of <10 copies/mL) and the Prism HBcore assay to retrieve previously-deferred donors. Roche may submit data for a supplement to its BLA for the Cobas AmpliScreen HBV test to be used for donor re-entry.

Chiron displayed a Procleix Tigris system in its booth and, across an aisle from its main booth, had a science centre with posters, abstracts and computer demonstrations of new assay product development, including an assay for vCJD. In addition, Chiron, Gen-Probe and ZymeQuest scientists staffed the science centre throughout the conference to answer questions.

The addition of the science centre underscored Chiron's work to expand its business from purely NAT-based blood donor screening to broader applications in blood safety, an investment to help sustain long-term growth. For example, Chiron and ZymeQuest are working to move their product for the enzyme conversion of blood type A and B to type O into clinical safety trials. Although Gen-Probe issued two press releases in the week leading up to AABB 2005 that dealt with regulatory questions raised by the FDA surrounding the Procleix Ultrio assay on the Procleix Tigris system and their subsequent delay, customer interest remained high for Chiron's products.

Similar to last year's conference, Roche displayed the Cobas AmpliCor as well as the Cobas s201* (formerly known as the

Cobas s200 and Blood Screening System 200) in its booth. The Cobas s201 consists of the Hamilton Microlab Star pipettor, Cobas AmpliPrep, and Cobas TaqMan 96 instruments, linked by a new version of AmpliLink and Pooling Data Management software. US clinical trials of the Cobas s201 using the Cobas TaqScreen MPX multiplex assay (HIV-1 (M/O), HIV-2, HBV and HCV) were conducted in 2005. Trials are beginning in Australia, Scotland, France and Italy.

By year-end 2005, Roche expects to file for European approval of its Cobas s201 blood screening platform and Cobas TaqScreen MPX multiplex assay. The Cobas s201 system and Cobas TaqScreen MPX multiplex assay are slated for launch in Europe in 2006 followed by launch in the US in 2007.

The Cobas s401, Roche's fully-automated blood screening system, will be sent to Roche's Japan affiliate by year-end 2005, followed by evaluation at the Japanese Red Cross (JRC) in the spring of 2006. Roche is already looking ahead to the next-generation blood screening system, now called the Cobas s801.

Automation for IAS-based testing

Although Abbott and Ortho-Clinical Diagnostics (OCD) promoted new automated instruments last year, the companies stepped up efforts due to timely regulatory approvals and development progress, respectively.

Just prior to the start of the AABB conference, Abbott received FDA approval of the Abbott Prism HBcore assay, a major milestone for the company. [Note: the Prism instrument was 510(k) cleared in 1999.] Abbott displayed a Prism instrument and literature in its scientific resource centre. The Abbott Prism HBcore assay may be used to help preserve the donor pool by limiting deferrals based on false-positive HBV test results.

As mentioned previously, the Abbott Prism HBcore assay is currently being used in an ongoing study along with HBV NAT for donor re-entry.

Approval of the Prism HBsAg assay is expected in the first half of 2006, with manufacturing of the first lots underway. The company will focus on completing the panel of five mandated serological tests first, and then work on other innovative assays, including next-generation versions, as well as tests for Chagas, malaria, and vCJD detection. In addition, the company is working on front-end automation and LIS middleware for blood donor testing.

For the first time at any worldwide venue, OCD displayed a prototype of its next-generation system for blood donor testing, the Ortho Paradigm system.

The system automates all pre-analytical functions and analytical serology testing, while interfacing sample transport and data integration for NAT and immunohaematology. The system displayed at the AABB included pre-analytical, analytical and storage modules connected by a track system. When using the Paradigm system, all processes are tracked and documented using RFID technology. The development programme draws on OCD's long history in transfusion medicine laboratory automation and expertise of their development partners, Sanguin, Tecan and Thermo Electron.

Emerging analytes

Seven cases of transfusion-transmitted Chagas have been documented in the US and Canada. Although there are 30+ assays approved for diagnostic use, a test with a blood donor screening claim has not yet been approved. OCD read one abstract on its lysate-based Chagas assay and sponsored a workshop on the need for Chagas testing, development of OCD's Chagas assays and confirmatory testing for Chagas.

The Ortho T cruzi ELISA Test System (IND) recently finished clinical trials on the OSP and features a lysate manufactured by OCD from master/working cell banks. Advantages of the lysate include the following:

- it provides complete antigen set;
- multiple antigens provide maximum sensitivity; and
- increased probability of detecting geographically diverse samples.

However, achieving consistent performance and manufacturing of a lysate has been challenging; as a result, OCD established in-process controls for all reagents in the assay (including the lysate) to aid in manufacturing a standardised, simplified and robust assay. Process validation and product transfer to manufacturing are complete, and the company is optimistic that it will have an FDA-approved Chagas assay in the next 6-12 months.

A Radioimmune Precipitation Assay (RIPA), using I125, was developed as a confirmatory assay, and OCD is in discussions with reference laboratories to make sure sufficient capacity for RIPA testing is available at the time of launch. RIPA is being validated by OCD as a reference assay in the clinical trials.

Abbott presented two abstracts on its recombinant-based Chagas assay, which has been moved from the research to development phase. The company is developing a confirmatory assay that resembles a line blot.

In contrast to last year's conference, Chiron presented an abstract on its prototype vCJD test, which is performed as follows:

- abnormal prion aggregates are bound to PrP^{Sc} specific binding reagents that are coated on magnetic beads and washed; and
- a chemical treatment is performed to convert bound abnormal prions to normal prions, which are then detected by sandwich ELISA.

Chiron has completed the discovery phase and is moving work into the research phase. The vCJD assay will be designed for a high-throughput, automated platform. Chiron hopes to have the vCJD assay CE-marked for IVD use. However, the first application of the technology could be for veterinary use.

Pall continued to highlight its Leukotrap Affinity Prion Reduction Filter system, which is currently being evaluated by National Blood Authorities in the UK and Ireland, and will be expanding soon to continental Europe; patient trials by these authorities are expected to be completed in 2006. In October 2005, the company presented data at the FDA's Transmissible Spongiform Encephalopathies (TSEs) Advisory Committee as part of its discussion with the agency on prion filtration of US blood products.

Blood grouping and typing (BGT)

The only new automated BGT system was the Galileo Echo from Immucor, the company's third-generation system, which is designed for the small- to medium-sized laboratory or as a backup to a larger automated BGT system. The product should be released on a worldwide basis in mid- to late-2006, depending on regulatory approvals. Distinguishing features of the system are summarised as follows:

- benchtop instrument with dimensions 43" (W) x 23" (D) x 19" (H);
- weight of approximately 75 pounds;
- targeted throughput of approximately 16 samples/hour;
- capacity for 20 samples, continuous feed using linear racks;
- capacity for 16 reagents;
- capacity for 32 microstrips;
- touchscreen user interface with Windows-based software;
- reflex testing; and
- bi-directional interface.

Like the Galileo, the Galileo Echo will use haemagglutination for blood typing assays and Immucor's Capture solid phase assays for antibody screening, antibody identification, Weak D, DAT and IgG crossmatch.

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Bacterial screening

Last year's AABB conference focused on the initial survey data from testing centres and hospitals after implementation of the AABB guidelines in March 2004. This year's conference included additional discussion on seven-day platelets and new technologies. Of note, New York Blood Center (NYBC) was the first site to begin releasing seven-day platelets.

bioMérieux supports Gambro's FDA approval (March 2005) for shelf-life extension of apheresis platelets collected with its Trima and COBE Spectra collection systems for routine storage and patient transfusion up to seven days when tested with bioMérieux's BacT/Alert Microbial Detection System as a release test. More recently, on November 18 2005, Baxter received 510(k) approval for seven-day storage of leukoreduced, apheresis platelets collected on the Amicus Separator and stored in the company's PL 2410 collection container; bioMérieux's release test must also be used with these products.

The FDA currently requires testing of both aerobic and anaerobic BacT/Alert bottles for release of seven-day platelets to aid in the detection of strict and facultative anaerobes. Both Gambro and Baxter are conducting post-market surveillance studies to evaluate system performance characteristics and compliance with ongoing evaluation requirements.

Prior to the 2005, Pall received FDA clearance to market its new Pall Acrodose PL system, the first whole blood-derived system for pre-storage pooling and testing of leukoreduced whole blood-derived platelets, resulting in a transfusion-ready product for hospitals. An Acrodose Platelet represents a new product for platelet transfusions that provides many of the benefits of apheresis platelets, but at a lower cost.

Currently, most hospitals perform pH or glucose dipstick testing prior to transfusion of whole blood-derived platelets, and testing centres perform culture on apheresis platelets. Dipsticks represent a detection technology that is considerably less sensitive to culture-based testing, thereby resulting in a two-tiered level of safety between platelet products. The Acrodose PL

System now allows blood centres to cost-effectively adopt culture-based testing for their whole blood platelet, providing the same level of safety for all platelet products.

15 million whole blood units donated annually in the US with five whole-blood derived platelets per therapeutic unit could help meet the need of approximately three million platelet transfusions per year in the country; the Pall Acrodose PL System provides another solution to help in meeting this need.

Still in development, Verax's Pan Genera Detection (PGD) product is a point-of-care cartridge that detects both gram-positive and gram-negative bacteria. Results are provided within 20 minutes of sample application (no more than 500 µL), which requires less than three minutes of hands-on time. If bacteria are present, a red line appears, similar to a pregnancy test.

Built-in procedural controls confirm sample addition and test completion. The PGD test may be used on either whole-blood derived or apheresis platelets. Verax finished pre-clinical trials and is now working with the FDA to determine if a 510(k) submission is appropriate with clinical trials, utilising \$15m of funds raised, beginning in January 2006. The company hopes to have a marketable product by next year's meeting.

UK-based Acolyte Biomedica and the Scottish National Blood Transfusion Service are collaborating on a prototype assay to detect clinically significant bacterial contamination of platelets within four hours. The results of Acolyte's feasibility study presented at the AABB showed that Acolyte's unoptimised prototype assay can detect 50 bacteria – both aerobic and anaerobic bacteria – in three hours using spiked platelet samples. The assay uses adenylate kinase (AK) as a highly sensitive, rapid bacterial detection system end point.

** For investigational use only.*

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