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ABC NEWSLETTER

CURRENT EVENTS AND TRENDS IN BLOOD SERVICES

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2013 #3 **January 25, 2013**

INSIDE:

Should WHO Consider Blood an Essential Medicine?

In 1977, the World Health Organization (WHO) compiled a Model List of Essential Medicines to guide countries in providing access to cost-effective medicines that are vital for public health. The list is updated every two years and shapes national drug policies in many countries. Although blood for transfusion saves millions of lives and is regulated as a drug in the US and many other countries, it is not included on the WHO Model List of Essential Medicines.

Harvey G. Klein, MD, of the National Institutes of Health, asked in a commentary, published on Jan. 17 in the *New England Journal of Medicine*, "Should blood be an essential medicine?" He argues that adding it to the list would underscore governments' responsibility to invest in the necessary infrastructure to support a safe, adequate, and accessible blood supply, thereby improving health globally.

A group of blood donation organizations agrees with Dr. Klein and has submitted an application to the WHO expert committee responsible for updating the Model List of Essential Medicines, asking that whole blood and red blood cells be added to the list. AABB, the American Red Cross (ARC), Canadian Blood Services (CBS), and ISBT cited in their application many of the points that Dr. Klein made in his editorial, including that adding blood to the list would bring awareness to the need for blood in protecting the public health. America's Blood Centers is drafting a letter of support for the application.

Defining an Essential Medicine. WHO defines a "medicine" as "any substance or pharmaceutical for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient." Dr. Klein writes that "blood is certainly a substance used to treat, mitigate, or prevent disease." While whole blood and red cells differ from small-molecule pharmaceuticals in their unit-to-unit heterogeneity, blood components are biologics that share many attributes with those medicines, said Dr. Klein.

Although blood transfusion originated as a medical practice whereby the donor would be drawn and the patient immediately transfused with that blood, preservative solutions and plastic blood bags have permitted blood to be collected and stored, distinguishing the product from the medical practice of transfusion.

Technical and regulatory advances during the past half-century have led to the manufacture of blood components with unprecedented purity, potency, and safety.

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OUR SPACE

ABC Executive Vice President Louis Katz, MD

Pet Peeves: Confounded Observational Studies that Say Blood Hurts People

The first lesson in med school is (or was 40 years ago) *primum non nocere:* "first, do no harm." In blood banking, we like to see ourselves as the "good guys," persuading a busy, sometimes reluctant, donor population, to have 16-gauge needles stuck in their arms, and distributing their "gift of life." It's distressing then when we are told that what we distribute is injurious to patients. And there's a lot of recent literature saying that.

Most recently, the *Archives of Internal Medicine* (Chatterjee, *et al.*) published such a study. After reviewing 10 studies including >200,000 patients, the investigators alleged that liberal transfusion was associated with increased mortality and subsequent myocardial infarction risks in patients transfused during heart attacks. The study got media coverage, and I got a handful of patient and "worried-well" inquiries.

The timing of the article was particularly unfortunate since the Myocardial Infarction and Transfusion trial (MINT), a randomized controlled trial (RCT) of conservative and liberal transfusion in the face of myocardial infarction or hospitalization for stable coronary artery disease, is in progress, exploring the feasibility of a larger trial to actually answer the question.

Is it true that blood is harmful in this setting? Perhaps, but what got less ink was an accompanying commentary in *Archives* by Jeff Carson, MD, and Paul Hebert, MD, authors of the two pivotal RCTs of transfusion triggers in adults (FOCUS and TRICC), reminding us of the (sometimes fatal) flaws in much of this literature. There was a single RCT included in the *Archives* review – the rest were essentially observational, and thus does not account for what all of us who have stood at the bedside understand – sicker patients get blood, and sicker patients do worse than less sick patients.

Dr. Carson, Dr. Hebert, and their colleagues, understanding that avoiding this "confounding" requires RCTs, have demonstrated (as have a number of pediatric and other trials), in large, mixed clinical populations, that, while liberal transfusion did not improve their primary outcomes, it was not generally harmful.

This distinction is critical when addressing other poorly studied populations, like patients with acute coronary syndromes. It requires a default of conservative transfusion because of absence of benefit, not evidence of harm, while awaiting definitive trials. Given the evidence base of RCTs, journal editors and referees should ask themselves whether they bring readers (medical, media, or lay) value by publishing more observational studies and meta-analyses of inevitably confounded studies.

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ABC is an association of not-for-profit, independent community blood centers that helps its members provide excellence in transfusion medicine and related health services. ABC provides leadership in donor advocacy, education, national policy, quality, and safety; and in finding efficiencies for the benefit of donors, patients, and healthcare facilities by encouraging collaboration among blood organizations and by acting as a forum for sharing information and best practices.

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Is Blood an Essential Medicine? (continued from page 1)

Many countries have developed hemovigilance systems that parallel pharmacovigilance systems. Furthermore, blood is already regulated as a drug in many countries, including the US, where blood became subject to regulation as medicines under the Food, Drug, and Cosmetic Act in 1938, and subject to licensing in 1944.

As to whether blood is an *essential* medicine, red-cell transfusion is one of the few treatments that adequately restore tissue oxygenation when oxygen demand exceeds supply, writes Dr. Klein. In developed countries, many surgeries are not undertaken without available blood. Most blood transfusions support surgery, chemotherapy, stem-cell transplantation and management of inherited disorders, such as sickle cell disease. In developing countries, many deaths result from trauma, hemorrhage during childbirth, and malaria, because safe blood is not readily available.

Bringing Awareness to Need for Blood. Aside from promoting awareness of the need for blood and its role in public health, including blood in the list would highlight the importance of appropriate regulatory oversight of blood systems, as well as the need for adherence to guidelines for clinical use. Adding blood would also emphasize the need to ensure that blood is cost-effective and affordable. These goals are particularly important in low- and middle-income countries where many die for lack of safe blood, said Dr. Klein.

Concerns. Some people have expressed concerns that adding blood to the Model List would erode volunteerism and altruism and increase the cost of blood. Dr. Klein does not believe that this would happen, however. Including blood on this list would likely emphasize the importance of voluntary, non-remunerated blood donation and the non-profit status of blood centers – policies that WHO endorses and that were stressed again in a 2011 WHO Assembly resolution, he adds.

Others are concerned that treating blood as a medication will increase costs and interfere with blood systems that developed without oversight from health ministries or regulatory agencies. Dr. Klein agrees that the initial costs of introducing regulated manufacturing systems are high, but adds that the indirect long-term savings in improved donor and patient safety are substantial. Lastly, and perhaps most importantly, "national investment in oversight of blood systems ... have led to improved availability and quality of blood for transfusion."

Dr. Klein concludes that "Adding blood to the Model List would encourage governments to invest in infrastructure and the governance of blood systems and increase their efforts in blood-donor recruitment and blood collection, which should lead to the provision of a safe and cost-effective therapy, prevent deaths and disabilities from blood shortages, and improve health globally."

Support from Blood Community. Several other blood collection agencies and blood-related organizations have posted comments supporting the application to add blood to the list, including the Paul-Erlich-Institut, the Canadian Society for Transfusion Medicine, the Indian Society of Transfusion, the Japan Society of Transfusion Medicine and Cell Therapy, the Russian Transfusionist Association, WHO Blood Regulators Network, and Swissmedic. The US Food and Drug Administration wrote a letter supporting the addition of whole blood and red blood cells to the list saying that "they satisfy the priority healthcare needs of the population in all countries."

ABC is drafting a letter of support. The application and comments can be found at http://bit.ly/W0i10v.

Citation: Klein HG. Should blood be an essential medicine? N Engl J Med. 2013 Jan 17; 368(3): 199-201.

NIH-Developed Dengue Virus Vaccine Candidate Shows Promise

A candidate dengue vaccine developed by scientists from the National Institutes of Health has been found to be safe and to stimulate a strong immune response in most vaccine results in an early-stage clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). The trial results were published in the Jan. 17 issue of the *Journal for Infectious Diseases.*

Background. The World Health Organization estimates that every year, 50 million to 100 million cases of dengue occur worldwide, resulting in 500,000 hospitalizations of patients with severe disease, many of them children. Dengue is a mosquito-borne virus that is highly endemic in most tropical and subtropical areas of Asia and the Americas. In the continental US, dengue is less common but has been transmitted in recent years in Florida, Texas and Hawaii. Dengue is the most frequently diagnosed cause of fever in travelers returning from Asia and the Americas.

Dengue causes high fever, severe headache, severe pain behind the eyes, joint pain, muscle and bone pain, rash, and mild bleeding. Severe dengue results in capillary leakage, which can lead to failure of the circulatory system and shock, followed by death, if circulatory failure is not corrected. There is currently no vaccine or cure for dengue.

It is caused by any of four related viruses – DENV-1, DENV-2, DENV-3, and DENV-4 – transmitted to humans by Aedes mosquitoes. Infection with one dengue strain results in immunity to that strain but not to the other three. Severe disease increases when a person with a prior infection is subsequently infected with a different dengue strain. This observation suggests that the ideal dengue vaccine would be tetravalent (protective against all four dengue viruses).

“The global burden of dengue is enormous – and it is growing,” said NIAID Director Anthony S. Fauci, MD, in the NIH press release. “We are cautiously optimistic about these recent clinical trial results with this candidate tetravalent vaccine developed at NIAID; however, much more work still needs to be done.”

Methods. The phase I clinical trial, led by Anna Durbin, MD, at Johns Hopkins Bloomberg School of Public Health in Baltimore, tested a single dose of each of four versions of the investigational live-attenuated vaccine TetraVax-DV. These four vaccines included different mixtures of components designed to protect against all four dengue viruses.

The final study analysis included 112 healthy men and women 18 to 50 years old, who had not previously been exposed to dengue or related flaviviruses, such as West Nile virus (WNV) and yellow fever.

Participants were randomized into four groups, with 20 in each group receiving a single 0.5 mL subcutaneous injection of one of the vaccine combinations, and eight others received a placebo. The investigators monitored participants for immediate adverse reactions and fever three times daily for 16 days. Participants underwent a physical exam every other day up to day 16, and again on study days 21, 28, 42, and 180, when blood tests were also performed.

Results. All four vaccine combinations induced antibody responses against each of the dengue viruses. However, one vaccine combination, TV003, induced the most balanced antibody response. A single dose of TV003 resulted in an antibody response to all four dengue viruses in 45 percent of participants and against three viruses in an additional 45 percent.

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Dengue Virus Vaccine Candidate (continued from page 4)

"What is promising about TV003 is that it elicited solid antibody responses after just one dose," explained Stephen Whitehead, PhD, of NIAID's Laboratory of Infectious Disease, who led the development of the vaccine candidates. "Other vaccines in development require two or three injections at higher doses to achieve similar results."

All four candidate vaccines were found to be safe, and no participants experienced fever or dengue-like illness. The most common side effect was faint rash (in 64 percent of vaccine recipients) that resolved within five to seven days. Ninety-seven percent of white vaccine recipients developed antibodies to at least three of the dengue viruses, compared to 60 percent of African-Americans.

Conclusions and Future Research. It is unclear what caused the racial difference, but previous studies of severe dengue outbreaks in Brazil, Cuba, and Haiti suggest that black people may have some inherent protection from dengue infection, said the release. Alternatively, unknown factors may have resulted in a weaker antibody response to the vaccine among African-Americans. Additional research to evaluate racial differences in dengue infection and antibody response rates to dengue vaccines is needed.

Additional studies are underway to further evaluate the vaccine's safety and ability to stimulate immune response in healthy volunteers and in people who have been infected previously by dengue or related viruses. Phase II trials to evaluate the safety of TV003 and its capacity to create an immune response will begin soon in Brazil and Thailand, where dengue is prevalent.

TV003's inexpensive production cost – less than $1 per dose – is critical to its potential use in developing countries, said Dr. Whitehead. More information about the phase II trial is available at www.clinicaltrials.gov/ct2/show/NCT01696422, and details about the phase I trial can be found at http://clinicaltrials.gov/ct2/show/NCT01072786.

Dengue and Transfusion Medicine. Although dengue virus is spread primarily by mosquito bites, transfusion-transmitted cases have been documented in Hong Kong, Singapore, and Puerto Rico. Transmission has also been observed after needle stick exposure and in bone marrow and kidney transplant recipients.

There is currently no Food and Drug Administration-approved blood donor screening test and there is no specific donor screening question related to dengue. Current travel-related questions for malaria deferral catch many travelers in dengue endemic areas, but since dengue is more widespread geographically than malaria, specific dengue deferral guidelines would result in many more travel deferrals than with current travel screening. Investigational dengue donor nucleic acid testing programs by the American Red Cross in Puerto Rico have demonstrated prevalences of infected donors in Puerto Rico consistent with those found for WNV in the continental US. (Sources: NIH press release, 1/23/13; AABB Dengue Factsheet)

Citation: Durbin AP, *et al*. A single dose of any of four different live attenuated tetravalent dengue vaccines is safe and immunogenic in flavivirus-naive adults: a randomized, double blind clinical trial. J Infect Dis. 2013 Jan 17. [Epub ahead of print]

America's Blood Centers® It's About Life

REGISTRATION NOW OPEN

America's Blood Centers'
51st Annual Meeting
March 15-19, 2013 - Washington, DC
Ritz Carlton (Pentagon City)

2013 Annual Meeting Schedule

Friday, March 15:
International Blood Safety Forum

Saturday, March 16:
GSABC Members Meeting (members only)
GSABC Member/Vendor Reception
Hospitality/Networking

Sunday, March 17:
ABC Members Meeting (members only)
Scientific, Medical and Technical Forum
The Foundation for America's Blood Centers' Reception
Hospitality/Networking

Monday, March 18:
Blood Center Leadership Forum
ABC *Awards of Excellence* Reception and Banquet
Hospitality/Networking

Tuesday, March 19:
Legislative Session and Capitol Hill Visits

"ABC's Annual Meeting is a time when blood center leaders from North America and other parts of the world gather together. We not only discuss what challenges and opportunities we face today and in the future, but reflect on our collective accomplishments in the last year. Register now, and don't miss the opportunity to be a part of the discussions and this exceptional annual event."

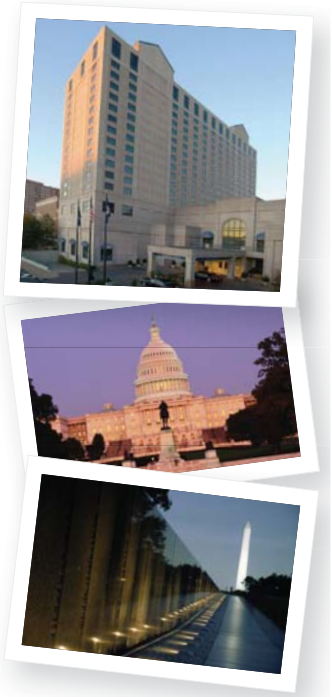
– Dan Waxman, President
America's Blood Centers

Register and reserve hotel by February 22.

Meeting Fees
International Blood Safety Forum: $250
ABC Annual Meeting: $695
For ABC member registration information, go to http://bit.ly/ABC_AM_13.

Non-members (non-vendor), contact Lori Beaston at *lbeaston@americasblood.org* for invitation and registration fees and information.

Sponsorship opportunities available. Contact Abbey Nunes at *anunes@americasblood.org* for details.



RESEARCH IN BRIEF

A recent study found that Factor VIII clotting factors derived from donor plasma and recombinant products are equally likely to induce inhibitory antibodies in previously untreated children with hemophilia A. The study, published in the Jan. 17 *New England Journal of Medicine*, was led by H. Marijke van den Bert, MD, PhD. In the study of 574 consecutive pediatric patients with severe hemophilia A, the adjusted hazard ratio for development of inhibitory antibodies within 75 days of starting treatment for plasma-derived products was 0.96 (95 percent confidence interval 0.62 to 1.49) relative to recombinant Factor VIII analogs. The development of inhibitor antibodies at high titers – at least 5 Bethesda units per mL – was equally common between plasma-derived and recombinant products. However, they did find significant differences between synthetic products. Specifically, second-generation recombinant Factor VIII analogs were more likely to induce inhibitory antibodies than were third-generation agents. "There is no straightforward biologic explanation for a difference in immunogenicity among recombinant factor VIII products. Further studies are needed to verify these observations and to identify biologic explanations," said the authors. The study was conceived to examine whether plasma-derived Factor VIII is less immunogenic than recombinant products, as commonly believed. Patients in the study were born between Jan. 1, 2000 and Jan. 1, 2010, and had severe hemophilia A. The researchers collected data on the clotting factors administered and results of blood analyses through the first 75 days of treatment exposure. According to earlier studies, development of inhibitory antibodies later than 75 days after initiation of replacement therapy is rare. They found that 177 patients (32.4 percent) developed inhibitor antibodies within 75 days of starting Factor VIII replacement therapy, with 116 showing titers above 5 Bethesda units per mL. First-generation recombinant products – those for which mammalian proteins were used in production and had human serum albumin as a stabilizer – were little used in the cohort (2,464 exposure days), whereas second- and third-generation agents accounted for more than

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RESEARCH IN BRIEF (continued from page 6)

9,000 exposure days each. Second-generation products were those in which human plasma protein solutions were used in cell culture media, and third-generation agents did not use mammalian proteins in production or as additives. The researchers also examined whether switching between different brands raised the risk of inhibitory antibody development, and found that it did not. In their analyses, the researchers adjusted for race and ethnicity, age at first exposure to Factor VIII therapy, reason for treatment, dosage, dosing frequency, genotype, and a variety of other factors. Despite these adjustments, the authors noted that they could not rule out the possibility of confounding by unmeasured factors. They also wrote that because of their cohort size and the large number of different Factor VIII products available, they may not have been able to detect differences in inhibitor development between specific brands. (Source: *MedPage Today*, 1/17/13)

Citation: van den Berg HM, *et al*. Factor VIII products and inhibitor development in severe hemophilia A. N Engl J Med. 2013 Jan 17;368(3): 231-9.

Researchers find no relationship between red blood cell (RBC) age and mortality in a retrospective analysis of 7,000 non-cardiac surgical patients. The study was conducted by Leif Saager, MD, and colleagues of Cleveland Clinic, and was published in the January edition of *Anesthesiology*. Previous studies have linked storage duration of RBCs to the risk of postoperative complications, while others have suggested that storage duration does not affect outcomes. An association between storage duration of transfused RBCs and postoperative all-cause mortality among general surgery patients was evaluated. The investigators gathered data on 63,319 adult, general surgery patients from Cleveland Clinic's registry. Only patients who received leukocyte-reduced, allogeneic RBC transfusions were included. The relationship between median RBC storage duration and postoperative mortality was analyzed, adjusting for characteristics plausibly influencing the storage duration of RBCs. Of the 6,994 patients in the final analysis, 23, 44, 11, 9 and 13 percent received, 1, 2, 3, 4, and $\geq$5 RBC units, respectively. The authors found no evidence that increasing median storage duration was associated with increased postoperative mortality. The findings "support the recent literature in surgical and medical patients and underlines the importance of sufficiently powered randomized trials to finally resolve the erythrocyte storage duration debate." In an accompanying editorial, Jerrold H. Levy, MD, and Marie E. Steiner, MD, write, "Although multiple studies on outcomes associated with erythrocyte storage and transfusions have been reported, many of these studies have a multitude of limitations, including retrospective analysis, different methodological and analytical approaches insufficiently adjusting for confounding factors or disease severity, single- *versus* multiple-center populations, retrospective *versus* prospective evaluation, variable populations sizes, accrual time range, divergent patient populations, and variable erythrocyte processing and storage methods." They note that these confounding variables make it difficult to compare the results of a single study with another. "The current study is an important addition to the literature because these surgical patients represent a less critically ill patient population compared with other age of erythrocyte storage studies," write the authors. However, the available data does not answer whether the age or RBC transfused has a significant effect on clinical outcomes. The editorial cites large ongoing randomized controlled trials that may shed light on this subject, including the ARIPI, ABLE, and RECESS trials.

Citations: Saager L, *et al*. Erythrocyte storage duration is not associated with increased mortality in noncardiac surgical patients: a retrospective analysis of 6,994 patients. Anesthesiology. 2013 Jan.; 118(1): 51-8.

Levy JH, Steiner ME. Clinical studies of erythrocyte outcomes and mortality: size really counts. Anesthesiology. 2013 Jan; 118(1): 10-12. ♦

BRIEFLY NOTED

The National Collegiate Athletic Association (NCAA) has approved mandatory confirmation of sickle cell trait status in Division III student athletes, despite objections from the American Society of Hematology (ASH), reported *MedPage Today* on Jan. 21. Confirmation of sickle cell status will be required of all incoming athletes in the 2013-2014 school year and for all athletes by 2014-2015. The NCAA already requires mandatory sickle cell screening for Division I and II athletes. Last year, ASH issued a statement opposing the mandatory screening, saying that this policy may harm and stigmatize the sickle cell community (see *ABC Newsletter*, 2/3/12). This past week, ASH said in a statement that the "NCAA policy is medically groundless – perhaps even dangerous – and is focused more on protecting the NCAA from legal liability than protecting the health of students." Sickle cell disease affects 8 to 10 percent of African-Americans, and some people from South and Central America, the Carribbean, and the Middle East. It is hereditary and is caused by an abnormal type of hemoglobin that makes red blood cells assume a crescent shape when in an environment with low oxygen. These red cells have difficulty circulating through tissues and are eliminated, causing anemia, pain, disability, and in some cases death. People with sickle cell trait, however, live fairly normal lives unaffected by the genetic abnormality (except in rare cases), because they have only one defective gene, unlike sickle cell disease patients, who have two. In 2010, the NCAA adopted the policy for Division I athletes, requiring that students may provide test results or sign a waiver of liability against the university and the NCAA to opt out of testing. The requirement was sparked by a lawsuit against the NCAA and Rice University following the death of a football player after practice caused by acute exertional rhabdomyolysis, which was linked to sickle cell trait. ASH has argued that instead of requiring sickle cell screening, NCAA should implement several interventions to protect all student-athletes, such as environment-based work-rest cycles, heat acclimation monitoring, hydration guidelines, and rapid detection of and treatment for heat illness. Beginning Aug. 1, the guidelines will require schools to confirm the sickle cell trait status of incoming students in one of three ways: providing documented results of sickle cell solubility test taken before participation in sports; signing a waiver and submitting to "appropriate precautions as set forth by the institution" following pending results of a sickle cell solubility test; or opting out and signing a waiver to decline confirmation of sickle cell status after receiving education on the implications of signing the waiver and about sickle cell trait status. The ASH statement is available at www.hematology.org/Advocacy/Policy-Statements/7704.aspx. (Source: *MedPage Today*, 1/21/13)

The British Committee for Standards in Hematology (BCSH) recently published an updated version of its "Guidelines for Pre-Transfusion Compatibility Procedures in Blood Transfusion Laboratories." The guidelines were published on Dec. 6, 2012 in *Transfusion Medicine*, and are also available for free on the BCSH website at http://bit.ly/SH522V. These guidelines are meant to replace those published in 2004, and were authored by a BCSH convened writing group. They were subsequently revised by members of the Transfusion Task Force of the BCSH. "The BCSH guidelines on pre-compatibility testing have been through three metamorphoses since the first guideline in 1991. They have grown in length and detail over the years and are appropriately regarded as standards that all laboratories in the UK should follow," wrote Jonathan P. Wallis, MD, in an accompanying editorial in *Transfusion Medicine*. There are several major changes since the last guideline in 2004, and the authors give 19 key recommendations. Five of these refer directly to ABO typing and compatibility, whereas six refer to detection of atypical red cell antibodies and the remainder to processes within the blood transfusion laboratory. There are three recommendations that will lead to changes in practice in UK blood transfusion laboratories, notes Dr. Wallis. There are also significant changes about ensuring ABO compatibility. "In summary, the new guidelines on pre-transfusion compatibility procedures offer a welcome clarification in a number of areas including validity of samples for crossmatching. They have promoted the use of a second sample for confirmation of the ABO blood group for first-time patient prior to transfusion, and

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BRIEFLY NOTED (continued from page 8)

offered guidance on storage of blood and plasma samples for three and 10 days, respectively, post-transfusion," writes Dr. Wallis. He concludes that implementing the changes will require considerable thought and effort but will improve blood safety.

Citations: British Committee for Standards in Haematology. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. Transfus Med. 2013 Feb; 23(1): 3-35.

Walls, JP. Pre-transfusion compatibility guidelines: a new edition. Transfus Med. 2013 Feb; 23(1): 1-2.

REGULATORY NEWS

The Food and Drug Administration announced on Jan. 17 that it has approved Octaplas, a pooled plasma (human) blood product for the replacement of clotting proteins (coagulation factors) in certain medical conditions where patients have insufficient levels. It is indicated for replacement of multiple coagulation factors in either patients with acquired deficiencies due to liver disease or in those undergoing cardiac surgery or liver transplant, and during plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP). Manufactured by Octapharma, it is a sterile, frozen solution of pooled human plasma from 630 to 1,520 individual donors that has been treated with a solvent detergent process. This process inactivates enveloped viruses (e.g. HIV, hepatitis C virus, hepatitis B virus, West Nile virus) to reduce the risk of virus transmission. Nonenveloped viruses like hepatitis A virus and Parvovirus B19 are not effectively inactivated. The plasma used to manufacture Octaplas will be collected from US donors, both source and volunteer non-remunerated, who have been screened for infections transmitted by blood, and determined to be suitable donors. Octaplas must be matched to the recipient's blood group to help avoid transfusion reactions. Octaplas has been used extensively in Europe and other countries. More than 2 million patients have been treated with more than 7 million doses of Octaplas outside the US. The licensing of Octaplas was primarily based on clinical studies conducted in patients with liver disease, liver transplant, heart surgery, and thrombotic thrombocytopenic purpura. Additional data supporting the safe use of Octaplas for the US market came from prior use of the products in Europe and other approved markets. The initial dose is 10-15 mL/kg, similar to that recommended for FFP. It is supplied in 200 mL aliquots. The most common adverse reactions observed in clinical studies included shortness of breath, dizziness, chest discomfort, skin itchiness, and rashes, headache, and tingling sensations. The FDA documents regarding this product's approval are available at http://1.usa.gov/14afOSI. (Source: FDA press release, 1/17/13)

The FDA published this week a final rule governing the Current Good Manufacturing Practice (cGMP) requirements for products that combine devices, drugs, and/or biological products. The rule is meant to provide clarification on cGMP requirements for products that include any fusion of the medical products either as packaged together or as a "single-entity" combination. The final rule is "largely identical" to what FDA proposed in September 2009, based off of a draft guidance first published in 2004. The new guidelines apply equally to existing, as well as new products, despite some requests that the regulation be forward-looking only. FDA asked members of existing combination products to comply with the new cGMP guidelines but promised to issue guidance to help manufacturers alter systems as need be for products already on the market. FDA also shielded certain manufacturers from the cGMP rules, applying the guidelines to both "specification" developers and contract manufacturers, but left out component manufacturers, even if a component will be incorporated into the final product. Guidelines for

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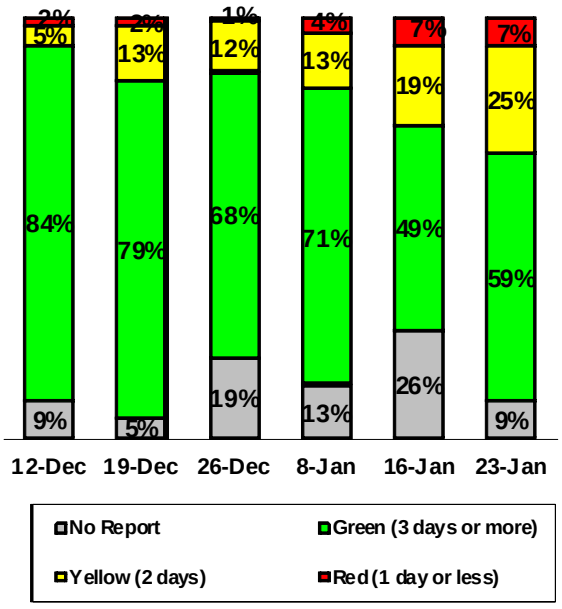
REGULATORY NEWS (continued from page 9)

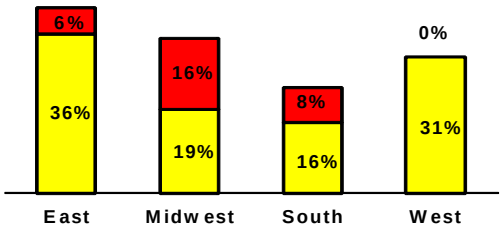
certain combination products, such as those including parts that are separately manufactured and marketed, are straightforward, with each piece regulated under existing guidelines for its respective category. For packages that FDA calls "single-entity and co-packaged combination products" the rules are less clear, and those combinations are the focus of this new rule. The final rule can be accessed at www.gpo.gov/fdsys/pkg/FR-2013-01-22/html/2013-01068.htm. (Sources: Federal Register, 1/22/13; *MassDevice*, 1/22/13) ♦

STOPLIGHT®: Status of America's Blood Centers' Blood Supply

Total ABC Red Cell Inventory



Percent of Regional Inventory at 2 Days Supply or Less, January 23, 2013



Percent of Total ABC Blood Supply Contributed by Each Region

East: 20%; Midwest: 25%; South: 24%; West: 31%

Daily Updates are available at:
www.AmericasBlood.org

We Welcome Your Letters

The *ABC Newsletter* welcomes letters from its readers on any blood-related topic that might be of interest to ABC members. Letters should be kept relatively short and to the point, preferably about a topic that has recently been covered in the *ABC Newsletter*. Letters are subject to editing for brevity and good taste. Please send letters to ABC Publications Editor Betty Klinck at newsletter@americasblood.org or fax them to (202) 393-1282. Please include your correct title and organization as well as your phone number. The deadline for letters is Wednesday to make it into the next newsletter.

MEMBER NEWS

Héma-Québec announced in a recent press release that it has chosen the future site for the first donor center exclusively for plasma collection in Québec. Héma-Québec will build its plasma collection center in the city of Trois-Rivières, and plans to open the center in fall 2013. The purpose of the center is to increase the number of plasma donations by apheresis. Plasma is often used in producing medications for patients with immune system disorders and to treat many other diseases. Currently, Québec depends heavily on plasma collected abroad, and a strategy is needed to achieve an acceptable degree of self-sufficiency in donations for these plasma-derived medications and treatments, said the press release. "We are proud to be joining forces with the city of Trois-Riviéres for this Québec first and to be contributing to creating jobs in the area, as well as in Québec ... Trois-Riviéres is unquestionably an excellent incubator for this innovative initiative that we hope to be able to reproduce elsewhere in Québec," said Jean De Serres, MD, president and CEO of Héma-Québec. The establishment of this plasma collection center could lead to the establishment of other plasma donor centers in the main urban areas of Québec within the next five years, said the release. (Source: Héma-Québec press release, 1/22/13)

HÉMA-QUÉBEC
Blood Products
Stem Cells
Human Tissues

Florida's Blood Center (FBC), a division of OneBlood, recently recognized Wayne Zdrojewski, of Kissimmee, Fla., for donating his 100th gallon of blood on Monday. His donations have affected the lives of at least 2,400 patients during his time as a blood donor. Mr. Zdrojewski is one of a few active blood donors at FBC who have donated 100 gallons or more. He has helped save lives through making apheresis platelet donations. Platelets which are used in the treatment of cancer patients undergoing chemotherapy, and are vital to keeping many cancer patients alive throughout their treatment. FBC staff celebrated Mr. Zdrojewski's 100th platelet donation with a cake and congratulations on this important milestone. (Source: FBC press release, 1/22/13)

During the month of February, Hoxworth Blood Center is challenging charitable non-profit organizations to recruit blood donors for its Bleed for a Cause campaign. The charities will be competing with other non-profits to see who can score the most points by recruiting blood donors, and the top three charities will win cash prizes. "Hoxworth Blood Center is proud to partner with 63 of Greater Cincinnati's 501(c)3 charitable organizations on our inaugural Bleed for a Cause campaign," said Eric Langevin, assistant division director for Donor Recruitment & Community Relations at Hoxworth Blood Center. "We've worked with numerous non-profit organizations in the past. Now, as part of our branded Amplified Altruism program, and sponsored by the good folks at Toyota and Montgomery Inn, we can work with so many more – and help one of them win up to $10,000!" Bleed for a Cause is sponsored by Montgomery Inn and Toyota Motor Engineering & Manufacturing North America, allowing for the winning charities to receive direct financial support for their efforts. Non-profits were asked to sign up in December to participate in the month-long challenge during February. Each charity will encourage people to donate blood, and that organization receives points for each blood donor that donates in the charity's name. The non-profits will receive one point for each whole blood donation, two points for a double red donation, three points for a platelet donation, and two bonus points for each first-time donor. The 1st place winner will receive $10,000; 2nd

Hoxworth BLOOD CENTER
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place will receive $5,000; and 3rd place will receive $2,500. The standings of each non-profit will be released weekly and the winners will be announced in early March, when they will be invited to a check presentation event. More information about Bleed for a Cause is available at www.hoxworth.org/groups/cause.html#overview. (Source: Hoxworth Blood Center website, 1/22/13)

PEOPLE

Jim Fox, director of communications at New York Blood Center, wrote an article that was recently published in the *New York Daily News* about *Good Morning America* host, Robin Roberts, who became a bone marrow donation advocate due to her experience with cancer. In June 2012, Ms. Roberts announced that she has been diagnosed with myelodysplastic syndrome, an after-affect of chemotherapy treatments that she underwent five years ago for breast cancer. Ms. Roberts was in need of a bone marrow transplant and, luckily, her sister was a match. Ms. Roberts underwent a bone marrow transplant in September, and recently passed the critical 100-day mark after her transplant. Like Ms. Roberts, Mr. Fox's sister-in-law Theresa has breast cancer and later developed leukemia due to the chemotherapy; she too received a stem cell donation from a sibling. He explains that despite the unfortunate circumstances of both women, they were lucky to find a match. "Siblings have only a 30 percent chance of matching," he writes. If Ms. Roberts had to seek a donor through the bone marrow and stem cell registry, she may not have been able to find a match. Generally, the best genetic match for someone seeking a stem cell transplant is a donor within the same racial or ethnic group. Unfortunately, just 30 percent of donors in the stem cell donation registry are members of an ethnic minority. Mr. Fox says he hopes Ms. Roberts' efforts to raise awareness of the need for more minority donors helps to diversify the bone marrow and stem cell registry. "I've seen first-hand how tough it is to navigate the tragic two-fer of breast cancer and then a secondary blood cancer. The odds of survival should not be based on whether a woman was born black or white." The article is available at http://nydn.us/VlUnwU. (Source: *New York Daily News*, 1/14/13)

Linda S. Barnes recently joined Puget Sound Blood Center (PSBC) as its chief quality officer, PSBC announced on Jan. 22. In her new role, Ms. Barnes will be focused on aligning quality with business goals, and overseeing all aspects of quality programs and systems, regulatory affairs, records management, and occupational health. "PSBC is committed to continuously improving our quality and compliance processes," said James P. AuBuchon, MD, president and CEO of PSBC. "Linda brings both depth and breadth of experience in health care and medical research that will sharpen our quality focus and improve performance across our operations." Prior to joining PSBC, Ms. Barnes served in global commercial and technical operation leadership roles with Dendreon Corp., as program director for the University of Washington International Clinical Research Center, and as director of diagnostic and treatment services at Seattle Cancer Care Alliance. Earlier in her career, Ms. Barnes served for more than 12 years as PSBC's director of quality and regulatory assurance. She began serving in her new role on Jan. 22. (Source: PSBC press release, 1/23/13)

COMPANY NEWS

Baxter International recently reported positive results from a late-stage study evaluating routine use of its anti-inhibitor coagulant complex to treat hemophilia, reported Reuters. The data will form the basis of a biologics license application to be filed with the Food and Drug Administration in the first quarter of 2013. The phase 3 clinical trial investigated the efficacy, safety, and health-related quality of life benefits of its anti-inhibitor coagulant complex prophylactic treatment given to maintain health and

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prevent bleeds compared with on-demand treatment. The study included 36 patients with hemophilia A or B and inhibitors over a 12-month period. There was a 72.5 percent reduction in bleed rates for the prophylactic treatment group, according to Baxter. The most commonly reported negative side effects observed were hypersensitivity, dizziness, headache, rash, hypotension, and hepatitis B surface antibody positive laboratory test result. The occurrence of a transitory increase in hepatitis B surface antibodies has been seen in certain plasma-derived products and could be attributed to the passive transfer of antibodies following treatment, reported Reuters. None of the subjects showed any signs or symptoms of hepatitis B infection. If approved, Baxter's drug would potentially compete with drugs being developed by Biogen Idec Inc. In October, Biogen said its experimental treatment for patients with hemophilia A controlled bleeding with fewer treatments in late-stage clinical trials. (Source: Reuters, 1/8/13) ♦

Correction

In last week's *ABC Newsletter* on page 4, we incorrectly stated, "Approximately 500,000 potential blood donors present to give blood in the US each day ..." It is actually approximately **50,000** potential blood donors who present to give blood in the US each day. We apologize for this error and thank our readers who bring such issues to our attention.

MEETINGS

Feb. 12 **FDA Blood Products Advisory Committee Meeting, Rockville, Md.**

The Food and Drug Administration announced that the next Blood Products Advisory Committee Meeting will be held on Feb. 12 from 8:30 a.m. to 5 p.m. in Rockville, Md. The committee will meet to discuss Cangene's biologics license application for Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)-(Equine). The meeting will be held at 5630 Fishers Lane, Room 1066, in Rockville, Md. More information and materials can be accessed at: http://1.usa.gov/UohBQo. ♦

Don't Miss Out on Your Chance to Participate in BOOTS!

Registration is open for the Blood Bank Operations Optimization Training Sessions (BOOTS), which will take place throughout 2013. BOOTS is a specialized training program consisting of 10 individual three-day sessions. The program is aimed at assisting blood center leadership in getting the most out of their numerous assets: labor, equipment, processes, cash flow, and capacity. The past two cycles of BOOTS have facilitated projects with savings commitments exceeding $15 million. The first BOOTS sessions are already underway – don't miss your chance to participate in this valuable training opportunity. The agenda can be viewed at http://bit.ly/BOOTS_Agenda and registration can be accessed at http://www.cvent.com/d/1cqxb51Q.

CLASSIFIED ADVERTISING

Classified advertisements, including notices of positions available and wanted, are published free of charge for a maximum of three weeks per position per calendar year for ABC institutional members. There are charges for non-members: $139 per placement for *ABC Newsletter* subscribers and $279 for non-subscribers. Notices ordinarily are limited to 150 words. To place an ad, contact Leslie Norwood at the ABC office. Phone: (202) 654-2917; fax: (202) 393-5527; e-mail: mnorwood@americasblood.org.

POSITIONS AVAILABLE:

Director, Reference and Transfusion Services. Carter BloodCare is currently seeking a Director of Reference and Transfusion services. The position is responsible for all technical activities in the R&T Service Laboratory and satellite locations. The Director will oversee the operation of all laboratory activities, explore opportunities to diversify services and/or expand service areas, and manage compliance. By working with and mentoring department managers, the Director ensures that daily operations meet and follow all established guidelines, operate within budget and provide excellence in service. Carter BloodCare is the largest blood center in the state of Texas. We are more than 1,000 employees strong and we offer a variety of great benefits! We have competitive salary and pay for skills and experience! Education: Bachelor's degree in Biology/Laboratory Sciences. MT (ASCP) or equivalent (HEW, NCA, AMT, etc.) required. Specialty in Blood Banking, SBB. Experience: Minimum 10 years of general laboratory experience. Minimum seven years of blood banking. Minimum four years reference laboratory experience. Minimum three years of supervisory experience. Apply online at www.carterbloodcare.org or email cmcfadden@carterbloodcare.org. We are proud to be an EEO/AA employer M/F/D/V.

Reference Technologist. LifeStream, a $53M healthcare organization providing blood service to more than 70 hospitals in Southern California, is searching for a Clinical Laboratory Scientist to resolve serologic problems and provides technical advice to hospital transfusion service personnel. Performs compatibility testing; provides CMV screened, antigen screened, and hemoglobin screened donor units. Performs platelet antibody screens and cross match studies and selects potential platelet donors for a given patient. Requirements: Four-year Bachelors of Science Degree (BS) in Clinical Laboratory Science or related field (e.g. Medical Technology). Current California Clinical Laboratory Scientist License. One to two years experience in antibody identification and transfusion service to grasp the more complex testing procedures. LifeStream is an Equal Opportunity Employer, M/F/D/V. Bonus Opportunity and Excellent Benefit Package! Apply online: www.LStream.org.

Clinical Lab Specialist II. Under direct supervision, this position is responsible for performing routine testing of biological specimens. Works with other team members to ensure timely and quality test results. Education: Bachelor's degree required. Must satisfy CLIA requirements for High Complexity Testing required. California testing requirements must be met within one year, where applicable, required. Experience: None. License/Certifications: Appropriate state licensure and/or certificate, for Florida is required. Send your resume to: Creative Testing Solutions, ATTN: jtueller@mycts.org, Job Code: Clinical Lab Specialist. **Closing Date: 2/1/2013**. Employee Drug Testing Required. EOE M/F/D/V. Fax: (602) 343-7125

QA Specialist. This position reports to the Director, QA & Compliance. Coordinate quality assurance activities with management and front-line staff. Develop and conduct internal audits for all areas of the SDBB. Complete and review Post Donation Information reports including consignee notification. Perform review and approval of Quality Incident Reports. Review and approve Standard Operating Procedures and Validations. Complete documentation and submit license amendments. Knowledge, Skills, Abilities: Education: Bachelor's degree required. Advanced degree preferred. Experience: Minimum five years of experience in Quality Assurance in Blood Banking or in a related area such as cord blood. Certifications/Licenses: RN, CLS, SBB, ASQ certification preferred. To apply online, please visit http://www.sandiegobloodbank.org/find-a-career. AA/EEO/V/D/M/F

Lead Medical Technologist. BloodCenter of Wisconsin seeks experienced Medical Technologist to join our Transfusion Services team. This position is based with Children's Hospital of Wisconsin, in Milwaukee, Wis. Lead Tech provides leadership and technical expertise, coordinates workflow, training, and quality activities. Successful candidate will have strong leadership skills, effective communication skills, and strong technical skills. Position requires bachelor's degree, ASCP certification, and experience working in a transfusion service. SBB preferred. We offer a competitive salary

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and excellent benefits. Apply online at www.bcw.edu/careers. We embrace and encourage diversity in our workforce. EEO/AAP

Cellular Therapy Collection Nurse/Blood Collections. Kentucky Blood Center, located in Lexington, Ky., is seeking a reliable Registered Nurse to collect mononuclear cells/stem cells while providing the best possible care, safety, and outcomes for donors/patients undergoing cellular therapy procedures. Job duties include, but are not limited to: performing apheresis procedures on automated cell separators; performing venous assessments on donors/patients; monitoring donors/patients during apheresis/phlebotomy procedures; administering medications to donors/patients; providing education to patients, donors, families and providers; developing and revising procedures, policies and training materials; and ensuring donor/patient records are complete. Requirements for this position include RN certification; experience in blood banking, apheresis, dialysis, ICU or equivalent experience; proficient in Microsoft Office; and excellent written and verbal communication skills. Competitive salary, comprehensive benefits including health/dental/life, LTD, paid sick/vacations/holidays, EAP, 403(b) retirement savings plan, and pension plan. For more information or to apply online, please visit www.kybloodcenter.org/. Drug-free and EOE/AAP

Director of Quality Systems (Rock River Valley Blood Center, Rockford, Ill.). RRVBC's successful candidate is a self-motivated professional who will lead and champion all quality initiatives from start to finish in an influential, collaborative, and business-friendly manner. This position is accountable for overseeing the strategic planning, development and execution of all quality systems and process improvement initiatives center-wide. This includes business operations relating to blood collection, testing, manufacturing, distribution, document control, customer service, safety, risk management, training, internal and external audits/inspections. This position will take an inquisitive and systematic approach in the identification of potential areas of quality systems vulnerability and risk and will ensure the organization is in full compliance with all applicable federal and state regulations and professional contract requirements, including but not li-mited to FDA, CLIA, HIPAA, AABB, OSHA and NMDP. Five plus years QA management experience in a highly regulated work environment required. Certification such as CMQ/OE or CQA with FDA experience preferred. Please visit us online at www.rrvbc.org to apply online. Email resume to jobs@rrvbc.org. EOE M/F/D/V

CALENDAR

Note to subscribers: *Submissions for a free listing in this calendar (published in the last issue of each month) are welcome. Send information to Leslie Norwood by e-mail* (mnorwood@americasblood.org) *or by fax to (202) 393-5527. (For a more detailed announcement in the weekly "Meetings" section of the Newsletter, please include program information.)*

2013

Jan. 28-29. **16th Annual Blood Conference FDA and Current Issues in Blood Banking, San Antonio, Texas.** More information is available at http://bit.ly/115IFGm. Interested participants may register online at www.pharmaconference.com/registration.htm.

Feb. 9-10. **SBB Last Chance Review, Houston, Texas.** Details and registration form are available at http://www.giveblood.org/services/education/sbb-last-chance-review. Contact: Clare Wong, cwong@giveblood.org.

Feb. 13-15. **Children's Medical Center Sixth Annual Transfusion Medicine Conference, Plano, Texas.** Contact LENA.PATE@childrens.com with questions or comments.

Feb. 15. **CBBS Transfusion Medicine Regional Seminar, Calif.** Early registration prices apply prior to Feb. 9. More information and registration can be accessed at http://bit.ly/SmWAXP.

Feb.15-18. **International Meeting on Emerging Diseases and Surveillance, Vienna, Austria.** More information about the meeting is available at http://www.isid.org/imed/.

Feb. 25-26. **AdvaMed 510(k) Submission Workshop, Arlington, Va.** More information and registration links can be accessed at www.advamedmtli.org/go.cfm?do=Wercs.Show&wid=193.

Mar. 5-6. **International Plasma Protein Congress, Dublin, Ireland.** More information is available at www.ippc.net/.

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Mar. 16-19. **Annual Meeting, America's Blood Centers, Washington, DC.** Attendance restricted to ABC members and invited guests. Contact: ABC Meetings Dept. Phone: (202) 654-2901; fax: (202) 393-1282; e-mail: meetings@americasblood.org.

Mar. 20-22**. BBCS' Annual User Group Meeting, Seattle, Wash.** More information and online registration are available at http://conta.cc/11ksK8J.

April 23-24. **IPFA/PEI 20th International Workshop on "Surveillance and Screening of Blood Borne Pathogens," Helsinki, Finland.** Visit www.ipfa.nl/events/ipfa-pei-workshop-2013-20th_anniversary for more information and registration details.

May 7-9. **Technical/Lab Directors &Quality Workshop, America's Blood Centers, Atlanta , Ga.** Attendance restricted to ABC members and invited guests. Contact: Leslie Norwood. Phone: (202) 654-2917; fax: (202) 393-1282; e-mail: mnorwood@americasblood.org.

June 2-5. **23rd Regional Congress of the ISBT, Amsterdam, The Netherlands**. For more information please visit www.isbtweb.org/amsterdam.

June 18-21. **Fund Development, Donor Recruitment and Communications Workshop, America's Blood Centers, San Antonio, Texas.** Attendance restricted to ABC members and invited guests. Contact: Abbey Nunes. Phone: (202) 654-2980; fax: (202) 393-1282; e-mail: anunes@americasblood.org.

Aug. 3. **Medical Directors Workshop, America's Blood Centers, Milwaukee, Wis.** Attendance restricted to ABC members and invited guests. Contact: ABC Meetings Dept. Phone: (202) 654-2901; fax: (202) 393-1282; e-mail: meetings@americasblood.org.

Aug. 4-5. **Interim Meeting, America's Blood Centers, Milwaukee, Wis.** Attendance restricted to ABC members and invited guests. Contact: ABC Meetings Dept. Phone: (202) 654-2901; fax: (202) 393-1282; e-mail: meetings@americasblood.org.

Oct. 12-15. **AABB Annual Meeting and CTTXPO, Denver, Colo.** For more information: www.aabb.org/events/annualmeeting/attendees/Pages/future.aspx.

2014

June 5-8. **5th International Monoclonal Antibody Workshop, New York, N.Y.** Contact: Gregory Halverson, New York Blood Center. Phone: (212) 570-3026; e-mail: ghalverson@nybloodcenter.org.

Aug. 5 Tuesday (Please note: new date and day) **Medical Directors Workshop, America's Blood Centers, Seattle, Wash.** Attendance restricted to ABC members and invited guests. Contact: ABC Meetings Dept. Phone: (202) 654-2901; fax: (202) 393-1282; e-mail: meetings@americasblood.org.

Aug. 6-7 Wednesday-Thursday (Please note: new dates and days) **Interim Meeting, America's Blood Centers, Seattle, Wash.** Attendance restricted to ABC members and invited guests. Contact: ABC Meetings Dept. Phone: (202) 654-2901; fax: (202) 393-1282; e-mail: meetings@americasblood.org.

Oct. 25-28. **AABB Annual Meeting and CTTXPO, Philadelphia, Pa.** For more information: www.aabb.org/events/annualmeeting/attendees/Pages/future.aspx.