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ABC NEWSLETTER

CURRENT EVENTS AND TRENDS IN BLOOD SERVICES

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2017 #43 **December 8, 2017**

INSIDE:

Early Phase Trials of 3 Zika Vaccines Reported

The Zika epidemic, with its associated fetal morbidity, resulted in a wide variety of emergency responses ranging from mosquito control initiatives, to blood donor screening in the United States, and accelerated vaccine development. The findings from Phase 1 clinical trials are now available and demonstrate that three vaccines are "safe and induc[e] an immune response in healthy adults, according to results published in *Lancet* and an National Institutes of Health news release. "Following early reports that Zika infection during pregnancy can lead to birth defects, [National Institute of Allergy and Infectious Diseases] scientists rapidly created one of the first investigational Zika vaccines using a DNA-based platform and began initial studies in healthy adults less than one year later," said NIAID Director Anthony S. Fauci, MD. "NIAID has begun Phase 2 testing of this candidate to determine if it can prevent Zika virus infection, and the promising Phase 1 data published today support its continued development." Three phase 1 placebo controlled trials of a formalin-inactivated whole virus and two Zika DNA vaccines are reported in two *Lancet* papers. Adverse reactions were acceptable in all the reports, "[v]accinations were safe and well-tolerated in both trials, although some participants experienced mild to moderate reactions such as tenderness, swelling and redness at the injection site," stated the release. The vaccines produced what appear to be clinically relevant humoral immune (antibody) responses.

Additional studies are being planned. The authors of an accompanying commentary note the association of natural Zika infection with Guillain-Barré syndrome, asking if the vaccine antigens might pose a risk of this immune complication, and whether the immune response to the vaccines might alter the clinical behavior of related flaviviruses, i.e. dengue, where prior infections can be associated with adverse clinical outcomes during subsequent infections. They emphasize the difficulty of completing the necessary assessments of the candidate vaccines effectiveness, especially in women of child bearing age, at a time when the epidemic has declined dramatically, and any recrudescence is unpredictable. This limits the pool of susceptible potential vaccines needed to demonstrate efficacy in controlled trials.

Citations: Modjarrad, K., Lin, L., George, S. *et al.* Preliminary aggregate safety and immunogenicity results from three trials of a purified inactivated Zika virus vaccine candidate: phase 1, randomised, double-blind, placebo-controlled clinical trials. *Lancet*. 2017. http://dx.doi.org/10.1016/S0140-6736(17)33106-9.

Gaudinski, M.R., Houser, K.V., Morabito, K.M. *et al. Lancet*. 2017. http://dx.doi.org/10.1016/S0140-6736(17)33105-7.

Marques, E.T.A., Burke, D.S. Tradition and innovation in development of a Zika vaccine. *Lancet*. 2017. http://dx.doi.org/10.1016/S0140-6736(17)33107-0 .

OUR SPACE

Louis Katz, MD; Chief Medical Officer & Interim CEO

BPAC Outcomes

Last week, the U.S. Food and Drug Administration's (FDA) Blood Products Advisory Committee (BPAC) met for two full days of sausage making—not always pretty, but the committee came up with a tasty product. Two topics were of particular interest to ABC member blood centers. Bacterial contamination of platelets was the subject of draft guidances from the agency in December 2014 and again in March 2016. ABC commented repeatedly on these, last in late winter of this year to urge FDA to make available an approach like that used in the United Kingdom, Héma-Québec and most recently Canadian Blood Services. It is delayed, high volume primary culture, in return for 7-day platelet dating without secondary bacterial testing on day 4 and later during storage. If the FDA accepts the recommendation of the BPAC (it is not required to do so), we can deliver to hospitals a safe, ready-to-use platelet that requires no further testing and/or relabeling there. Extended dating will be associated with lower outdates and offer operational advantages in collection facilities that will offset at least part of the increased cost of enhanced sensitivity. Consider this a victory for safety, customer service, and blood center operations—win-win-win. If pathogen reduction is the most effective approach to bacterial safety in platelets, then we now have a rest stop on the road to that approach while manufacturers make the process(es) more "user friendly."

The urgent August 2016 guidance about the threat to recipients from Zika virus was not free of controversy. It was issued at a time of uncertainty about the importance of Zika to transfusion medicine, and the requirement for universal individual donor nucleic acid testing. Many of us asked if it was commensurate with what we estimated to be a low, but admittedly not zero, risk from the virus. I certainly questioned whether consuming the time and money required, without a more formal public assessment, was appropriately risk-based decision-making from a societal standpoint. At the time, and in part in response to our (the blood community's) position, leadership at the FDA's Center for Biologics Evaluation and Research and its Office of Blood Research and Review committed to timely reassessment of the guidance based on experience and new data. The discussion last week fulfilled that commitment and has resulted in what can be characterized as an evidence-based approach. The BPAC has recommended a strategy going forward that looks very much like that in use, with great success, for West Nile virus. Given that our vendors charge per donor tested, not per assay run, it will not save us much money, but it does simplify and rationalize our approach while we watch the progress of the Zika pandemic unfold. Explicit in BPAC discussions of Zika testing was the fact that no strategy will be perfect—there is no such thing as *zero* risk—but there was implicit and explicit recognition in the recommendation that there is such a thing as *tolerable* risk when it is managed appropriately. Development of ABC's positions on these two subjects has been a bit like sausage-making too, but a messy, difficult process does not make it any less important. Members' responsiveness to our request for thought, advice, criticism, and finally consensus is the core of our increased focus on advocacy—this makes your participation only ***more*** important. Stay tuned.

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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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INSIDE ABC

The programs and services described in the Inside ABC section are available to ABC member blood centers and their staff only, unless otherwise specified.

ADRP Registration & Call for Speaker Abstracts Open

Early bird registration for the ADRP, an international division of ABC, 2018 Conference and Expo is open. Register by December 31st to take advantage of the discounted rate ($525). ADRP also invites you to submit abstracts to speak at the conference in Dallas, Texas. All marketing and communications innovators, recruitment visionaries, and collections experts are invited to submit abstracts on topics including donor collections staffing, the impact of technology on donor flow, internal communications strategies for regulatory changes, reinventing your brand, fixed site recruitment, lead generation for new sponsor groups, first time donor retention programs, and emerging medical issues. Speakers who are chosen will receive a 30 percent discount off conference registration and a complimentary one-year subscription to ADRP. Interested individuals may submit abstracts here.

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INSIDE ABC (continued from page 3)

Reminder: ADRP Award Nominations Open

Recognize a peer or outstanding donor group by nominating them for an ADRP Award. Submissions are being accepted until December 31st via the online nomination form. This year's categories include: Donor Recruiter of the Year, Donor Collections Team Member of the Year, Leader of the Year (Recruitment & Collections), Franzmeier Lifetime Achievement Award, Gilcher MD/CEO Award, Media Partner Award, Blood Drive Award (Creative & Most Productive), School Blood Drive Award, and the Humanitarian Service Award.

RESEARCH IN BRIEF

A study in the *New England Journal of Medicine* examined the factor IX levels and clinical activity in patients with Hemophilia B after gene therapy supplying the Factor IX gene via a viral vector. The results of the study represent a progress towards a cure for the blood disorder. Currently, Hemophilia B patients are treated with plasma-derived or recombinant factors infused intravenously weekly. The authors hypothesized that "Endogenous factor IX expression after gene therapy could address many of the limitations of current therapies with the use of a single vector infusion to maintain factor IX coagulant activity above the threshold that is effective in preventing spontaneous bleeding and preserving joint function." The recombinant-adeno-associated viral (AAV) vector, consists of a bioengineered capsid (AAV-Spark100), and a transgene consisting of a liver-specific promoter sequence and the gene for factor IX-Padua. The 10 patients in the nonrandomized, multicenter study were men older than 18 with a factor IX coagulant activity of 2 percent or less than normal. Patients incurred 40 adverse events, but none were deemed serious. The range of participants' follow-up was 28 to 78 weeks with the annualized bleed rate reduced from a mean of 11.1 events per year [range, 0 to 48] before vector administration to 0.4 events per year [range, 0 to 4] after; P = 0.02. A drop in factor use from a mean dose of 2,908 IU per kilogram [range, 0 to 8,090] before vector administration to 49.3 IU per kilogram [range, 0 to 376] after; P = 0.004.

Citation: George, L., Sullivan, K., Giermasz, A., *et. al.*, Hemophilia B Gene Therapy with a High-Specific-Activity Factor IX Variant, *New England Journal of Medicine* 2017. 377:2215-2227, doi: 10.1056/NEJMoa1708538.

WORD IN WASHINGTON

Congress temporarily avoided a government shutdown by reaching agreement on a two-week funding bill extension. Funding for the government had been slated to run out on Friday prior to this temporary measure. President Trump continues to meet with congressional leaders to hash out a longer-term solution. "We had a good meeting. We agreed to keep on talking," said Senate Majority Leader Mitch McConnell (R-Ky.). "Everybody wants to get to an outcome." House Minority Leader Nancy Pelosi (D-Calif.) added, "[w]e had a productive conversation on a wide variety of issues. Nothing specific has been agreed to, but discussions continue."

(Source: *Politico*, Congress clears spending bill, averting shutdown, 12/7/17)

The Senate passed a tax bill last Saturday that would overhaul the federal tax code. The bill eliminates the Affordable Care Act's (ACA) individual mandate for health insurance and cuts the corporate tax rate by 20 percent. The bill differs from the House version, which did not repeal ACA individual mandates. According to the *New York Times*, the "budget office said [repeal of the ACA mandate] would save the federal government more than $300 billion over 10 years — mainly because fewer people would have Medicaid or subsidized private insurance." Lawmakers from the House and Senate will attempt to compromise on a unified version of the bill in conference before the end of 2017, "we will move quickly to a conference committee so we can get a final bill to President Trump's desk," said House Speaker Paul Ryan (R-Wisc.).

(Source: *New York Times*, Tax bill is likely to undo health insurance mandate, republicans say, 12/6/17)

RECENT REVIEWS

Clinical cases of variant Creutzfeldt Jakob disease (vCJD) have nearly disappeared, with only two deaths in the United Kingdom (U.K.) since 2011. One hundred seventy-seven of 178 of these cases were methionine homozygotes at the critical codon 129 of the prion protein (PrP) gene. But the last case, in 2016, was a methionine/valine heterozygote and the authors are concerned this may portend future waves of illness, or that subclinical infections (two are referenced) on the latter genetic background may be transmissible, including by transfusion, to susceptible individuals. The tissue distribution of the abnormal PrP is described, as are a series of surveillance studies (Appendix I-III). Estimates for the prevalence of the vCJD PrP in appendices center on 1/2-3000 patients in the U.K. population, but the initial studies included no negative control group. In Appendix III, appendices removed outside the years with the years of maximum dietary exposure were studied, demonstrating a similar rate, raising questions about the specificity of the initial studies or that the risk of exposure was more extended than believed. The only evidence to date of person-to-person transmission of vCJD is blood transfusion, and the evidence base requires continued careful surveillance, the authors conclude. This will be important moving forward as regulatory agencies, including the Food and Drug Administration, reassess existing blood donor deferral policies.

Citation: Diack, A.B., Will, R.G., Manson, J.C. Public health risks from subclinical variant CJD. *PLoS Pathogens*. 2017. 13(11): e1006642. https://doi.org/10.1371/journal.ppat.1006642.

BRIEFLY NOTED

AABB has issued its call for proposals to be presented at the 2018 AABB Annual Meeting in Boston from Oct. 13 to 16. AABB encourages individuals to submit proposals online to share knowledge with colleagues by completing submissions on or prior to January 10th. Preliminary acceptance notifications will be distributed in March. An education session proposal guide is available for download. More information and submission instructions can be found here.

REGULATORY NEWS

The U.S. Food and Drug Administration (FDA) issued a final guidance this week regarding donor screening for infection with the agent of Chagas disease. The guidance, "Use of Serological Tests to Reduce the Risk of Transmission of *Trypanosoma cruzi* Infection in Blood and Blood Components," "supersedes" the 2010 Chagas guidance and "finalizes" 2016 draft Chagas guidance with recommendations that include donor testing, deferrals, and reentry.

(Source: FDA Guidance, 12/5/17)

Members of the Department of Health and Human Services (HHS) Tick-borne Working Group will hold a meeting on December 11th-12th in Washington, D.C. The group includes 14 individuals who will serve in advisory committee roles providing recommendations regarding ongoing research and advancements in the fight against tick-borne diseases. A biennial report will be provided by the group to Congress on the federal response to tick-borne diseases. The meeting will be webcast for interested individuals who are unable to attend. While the focus of the advisory committee is much broader than the impact of tick-borne infections on transfusion recipients, it is anticipated this aspect will be discussed. Additional information including the meeting agenda and materials will be posted on the HHS site as they become available.

(Source: *Federal Register* Announcement, 11/24/17)

FDA issued a guidance on December 5th entitled "Technical Considerations for Additive Manufactured Medical Devices." The guidance addresses 3-dimensional (3D) printing and the agency's "initial" thoughts on medical devices manufactured in this manner. FDA Commissioner Scott Gottlieb, MD issued the following statement, "In order to help ensure the safety and effectiveness of these products, we're working to establish a regulatory framework for how we plan to apply existing laws and regulations that govern device manufacturing to non-traditional manufacturers like medical facilities and academic institutions that create 3D-printed personalized devices for specific patients they are treating... The FDA also plans to review the regulatory issues related to the bioprinting of biological, cellular[,] and tissue-based products in order to determine whether additional guidance is needed beyond the recently released regulatory framework on regenerative medicine medical products .The Center for Biologics Evaluation and Research has recently interacted with more than a half-dozen manufacturers who have expressed interest in using 3D printing in some capacity to produce their medical products."

(Sources: FDA Announcement, 12/4/17; FDA Guidance, 12/5/17) ♦

INFECTIOUS DISEASE UPDATE

SARS

Many of us recall the SARS outbreak(s) and the related U.S. Food and Drug Administration response related to blood donors in 2003. This coronaviral respiratory pathogen spread from China to more than 20 countries, including the U.S. and Canada, with a mortality rate of around 3.5 percent. While there was and is no evidence of spread by transfusion of this or other coronaviruses, urgent guidance at the time stated that "(T)he possibility of a viremic period, remains a an important concern regarding blood safety". This statement was based on the presence of viral nucleic acid in the blood of a single patient and in tissues outside the respiratory tract in others, suggesting the possibility of viremic spread from the lungs. The source of the epidemic was not conclusively identified at the time, and a variety of animals, especially in live animal markets in China, were implicated in the chain of transmission—especially palm civets. Transfusion services were required to ask every donor about a history of SARS, treatment for SARS, close contact

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INFECTIOUS DISEASE UPDATE (continued from page 8)

with SARS, and travel to areas affected by SARS, with a 30-day implementation timeline. Chinese investigators have now nearly conclusively identified the source of the virus in cave-dwelling horseshoe bats. They have sequenced multiple related coronaviruses in these bats in a single cave site that, in aggregate, represent the entire genome of the SARS-coronavirus. Recombination rates analyzed were high enough for them to hypothesize the evolution of the pathogen. The cave is 1,000 km from where human infection emerged, and whether and how the virus traveled that distance is unclear. The presence of these multiple coronaviruses "highlights the necessity of preparedness for future emergence of SARS-like diseases."

Citation: Hu, B., Zeng, L-P, Yang, X-L *et al.* Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog*. 2017. 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698 ♦

MEMBER NEWS

The National Marrow Donor Program (NMDP) honored **Rock River Valley Blood Center** (RRVBC) during its fall Council Meeting. RRVBC received recognition for "Tier 1 Donor Management Performance" and "Top Honors for Recruitment." According to the release, RRVBC was the only organization within "their category to receive these distinctions," and has been a donor center for NMDP's Be The Match® Registry for more than 25 years.

(Sources: Rock River Valley Blood Center News Release,11/29/17) ♦

GLOBAL NEWS

Facebook recently announced plans for expansion of a blood donation tool that debuted in India in September. More than 4 million people in India have registered as blood donors according to Facebook, which intends to unveil the program in Bangladesh to combat blood shortages. The feature allows individuals to sign-up to be blood donors on Facebook and receive alerts directly in their newsfeed when shortages arise. Blood organizations and hospitals in that country will be able to generate special posts or requests that Facebook will connect to individual donors nearby who will have the opportunity to respond directly from their mobile device via WhatsApp, Facebook Messenger, or by phone to the requests. "People were already using Facebook for blood donation and fundraising," said Naomi Gleit, Facebook vice president of Social Good. "We're building tools to make it even easier."

(Sources: CNN, Facebook wants to be seen as a force for good, 11/29/17; Facebook Announcement, 11/29/17) ♦

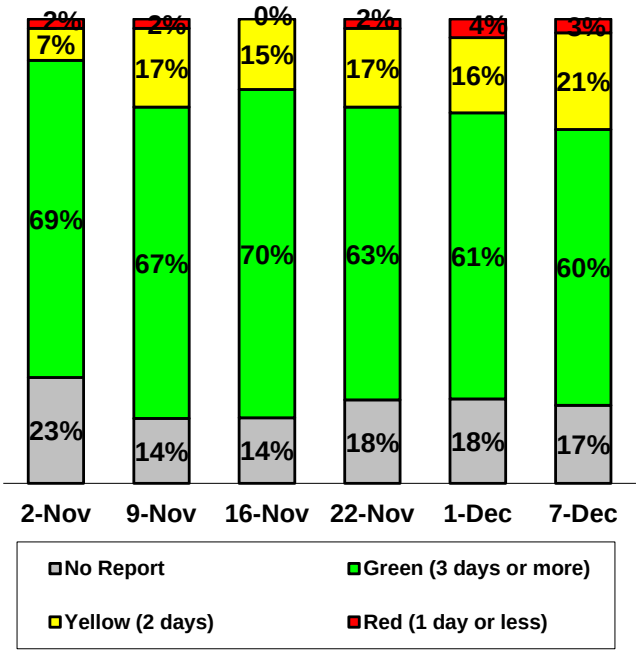
COMPANY NEWS

Terumo BCT has received a 3-year grant from the U.S. Department of Defense (DoD) for further advancement of its Mirasol® pathogen reduction technology system, as a part of the Peer Reviewed Medical Research Program. "A ready and safe supply of blood products for our [w]arfighters and beneficiaries around the world is fundamental to preparedness," said Col. Audra L. Taylor, director of the Army Blood Program. "This new grant extends our efforts with Terumo BCT to help us further explore increasing blood processing and pathogen reduction efficiencies." Mirasol® utilizes a combination of riboflavin and ultraviolet light to eliminate pathogens from blood products. "Our latest DOD grant is helping Terumo BCT directly address specific customer needs by engineering innovations that will have a lasting impact on patients throughout the world," said Palani Palaniappan, executive vice president, Innovation and Development at Terumo BCT.

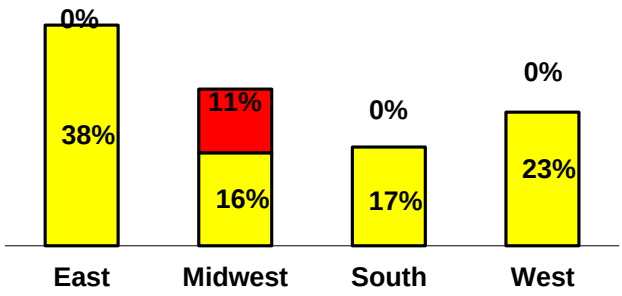
(Source: Terumo BCT News Release, 12/6/17) ♦

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

Total ABC Red Cell Inventory



Percent of Regional Inventory at 2 Days Supply or Less, December 7, 2017



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

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 Maundy by e-mail (lmaundy@americasblood.org) or by fax to (202) 393-1282. (For a more detailed announcement in the weekly "Meetings" section of the newsletter, please include program information.)*

2017

Dec. 9-12. **American Society of Hematology Annual Meeting & Expo., Atlanta, Ga**. Register here.

2018

Feb. 5-7. **14th Annual FDA and the Changing Paradigm for HCT/P Regulation., Alexandria, Va.** Register here.

Feb. 21. **General Topics for Blood Bankers in Clinical Laboratory Medicine, Orlando, Fla.** For more information, contact Nancy Benitez.

Mar. 17-19. **ABC Annual Meeting, America's Blood Centers, Scottsdale, Ariz.** More details available here.

Mar. 21-22. **IPFA 3rd Asia Workshop on Plasma Quality and Supply, Kuala Lumpur, Malaysia.** More details available here.

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CALENDAR (continued from page 10)

May 8-10. **ABC Human Resources and Training/Development Workshop, Dallas, Texas.** More details available here.

May 9-11. **ADRP Conference & Expo, Dallas, Texas.** More details available here.

May 16-17. **IPFA/PEI 25th Workshop on "Surveillance and Screening of Blood-borne Pathogens," Athens, Greece.** More details available here.

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. A six (6) percent processing fee will be applied to all credit card payments. Notices ordinarily are limited to 150 words. To place an ad, contact Leslie Maundy at the ABC office. Phone: (202) 654-2917; fax: (202) 393-1282; e-mail: lmaundy@americasblood.org.

POSITIONS

Medical Technologist (MT). Blood Bank of Hawaii is seeking a Medical Technologist (MT) to join our Laboratory team!! The candidate is responsible for: Component antigen testing in the donor blood testing section of the laboratory; and patient testing in the Immunohematology Reference Lab, including but not limited to ABO grouping, Rh testing, antibody screening, and antibody identification to include complex work-ups. The ideal candidate will: Encompass a high standard for accuracy, follow-up and follow-through; thrive in an environment where problem solving is a necessity; work with team members ensuring compliance at all times; and serve as a technical resource to hospitals and other departments. Minimum qualifications include Baccalaureate degree in Medical Technology or in a related science from an accredited college or university; Certified Medical Technologist by the ASCP; eligible for Clinical Laboratory Technologist license by the Department of Health of the State of Hawaii. Previous work experience as an MT in hematology and immunohematology is preferred; certification as a Specialist in Blood Banking (SBB) highly desirable. Visit our website at www.BBH.org to complete an online application.

Manager of Mobile Blood Drive Collection Operations. Do you have a passion for leadership and fostering great performance in your staff members? Are you a goal-oriented people person? Arkansas Blood Institute is seeking qualified candidates for Manager of Mobile Blood Drive Collection Operations in the Little Rock area. The position will focus on the staff performance of key metrics for the donor services Little Rock mobile operations. The manager will develop programs and work with individual staff to ensure key metric goals are achieved. Overall success will be realized with an acceptable incomplete, deferral and error rate in addition to conversion rates and excellent customer service scores. Qualifications: Three plus years of supervisory or management experience with blood bank focus helpful; post-secondary education required, bachelor's degree preferred; and a valid driver's license and good driving record with zero points and no moving violations in the past three years. Benefits: Arkansas Blood Institute offers a competitive salary, excellent benefits package including health, FSA, HSA Health Savings, dental, vision, and life insurance; LTD, 401(k), paid time off, and tuition reimbursement. Apply online only at http://arkbi.org/careers/. EEO M/F/D/V/Drug Free Work Environment.