Monitoring International Trends

**posted October-November 2014**

The NBA monitors international developments that may influence the management of blood and blood products in Australia. Our focus is on:

* Potential new product developments and applications;
* Global regulatory and blood practice trends;
* Events that may have an impact on global supply, demand and pricing, such as changes in company structure, capacity, organisation and ownership; and
* Other emerging risks that could potentially put financial or other pressures on the Australian sector.

A selection of recent matters of interest appears below. Highlights include:

* [CSL Behring](http://www.cslbehring.com/) at the 16th Biennial Meeting of the European Society for Immunodeficiencies (ESID) presented data evaluating flexible and individualized dosing and administration of Hizentra (immune globulin subcutaneous [human]) for the treatment of primary and secondary immunodeficiencies. (Section 1)
* Entegrion has $US7.8 million from the US Department of Defense to develop freeze-dried platelets to be used for emergency treatment of wounded soldiers. (Section 1)
* The US Food and Drug Administration (FDA) approved Baxter’s Obizur [Antihemophilic Factor (Recombinant), Porcine Sequence] for treating bleeding in adults with acquired Factor VIII deficiency. (Section 2)
* Health Canada, following a safety review, announced that the prescribing information (product monograph) for all immunoglobulin products had been updated to strengthen warnings on the rare but serious risk of blood clots. (Section 2)
* FDA has accepted Cerus’ clinical protocol to make the INTERCEPT Blood System for platelets available under an Expanded Access Investigational Device Exemption (IDE) to regions in the US with chikungunya and dengue outbreaks. (Section 2)
* Also in response to US public health concerns over chikungunya and dengue fever, Terumo BCT decided to file a submission with the FDA to allow expanded access use of the Mirasol Pathogen Reduction Technology System for the treatment of platelets. (Section 2)
* CSL announced expansion of its manufacturing site in Broadmeadows, Melbourne, to meet growing world demand for albumin. CSL recently increased its plasma processing and albumin production capacity at Kankakee, Illinois. (Section 3)
* A Canadian study found that patients transfused with recently donated blood had significantly fewer post-operative complications than those who were transfused with blood donated more than two weeks before their surgery. The study was presented at the Canadian Cardiovascular Conference. (Section 5)
* Another study presented at the Canadian Cardiovascular Congress said that robotically assisted coronary artery bypass grafting (CABG) surgery is a rapidly evolving technology that decreases the need for blood products, decreases recovery times, decreases the length of hospital stays and makes the procedure safer. Section 5)
* A study at Johns Hopkins found that patients who declined transfusions but were treated with blood-conservation methods suffered fewer deaths, infections and other morbid outcomes compared with those who accepted donor blood and received standard care.(Section 5)
* US research has concluded that the rate of postpartum haemorrhage is higher than generally recognised. (Section 5)
* Advanced Cell Technology announced that its human induced pluripotent stem cell platelet technology is potentially capable of producing large-scale quantities of universal donor platelets for transfusion in almost any patient. (Section 6)
* Zinc finger nucleases have been used to rewrite a disease-causing mutation in human primary hematopoietic stem cells from a patient with X-linked severe combined immunodeficiencies. (Section 6)

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# Products

*Here the NBA follows the progress in research and clinical trials that may within a reasonable timeframe make new products available, or may lead to new uses or changes in use for existing products.*

### Clotting factors

* 1. Grifols announced that the 40-g (400 mL) vial size for GAMUNEX-C (immune globulin injection [human], 10% caprylate/chromatography purified) became available on 3 November 3 in the US.
  2. **Peter W. Collins,** of the Arthur Bloom Haemophilia Centre at Cardiff University, led a team evaluating the safety and efficacy of nonacog beta pegol, Novo Nordisk’s recombinant glycoPEGylated [Factor IX](http://www.healio.com/hematology-oncology/hematology/news/online/%7Bb2c20fd4-69bf-4d85-916e-5989906ee5de%7D/recombinant-factor-ix-fc-fusion-protein-reduced-bleeding-in-hemophilia-b) with an extended half-life — in 74 previously treated patients with haemophilia B. They found the product effectively treated bleeding episodes and was associated with low annualized bleeding rates. They suggested: “Low bleeding rates were observed in patients on prophylaxis and are likely related to high trough levels due to the extended half-life of nonacog beta pegol.”

### Immunoglobulin

* 1. During the biennial congress of the European Society for Immunodeficiencies, held in Prague, Baxter International presented the results of a Phase II/III study of its 20 per cent concentration subcutaneous immunoglobulin treatment for primary immunodeficiencies (PI).
  2. Prophylix Pharma of Norway will conduct Phase I/II trials in 2015 of its novel prophylactic NAITgam (anti-HPA-1a Immunoglobulin). NAITgam protects newborns against the rare but potentially crippling or fatal bleeding disorder called foetal and neonatal alloimmune thrombocytopenia (FNAIT). This disorder results when a mother develops antibodies to her baby’s platelets[[1]](#footnote-1). Prophylix will apply to the FDA for fast track designation.
  3. [CSL Behring](http://www.cslbehring.com/) at the 16th Biennial Meeting of the European Society for Immunodeficiencies (ESID) presented data evaluating flexible and individualized dosing and administration of Hizentra (immune globulin subcutaneous [human]) for the treatment of primary and secondary immunodeficiencies.
  4. A study protocol has been issued for a randomized controlled trial of low-dose intravenous immunoglobulin treatment for complex regional pain syndrome.

### Devices and Services

* 1. At the [**2014 American College of Surgeons Clinical Congress (ACS)**](http://www2.facs.org/clincon2014/) in San Francisco,[**US Medical Innovations**](http://usmedinnovations.com/#sthash.lqseMPpK.dpbs) introduced its **Canady Hybrid Plasma Scalpel (CHPS)** handpiece design. This multifunctional electrosurgical scalpel allows a surgeon to simultaneously cut and coagulate through biological tissue at a temperature of less than 98 degrees Fahrenheit. This decreases intraoperative blood loss and operative time, improves wound healing, decreases the risk of hospital acquired infections and reduces the length of hospital stay.
  2. Harvard scientists[[2]](#footnote-2) have developed a new surface coating[[3]](#footnote-3) that prevents blood clots and bacterial infections around implanted devices such as catheters, central venous access devices and cardiac implants.
  3. Patches containing multiple microneedles have been used to capture two particular proteins with high sensitivity from fluid in the skin of mice[[4]](#footnote-4).
  4. A study by researchers at Northwestern University and University of Illinois at Urbana-Champaign report that a small new device, placed directly on the skin and worn 24/7, can alert the wearer if they are having cardiovascular trouble[[5]](#footnote-5).
  5. [Wei Shen](http://eng.monash.edu.au/about/people/profile/shen) and his group from Monash University have developed a paper-based blood type test and a smartphone app to interpret the result. The test can recognise all four blood types and the Rh factor.
  6. Portable devices using ‘near-infrared technology’ can map out a blood donor’s veins on the skin surface, reducing donor anxiety. “Veins have a lot of deoxygenated haemoglobin that absorbs near infrared light and the device is able to use this information to project the image,” explained[Dr Dan Waller](http://www.donateblood.com.au/media-centre/news/national/world-first-vein-viewing-tech-trial-is-not-in-vain), researcher at the Australian Red Cross blood service who is working on a study of the devices’s impact on donor retention. The study is assessing the responses of 300 first-time and 600 return donors aged 18-30 attending the Chatswood and Elizabeth Street donor centres in Sydney.
  7. The Medicines Company presented the results of the Phase III clinical trial of its investigational haemostatic agent RAPLIXA (fibrin sealant)[[6]](#footnote-6), at the 100th Clinical Congress of the American College of Surgeons in San Francisco. The Phase III trial, FINISH-3, included 719 patients, and met all primary and secondary haemostasis efficacy endpoints in four surgical indications: spinal surgery, hepatic resection, vascular surgery and soft tissue dissection. RAPLIXA, is under regulatory review with both the FDA and the EMA. It is a dry powder topical formulation of fibrinogen and thrombin.

### Other

* 1. Pluristem Therapeutics of Israel, which develops placenta-derived cell therapy products, announced that researchers at [Case Western Reserve University](file:///C:\Tracker%3fdata=tEt9GIOGhx6308dGEXDkG-HRR_KXor5Y9dlCz3IQfpRwgDGRABJ7LR4jE0FKZJNvx-e93TBhmvNrLgftAm3zVg==) will conduct a preclinical study of the Company's PLacental eXpanded (PLX)-RAD cells to evaluate whether cells increase the success rate of human umbilical cord blood transplantation (umbilical cord blood cells are transplanted to replace failed bone marrow cells).
  2. Entegrion was awarded $US7.8 million from the US Department of Defense to develop freeze-dried platelets to be used for emergency treatment of wounded soldiers. This funding should take the product Stasix to a stage where a regulatory application for human trials can be filed in 2016. In 2011 Entegrion was awarded $US43.7 million by the Pentagon to develop dehydrated plasma, which is now in the first phase of clinical trials.
  3. APT Therapeutics is developing a new drug, APT102, for heart attack and stroke patients. In animal model studies of heart attack, APT102 maintained optimal blood flow and reduced damage to the heart muscle by 80 per cent[[7]](#footnote-7).
  4. A phosphorescent transparent paint-on bandage developed at Harvard can provide both a view of the wound and an indication of the oxygen saturation below the bandage. When light shines onto the bandage, the phosphor molecules are activated and continue glowing after the light is turned off. The less oxygen is present around the molecules, the longer they glow[[8]](#footnote-8).
  5. Akebia Therapeutics has reported positive results from a Phase IIb clinical trial of AKB-6548 in patients with anaemia related to chronic kidney disease (CKD) who are undergoing dialysis. AKB-6548 is a once-daily, oral therapy which relies on the same mechanism of action used by the body to adapt to lower oxygen availability with increasing altitude.
  6. Kamada announced that a literature review of the data in support of the mechanism of action of its alpha-1 antitrypsin (Glassia) for the treatment of type-1 diabetes, was published in the August 2014 edition of the Journal of Diabetes Science and Technology. The online version of the review, “Mechanistic Evidence in Support of Alpha-1 Antitrypsin as a Therapeutic Approach for Type-1 Diabetes” can be accessed at: [http://dst.sagepub.com/content/early/2014/08/23/1932296814547096](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fdst.sagepub.com%2Fcontent%2Fearly%2F2014%2F08%2F23%2F1932296814547096&esheet=50965578&newsitemid=20141021005126&lan=en-US&anchor=http%3A%2F%2Fdst.sagepub.com%2Fcontent%2Fearly%2F2014%2F08%2F23%2F1932296814547096&index=1&md5=bb5400a729959721dcc39cb19b11916c)
  7. **bluebird bio** completed the infusion of its LentiGlobin BB305 drug product in the first patient suffering from sickle cell disease.

# Regulatory

*The NBA monitors overseas regulatory decisions on products, processes or procedures which are or may be of relevance to its responsibilities.*

### Plasma and recombinant products

* 1. The US Food and Drug Administration (FDA) approved Baxter’s Obizur [Antihemophilic Factor (Recombinant), Porcine Sequence] for treating bleeding in adults with acquired Factor VIII deficiency[[9]](#footnote-9). Obizur contains a recombinant analogue of porcine (pig) FVIII, used because it is similar enough to human FVIII to be effective in blood clotting, but less likely to be affected by the antibodies against human FVIII that are present in people with acquired hemophilia A.
  2. The FDA has received the investigational new drug (IND) application for ProMetic Life Sciences' IV plasminogen to treat hypoplasminogenemia (type I plasminogen deficiency). The FDA accepted the proposed Phase II/III clinical program represents an adequate surrogate endpoint for licensure using the accelerated approval pathway. The open label, single ascending dose Phase I trial enrolling before the end of 2014 will investigate safety, tolerability and pharmacokinetics in six patients suffering from hypoplasminogenemia. Progress to Phase II / III should occur in 2015, with 15 to 18 patients enrolled.
  3. [Octapharma USA](http://www.empr.com/octapharma/manufacturer/20727/) announced that Octagam 10% [Immune Globulin Intravenous (Human)] liquid preparation had been approved by the FDA for the treatment of adults with [chronic immune thrombocytopenic purpura](http://www.empr.com/immune-mediated-blood-disorders/category/69/0/) (ITP).
  4. The FDA approved a request from Wyeth (owned by Pfizer) to expand the indication for Xyntha to include all paediatric age groups following relevant clinical trials.
  5. China Biologic Products received approval from the China Food and Drug Administration (CFDA) for commercial manufacturing of human prothrombin complex concentrate at its Shandong Taibang facility[[10]](#footnote-10).
  6. Health Canada, following a safety review, announced that the prescribing information (product monograph) for all immunoglobulin products had been updated to strengthen warnings on the rare but serious risk of blood clots[[11]](#footnote-11).
  7. FDA has granted Kamada orphan drug designation for Glassia, its human alpha-1 antitrypsin, to treat graft-versus-host-disease. Orphan drug designation carries benefits, such as the availability of grant money, certain tax credits, seven years of market exclusivity, and the possibility of an expedited regulatory process.
  8. Octapharma Canada announced that Health Canada had approved Nuwiq (recombinant FVIII) for treatment and prophylaxis of bleeding in patients of all ages suffering with haemophilia A. Nuwiq is produced in a human cell line cultured without additives of human or animal origin or any exposure to human blood or plasma, so it is free from blood-borne pathogens. Nuwiq is also free of antigenic non-human protein epitopes, similar to FVIII produced in healthy humans. It has a high affinity for the von Willebrand coagulation factor.Nuwiq was previously approved in the European Union and Australia and is under review in the US
  9. The European Medicines Agency’s Pharmacovigilance Risk Assessment Committee examined evidence from two recently published studies suggesting that previously untreated haemophilia patients may be at greater risk of developing inhibitors (antibodies) if treated with the factor VIII product Kogenate by Bayer or Helixate NexGen from CSL Behring, than if treated with other factor VIII products. The PRAC recommended further examination of the available evidence.
  10. The European Medicines Agency (EMA) validated the Marketing Authorization Application of Elocta, a recombinant factor VIII Fc fusion protein product candidate for the treatment of haemophilia A. Elocta is the European trade name for the product known as Eloctate in the US, Canada, and Australia

### Blood donation, processing, storage and use; blood substitutes

* 1. The FDA has accepted Cerus’ clinical protocol to make the INTERCEPT Blood System for platelets available under an Expanded Access Investigational Device Exemption (IDE) to regions in the US with chikungunya and dengue outbreaks. The reviews of Cerus’ Premarket Approval (PMA) submissions for INTERCEPT plasma and platelets will continue in parallel with a Treatment Use IDE study. Approval decisions for both PMA submissions are expected in 2015. The American Red Cross will participate in Cerus’ IDE study.
  2. In response to US public health concerns over chikungunya and dengue fever, Terumo BCT decided to file a submission with the FDA to allow expanded access use of the Mirasol Pathogen Reduction Technology System for the treatment of platelets.

### Devices

* 1. **Welsh company Microvisk** won European CE Mark approval for the CoagMax PT/INR, its blood clotting analyzer that uses micro electro mechanical component at the core of its sensor.

### Other

* 1. In 2008, contaminated heparin marketed in the US was linked to the death of 80 patients. The FDA now has a list of 34 Chinese companies it will not permit to sell crude heparin into the US.
  2. The EMA has decided to publish the clinical reports that underpin the decision-making on medicines. The policy will take effect on 1 January 2015.
  3. The FDA granted fast track designation to NKTT120 as a potential treatment for sickle cell disease. The drug is a humanized monoclonal antibody that specifically depletes invariant natural killer T cells.

# Market structure and company news

*The NBA’s business intelligence follows company profitability, business forecasts, capital raisings or returns, mergers and takeovers, arrangements for joint research and/or development, contracts for supply of manufacturing inputs, and marketing agreements. Companies considered include suppliers, potential suppliers and developers of products which may be of interest.*

* 1. [CSL Behring](http://www.fiercedrugdelivery.com/tags/csl) has agreed with Ohio’s Enable Injections to use Enable's technology to deliver treatments for chronic diseases. Enable’s wearable bolus injector automatically mixes the solutions and warms the drug. The patient places the injector on his or her skin and presses a button. The injection’s process can be followed through a viewing window. The device includes a "pause" feature and an automatically retracting needle.
  2. CSL Plasma, Germany, has completed the transition to OrSense's NBM200, a non-invasive haemoglobin testing device for screening of Hb levels in plasma donors.
  3. CSL announced expansion of its manufacturing site in Broadmeadows, Melbourne, to meet growing world demand for albumin. Construction will take four years to complete. CSL recently increased its plasma processing and albumin production capacity at Kankakee, Illinois.
  4. CSL agreed to acquire Novartis’ global influenza vaccine business for US$275 million. The business will be combined with CSL’s subsidiary, bioCSL.
  5. [Swedish Orphan Biovitrum A (Sobi)](http://www.sobi.com/) formally opened its new North American office in Waltham, Massachusetts.
  6. Baxter announced plans for a new global innovation and research and development centre in Cambridge, Massachusetts, for its biopharmaceuticals business, which will become a separate, independent global company (Baxalta Incorporated) in mid-2015.
  7. Access Pharmaceuticals has signed an exclusive, global licence agreement with Plasma Technologies LLC (PlasmaTech) for the development and commercialisation of its proprietary plasma fractionation process. Access is now known as PlasmaTech Biopharmaceuticals. It holds the patent for a new extraction process for plasma biologics that it believes will alter the economics of blood plasma fractionation[[12]](#footnote-12), and make possible the extraction of further plasma proteins therapies as it says the process is less destructive than other fractionation processes. PlasmaTech believes that its prime product opportunity, alpha-1 antitrypsin, provides a low-risk, high revenue, product (AAT) for treatment of inherited COPD (pulmonary emphysema), and other indications.
  8. Kamada [extended its agreement](http://email.seekingalpha.com/track?type=click&mailingid=2005195&messageid=2900&databaseid=&serial=2900O2005195O1412013389.736ae0fa77db79dd49212fc3aa6ebffd&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://seekingalpha.com/pr/11150845-kamada-announces-second-extension-of-strategic-agreement-with-baxter?source=email_rt_mc_body&app=n) to supply its liquid [alpha-1 antitrypsin](http://email.seekingalpha.com/track?type=click&mailingid=2005195&messageid=2900&databaseid=&serial=2900O2005195O1412013389.736ae0fa77db79dd49212fc3aa6ebffd&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://en.wikipedia.org/wiki/Alpha_1-antitrypsin) , [Glassia](http://email.seekingalpha.com/track?type=click&mailingid=2005195&messageid=2900&databaseid=&serial=2900O2005195O1412013389.736ae0fa77db79dd49212fc3aa6ebffd&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://www.baxter.com/downloads/healthcare_professionals/products/Glassia_PI.pdf), to Baxter to the end of 2017. Baxter is the exclusive distributor of Glassia in the US, Canada, Australia and New Zealand. The transition to royalty payments for Glassia produced by Baxter will begin in 2018.

# Country-specific events

*The NBA is interested in relevant safety issues which arise in particular countries, and also instances of good practice. We monitor health issues in countries from which Australia’*s *visitors and immigrants come.*

### United States

* 1. In both the US and Canada, children have developed muscle weakness/ partial or full paralysis after a respiratory illness and some have been confirmed to have contracted Enterovirus D68. This is a virus in the Picornaviridae family, which also includes the polio virus, rhinoviruses and other enteroviruses. Some children who tested positive for D68 have died, possibly in some cases from other causes.
  2. The FDA has increased restrictions on who may donate blood as a precaution to prevent the spread of Mad Cow disease. Estimates predict anywhere from 4 per cent to 11 per cent of blood donors will no longer be eligible. Under the FDA's proposal, blood banks will have to bar donors who have spent three cumulative months or more in Britain from 1980 to 1996 inclusive; or spent five cumulative years or more in France from 1980 to the present; or spent six months or more, as American military personnel or dependents, on bases in Northern Europe from 1980 to 1990 inclusive, and elsewhere in Europe from 1980 to 1996 inclusive; or received a blood transfusion in Britain since 1980.

### Other

* 1. The Malaysian Health Minister Datuk Seri Dr S.Subramaniam announced that the number of reported dengue cases during the first 9 months of 2014 was 77,527 (with 149 fatalities) This compares with the 2013 numbers for the same period–23,099 cases (with 48 deaths).
  2. **Construction has begun on Scotland’s new national blood centre.** The centre has received £43m from the Scottish Government.
  3. In the UK the National Institute for Health and Care Excellence in October published draft proposals endorsing the use of Bayer's Xarelto as an option for preventing blood clots in patients who have suffered a heart attack from restricted flow in one of the blood vessels in the heart.
  4. SK Chemicals announced in Seoul that it will increase its plasma fractionation capacity by five times to 600,000 litres from the current 120,000 litres. It is likely to take about three years to build the facility.
  5. In Singapore, PrIME Biologics opened its plasma fractionation plant on October 8. PrIME plans to have its facility registered with the Singapore Health Science Authority and fully operational in January 2015.
  6. Canadian Blood Services launched a new, interactive website with improved navigation capabilities and content and a section dedicated to journalists. See [blood.ca](http://www.blood.ca/)

# Safety and patient blood management

*We follow current issues in patient safety and achieving favourable patient outcomes.*

### Appropriate transfusion

* 1. A study (published to coincide with the annual meeting of the European Society of Intensive Care Medicine in Barcelona[[13]](#footnote-13)) showed that for patients in the intensive care unit with septic shock, outcomes are similar for those who receive blood transfusion at a higher or lower haemoglobin threshold.
  2. A Canadian study found that patients transfused with recently donated blood had significantly fewer post-operative complications[[14]](#footnote-14) than those who were transfused with blood donated more than two weeks before their surgery. The study examined records at the New Brunswick Heart Centre in Saint John, Canada for heart surgeries over the previous nine years on patients given red blood cells during or after surgery. The study was presented at the Canadian Cardiovascular Conference.
  3. Another study presented at the Canadian Cardiovascular Congress said that robotically assisted coronary artery bypass grafting (CABG) surgery is a rapidly evolving technology that decreases the need for blood products, decreases recovery times, decreases the length of hospital stays and makes the procedure safer.
  4. The AABB (formerly the American Association of Blood Banks) has developed clinical practice guidelines for prophylactic platelet transfusion. They were published online 11 November in the *Annals of Internal Medicine*.
  5. A retrospective review of 591 primary total joint arthroplasties has suggested that using topical tranexamic acid in patients undergoing primary hip and knee arthroplasty reduced transfusion rate and cost[[15]](#footnote-15).
  6. US research has concluded that the rate of postpartum haemorrhage is higher than generally recognised[[16]](#footnote-16).
  7. Allegheny Health Network in Pennsylvania is using continuous, non-invasive haemoglobin monitoring on patients at risk for bleeding. This gives clinicians real-time data on changes in haemoglobin levels as the basis for informed and timely decisions about transfusion.
  8. A study at Johns Hopkins found that patients who declined transfusions but were treated with blood-conservation methods suffered fewer deaths, infections and other morbid outcomes compared with those who accepted donor blood and received standard care[[17]](#footnote-17).

### Treating iron deficiency

* 1. Researchers at UT Southwestern Medical Center found that giving acetate to anaemic mice stimulated the formation of new red blood cells[[18]](#footnote-18).

### Other.

* 1. Boehringer Ingelheim has initiated US phase III testing of its antidote to its anticoagulant Pradaxa (dabigatran). Testing is already underway elsewhere[[19]](#footnote-19).
  2. Portola Pharmaceuticals has engaged contract manufacturing and development organization Lonza to supply andexanet alfa, an FDA designated breakthrough therapy. The recombinant Factor Xa molecule reverses the effects of Factor Xa inhibitors. The anticoagulant antidote is needed for people undergoing emergency surgery or suffering from a major bleed.
  3. Two recent studies suggest that transfusion-related acute lung injury remains a perioperative hazard[[20]](#footnote-20). In the US it affects about one in 100 surgical patients, despite efforts to reduce its incidence[[21]](#footnote-21).
  4. During their 100-day life in the human bloodstream red cells lose membrane surface area, volume, and haemoglobin content. Of these, only the observed surface-area loss can be explained by red cells shedding small haemoglobin-containing vesicles budding off their cells' membrane.[[22]](#footnote-22)
  5. [University of Illinois](http://illinois.edu/) researchers have developed a new method to assess the freshness and clinical effectiveness of whole blood[[23]](#footnote-23).

# Research

*A wide range of scientific research has some potential to affect the use of blood and blood products. However, research projects have time horizons which vary from “useful tomorrow” to “at least ten years away”. Likelihood of success of particular projects varies, and even research which achieves its desired scientific outcomes may not lead to scaled-up production, clinical trials, regulatory approval and market development.*

* 1. Advanced Cell Technology of Massachusetts announced that its proprietary human induced pluripotent stem cell (iPSC) platelet technology is potentially capable of producing large-scale quantities of universal donor platelets for transfusion in almost any patient[[24]](#footnote-24). Generating universal platelets required removal of a gene essential to expression of the major histocompatibility (HLA) antigens. These are the molecules primarily responsible for cell and organ rejection.
  2. Zinc finger nucleases have been used to rewrite a disease-causing mutation in human primary hematopoietic stem cells from a patient with X-linked severe combined immunodeficiency[[25]](#footnote-25).
  3. Researchers at Emory University and Georgia Tech say platelets can “feel” their physical environment and respond to surfaces with greater stiffness by increasing their stickiness, the degree to which they “turn on” other platelets and other components of the clotting system[[26]](#footnote-26).
  4. New research shows red blood cells do more than just transport oxygen – they create new blood vessels from those that already exist[[27]](#footnote-27).
  5. A preliminary study[[28]](#footnote-28) suggests that measuring the activity of a type of white blood cell immediately after surgery could distinguish those patients likely to recover.
  6. Scientists from [Delaware Biotechnology Institute](http://www.dbi.udel.edu/) have studied the mechanism of platelet formation, hoping to speed up and enhance their production using stem cells found in bone marrow[[29]](#footnote-29).
  7. A Japanese team led by Koichi Tanaka has developed a blood test measure to detect signs of Alzheimer’s disease before patients show symptoms.
  8. Researchers at Sahlgrenska Academy of the University of Gothenburg have described growing new blood vessels in one week from two tablespoons of blood[[30]](#footnote-30).
  9. Swedish scientists suggest that a protein found in sugar beet could be used as a blood substitute. They say plant and human versions of haemoglobin are very similar.
  10. Researchers at the University of California, Santa Barbara, and Case Western Reserve University have developed synthetic platelet mimics that stopped bleeding in mouse models 65 per cent quicker than if nature were left to itself[[31]](#footnote-31).
  11. Researchers from the Stowers Institute for Medical Research showed that while megakaryocytes are best known for producing platelets, these cells found in bone marrow also play a role in regulating stem cells. This work is the first to show that hematopoietic stem cells (the parent cells) can be directly controlled by their own progeny (megakaryocytes).[[32]](#footnote-32)

# Infectious diseases

*The NBA takes an interest in infectious diseases because: the presence of disease in individual donors (e.g. influenza), or potential disease resulting from travel (e.g. malaria) means a donor must be deferred; temporary disease burden within a community (e.g. dengue in North Queensland) may limit blood collection in the community for a time; and some people may not be permitted to donate at all (e.g. people who lived in the UK for a period critical in the history of vCJD). Blood donations are tested for a number of diseases (e.g. HIV and Hepatitis B), but there are also emerging infectious diseases for which it may become necessary to test in the future (e.g. Chagas disease, and the tick-borne babesiosis and Lyme disease).*

### IMED 2014

* 1. The International Society for Infectious Diseases hosted IMED 2014 in Vienna from 31 October in Vienna. Ebola and MERS-CoV occupied the agenda on the first day[[33]](#footnote-33).
  2. Day 2 began with a plenary session on *The Global Emergence of Resistance,* followed by symposia on *Rapid Diagnostics for Emerging Infectious Threats, Ethics and Disease Surveillance,* *West Nile Fever in the European Union, Pathogen and Host Diversity-Are There Clues that Can Help Us Prevent Emerging Infectious Diseases,* and *Innovations in Outbreak Detection.*
  3. Day 3 launched the new OIE Global wildlife Disease Reporting System, examined FAO tools for animal health, considered emerging infectious diseases and climate change, heard five speakers on *Pastoralism, Rural Communities and the Human Animal Health Interface in East Africa,* heard about *Healthcare Associated Emerging Infections[[34]](#footnote-34),* and finished with *Emerging Viral Threats[[35]](#footnote-35).*
  4. Day 4 dealt with *Changing Disease Landscapes*, and in particular *From Research to Public Health.*
  5. The 17th International Congress on Infectious Diseases will be held in India, March 2-5, 1916 *with particular attention being paid to the major challenges of the region including AIDS, malaria, tuberculosis, pneumonia and enteric infections including typhoid fever and diarrhoea. In addition, major areas of neglected tropical diseases will be discussed and there will be a particular focus on disease prevention and vaccination.*

### Ebola virus disease

* 1. The World Health Organisation (WHO) on 7 November said there had been 13,268 reported Ebola cases in 8 affected countries since the outbreak began, with 4,960 reported deaths. In Liberia, Guinea and Sierra Leone, the three hardest hit countries, there had been 549 infections and 311 deaths of health care workers. Reported figures are generally regarded as underestimates of case numbers and deaths[[36]](#footnote-36). Analysis at Sierra Leone's Kenema Government Hospital found the fatality rate for patients under age 21 was 57 per cent; for those aged 45 or more the mortality rate was 94 per cent.
  2. Liberia has increased the proportion of safe burials of Ebola victims[[37]](#footnote-37).
  3. The US had its first death from Ebola, a man who had travelled from Liberia to Texas and was not appropriately dealt with on his first presentation to hospital. He was isolated on his second visit, but one of his nurses contracted the disease, and it became apparent that efforts to quarantine/ monitor others who had been involved in his care had been inadequate. The US Centers for Disease Control (CDC) on 20th October issued tighter guidelines for US healthcare workers on personal protective equipment for Ebola[[38]](#footnote-38).
  4. On 7 October the European Commission sought explanations from Spain as to how a nurse became infected with Ebola from contact with a Spansh priest who died of the disease, having been repatriated from Sierra Leone to Madrid.
  5. Early in October the US began monitoring travellers for Ebola at five airports. Australia and Canada introduced visa restrictions on people from Guinea, Liberia and Sierra Leone. An assessment of the potential for international spread of Ebola[[39]](#footnote-39) concluded that: “Exit screening of travellers at airports in Guinea, Liberia, and Sierra Leone would be the most efficient frontier at which to assess the health status of travellers at risk of Ebola virus exposure, however, this intervention might require international support to implement effectively.”
  6. Although health officials globally had been reassuring the public that Ebola could be spread only by physical contact or bodily fluids, some scientists have declared that assurance premature. A new CDC flyer describes  [the “droplet spread” of Ebola](http://www.cdc.gov/vhf/ebola/pdf/infections-spread-by-air-or-droplets.pdf), which “happens when germs traveling inside droplets that are coughed or sneezed from a sick person”. Health officials have also said that unless an air traveller has a fever of at least 101.5 degrees Fahrenheit, or other symptoms, other passengers are not at risk, but this too has been disputed[[40]](#footnote-40). The CDC has asked Johns Hopkins Medicine to lead the design of an interactive web-based learning program to instruct healthcare workers, nurses and physicians on government-approved protocols for Ebola care.
  7. Tekmira Pharmaceuticals, which develops RNA interference (RNAi) therapeutics, received authorisation from the US Food and Drug Administration (FDA) to provide TKM-Ebola[[41]](#footnote-41) for treatment under expanded access protocols to subjects with confirmed or suspected Ebola virus infections. Health Canada has established a similar framework.
  8. Fujifilm Corporation’s influenza medicine Avigan has been given to some Ebola patients.
  9. Mapp Biopharmaceutical exhausted supplies of its drug ZMapp in August, when it was given to seven American and non-American patients. The drug is made by infecting tobacco leaves with proteins, which proliferate as the plants grow. The extracted proteins are processed into ZMapp. The process takes weeks. Mapp is hoping to expand its tobacco-growing facilities, and has also been working with the Gates Foundation and a pharmaceutical company to speed manufacture of antibodies by substituting Chinese hamster ovary cells instead for tobacco plants. Unfortunately one of the antibodies in ZMapp doesn’t reproduce as well in animals as in plants.
  10. Mapp Biopharmaceutical also announced a partnership with researchers at Vanderbilt University to develop antibody therapies that can provide short-term protection in health workers and others at risk of exposure to the viruses. Vanderbilt researchers are generating antibodies from the blood of people who have survived Ebola and Marburg infections. The laboratory uses a high-efficiency human hybridoma[[42]](#footnote-42) technique for isolating human monoclonal antibodies, said Dr James Crowe, director of the Vanderbilt Vaccine Center.
  11. The Chimerix drug brincidofovir, primarily designed to treat cytomegalovirus and adenovirus, has been given to some Ebola patients.
  12. Thai scientists have created an antibody treatment for Ebola which has yet to undergo animal and human trials. It is designed to enter cells and destroy the virus.
  13. Sarepta Therapeutics has an Ebola treatment in the early stages of human testing. In animal testing it showed it could prevent disease development and death[[43]](#footnote-43).
  14. Inovio Pharmaceuticals will begin human testing of a DNA-based Ebola vaccine in the first half of 2015.
  15. GlaxoSmithKline revealed that it had contacted WHO a few months ago to see if its vaccine could help with the outbreak. The company was told the focus was on containment. Now GSK is trialling the vaccine in humans and hopes to have it in Africa by January, starting with 10,000 to 15,000 doses for healthcare workers. The vaccine is a chimpanzee cold virus that is injected with a small piece of the Ebola virus gene, which tricks the body into making an immune response against Ebola, even though it hasn’t been infected with the disease.
  16. Johnson & Johnson plans to start human testing in March and to have hundreds of thousands of doses available through the course of 2015 and more than a million in 2016. The vaccine uses an inactivated version of a cold virus to carry Ebola’s genetic information into cells. It’s then followed by a second booster shot from biotechnology company Bavarian Nordic A/S (BAVA) of Denmark.
  17. The University of Texas is developing an inhalable vaccine against Ebola under a grant from the US National Institutes of Health (NIH). It has worked well in monkeys.
  18. Vaxart has a temperature-stable tablet vaccine candidate for Ebola.
  19. Under a one-year contract with Profectus BioSciences, the US Biomedical Advanced Research and Development Authority (BARDA) will provide $US5.8 million in funding, expertise and technical assistance, to further develop the company’s experimental Ebola vaccine.
  20. The vaccine developed by the Public Health Agency of Canada and licensed to NewLink Genetics Corp. will undergo Phase II clinical efficacy trials in 2015.
  21. Pentamer Pharmaceuticals in October began a crowdfunding campaign to develop its Ebola vaccine, NoBola. Crowdfunding raises capital by seeking small sums from many people using the internet and social media.
  22. A number of new tests for Ebola infection have received emergency approval or are in the pipeline. The FDA has given emergency approval for a lab test that takes 45 minutes – made by BioFireDefense of Salt Lake City, a unit of France’s BioMerieux. France's Atomic Energy and European pharma company Vedalab are developing a system to diagnose Ebola in less than 15 minutes. "Ebola eZYSCREEN," includes a hand-held device that reads small samples of blood, plasma or urine. The ZOE Fluid Status Monitor, owned and marketed by Noninvasive Medical Technologies Inc., of Las Vegas has been previously approved for use by the FDA and is now being used in Ebola detection. Primerdesign Ltd, a spin-off company from the University of Southampton, says it has developed a fast and simple diagnostic test solution specific to the 2014 Ebola outbreak.
  23. A black market is allegedly emerging in the sale of the blood of Ebola survivors. This contains antibodies against the deadly virus and is believed to help Ebola patients fight the infection, or provide healthy people with immunity. The WHO has said that doctors should consider using Ebola survivor blood as a treatment until other treatments are available. However, people buying blood or plasma could expose themselves to other pathogens, or acquire Ebola, or their purchase may not be from recovering Ebola patients at all.
  24. The European Commission is providing €2.9 million, to fund a clinical trial of blood products from Ebola survivors as treatment. The trial will be led by the Institute of Tropical Medicine in Antwerp, Belgium. The Wellcome Trust will also provide support.
  25. CSL said in October that it is working on a hyperimmune plasma product to treat Ebola following a request from the Bill & Melinda Gates Foundation.
  26. Cerus Corporation sought from the FDA a “compassionate use” license to allow its INTERCEPT Blood System to treat blood plasma collected from Ebola survivors.
  27. Contributors to health care in West Africa include the US (which opened the first of 17 Ebola treatment units in Liberia on 10 November), the European Union, the UK, Norway, Japan, and Australia. South Africa’s first black billionaire, Patrice Motsepe donated $US1 million for Guinea.
  28. There are five strains of the Ebola virus. It is the Zaire (EBOV) strain which is currently raging in West Africa. Second in severity is the Sudan strain, SUDV, which has caused widespread illness in the past decade (most recently in 2012). Now researchers from Albert Einstein College of Medicine and other institutions have developed a potential therapy for SUDV[[44]](#footnote-44). This combines monoclonal antibodies, developed through synthetic antibody engineering. The antibodies block the virus from entering a cell by binding to a protein present on the outside of the Ebola virus particle. So far, antibodies that kill one strain of Ebola haven’t been shown to effective against other strains.

### Mosquito-borne diseases: dengue, chikungunya and malaria

* 1. Sanofi Pasteur announced publication of the results of the Phase III clinical efficacy study of its dengue vaccine in Latin America[[45]](#footnote-45). The company said the study met its primary objective and it will file for registration in several endemic countries in 2015.
  2. The 2013 dengue outbreaks in Malaysia and Singapore were associated with a switch in the predominant virus serotypes. In Singapore the predominantly circulating virus serotype switched from DENV-2 to DENV-1 at the beginning of 2013. Malaysia, however, saw an increase in the dominance of DENV-2. However, the second most common strain DENV-2 in Singapore has been on the rise since July 2014. This could mean a new wave of infections. The DENV-2 virus in Malaysia is especially predominant in the southern states of Johor and Malacca. It has also been associated with higher reported fatality cases in the two states.
  3. Researchers in Brazil have released ten thousand mosquitoes infected with the dengue-blocking bacteria*, Wolbachia*.
  4. French Polynesia confirmed 541 cases of chikungunya in the last three weeks of October, 509 being from Tahiti. At the same time, the region has been experiencing dengue and infections with the Zika virus[[46]](#footnote-46).
  5. Chikungunya has been raging in the Caribbean and Central America. The Dominican Republic has reported over half a million cases this year. A second strain is circulating in Brazil. Jamaica has declared its chikungunya outbreak to be a national emergency.
  6. On 21 October, France reported four cases of locally-acquired chikungunya in Montpellier, the first time that locally-acquired transmission of chikungunya has been detected in France since 2010.
  7. A large international multi-centre study showed that the severity of malaria infection is influenced by five human genes. The team, including Dr Sarah Dunstan of the Nossal Institute of Global Health at the University of Melbourne, reported in the journal *Nature Genetics*.
  8. A Japanese scientist has developed a new mosquito trap using human body odour as bait.

### Influenza: strains, spread, prevention and treatment

* 1. The FDA has granted Novovax Fast Track Designation for its H7N9 Virus-Like Particle Vaccine Candidate adjuvanted with Matrix-M™. H7N9 VLP is being developed under a Novovax contract with the US Biomedical Advanced Research and Development Authority (BARDA).
  2. A University of Adelaide-led project[[47]](#footnote-47) has developed a test that can distinguish between birds that have been vaccinated against the H5N1 influenza virus and those that have been naturally infected. Birds that have been vaccinated but still have live naturally infected H5N1 virus in their systems are the main source of emerging strains of the virus. The aim of the new test is to identify these birds and prevent the escape of any mutant strains. The researchers have been carrying out large surveillance programs in poultry farms across Indonesia.
  3. Health officials in the US reported that the nasal spray version of the flu vaccine did not protect young children against swine flu last winter, although it worked against other strains. "We are working with the CDC to try and understand why this observation is being seen," said Dr. Chris Ambrose of AstraZeneca.
  4. A universal flu vaccine developed by Israel’s BiondVax has now been granted patents by both the European Union and Japan. BiondVax’s technology already had patents in the US, Hong Kong, Australia, China, Russia and Mexico.
  5. At the 15th Annual World Vaccine Congress in Brussels, Vaxart announced clinical results demonstrating that its H1N1 tablet vaccine generates immunity comparable with protection afforded by currently licensed influenza vaccines, as measured by hemagglutinin inhibition assay (HAI).
  6. Developing a vaccine against avian influenza A/H7N9 has been hampered by poor immunogenicity of the H7 surface hemagglutinin. Researchers have found that response to vaccination can be improved by using an adjuvant[[48]](#footnote-48).
  7. Germany detected the H5N8 bird flu strain in turkeys, the first time this highly pathogenic strain has been reported in Europe. [China](http://uk.reuters.com/places/china) and Japan also reported cases of the H5N8 virus earlier this year.
  8. A report published in BMC Medicine in October said that some animal workers in southern China may have had asymptomatic infections with the H10N8 avian flu before the first human case was identified in November 2013. It recommended continued surveillance in this population and in healthcare workers.
  9. Human H7N9 infection continues to be reported from time to time China.

### MERS-CoV[[49]](#footnote-49)

* 1. MERS cases continue to be reported. In Saudi Arabia, two newly confirmed MERS-CoV cases and 2 deaths reported on 13 November 2014 and then one new case on 14 November brought the total number of laboratory-confirmed MERS-CoV infected individuals reported by Saudi Arabia since June 2012 is up to 805, including 342 deaths (case fatality rate 42.5 per cent). Saudi Arabia has been responsible for 86 per cent of global cases and 92 per cent of deaths.
  2. Research by a team from Colorado State University has proved for the first time that camels emit volumes of the MERS-CoV – confirming them as prime suspect in transmission to humans. CSU is one of the only research institutions in the US equipped to safely conduct tests on camels with such a contagious virus[[50]](#footnote-50), and the team worked with a section of the National Institutes of Health (NIH). The study will be published in the journal Emerging Infectious Diseases. Researchers **showed that three infected dromedary camels emitted high levels of the MERS virus-primarily from the nostrils. The virus developed in the animals' upper respiratory system and they shed the infectious virus for up to a week.** Within weeks, the camels overcame the virus as if it were a common cold. The researchers are now testing a vaccine developed by the US National Institutes of Health (NIH).
  3. The Abu Dhabi Food Control Authority (ADFCA) and Al Wathba Veterinary Laboratory say they have developed a technique to detect MERS in camels within just 20 minutes.

### Other diseases: occurrence, prevention and treatment

* 1. By 1 October 39 cases of measles had been reported in Western Australia, the highest number since 1998. The biggest cluster was seven people, with one infected in the Philippines and then spreading measles to six people in WA.
  2. From mid-August to 6 November the US recorded 1116 people with a respiratory illness caused by Entovirus D68. Most cases were in children. The illness led to a number of deaths. The illness appeared to carry with it focal limb weakness[[51]](#footnote-51). If this neurological facet was actually caused by EV-D68, then the reports of the illness as “polio-like” is understandable. EV-D68 was also detected in Canada and in the Netherlands, where there had been an outbreak in 2010. Neurological symptoms do not seem to have been associated with the Netherlands outbreak.
  3. The UK government is to investigate the extent of hidden Mad Cow disease in the British population using a new diagnostic blood test developed by Medical Research Council (MRC) scientists.
  4. NSW Health issued a bat lyssavirus alert after 32 people in one month had required rabies post exposure prophylaxis following high risk exposure.
  5. A recent survey by WHO suggests that tuberculosis has infected 400,000 more people globally this year than was estimated a year ago. There were nine million new cases reported across 200 countries which account for 99 per cent of cases.
  6. 300,000 people in the US are now estimated to be infected with Chagas disease.
  7. Residents of the Hunter region of NSW have been advised to avoid being bitten by mosquitoes following a surge in notifications for the Ross River Virus this year.

1. NAITgam contains antibodies against HPA-1a. The donors are women who have given birth to a baby who suffered from FNAIT. The antibodies are given as a single injection within the first 6 hrs after an HPA-1a negative woman has given birth to an HPA-1a positive child. They remove foetal HPA-1a positive platelets from the mother’s circulation before her immune system has had time to develop antibodies against the foetal platelets. NAITgam is therefore similar to Rh immune globulin, which for half a century has been used to prevent a related disorder, haemolytic disease of the foetus and newborn. [↑](#footnote-ref-1)
2. D Ingber , A Waterhouse, D Leslie, et al. “Bioinspired Blood Repellent Coating”, Nature Biotechnology. 2014. [↑](#footnote-ref-2)
3. Known as Tethered-Liquid Perfluorocarbon (TLP). [↑](#footnote-ref-3)
4. *Anal. Chem.* 2014, DOI: [10.1021/ac5031682](http://cgi.cen.acs.org/cgi-bin/cen/trustedproxy.cgi?redirect=http://pubs.acs.org/doi/abs/10.1021/ac5031682?source=cen) [↑](#footnote-ref-4)
5. [Li Gao](http://www.nature.com/ncomms/2014/140919/ncomms5938/full/ncomms5938.html#auth-1), [Yihui Zhang](http://www.nature.com/ncomms/2014/140919/ncomms5938/full/ncomms5938.html#auth-2), [Viktor Malyarchuk](http://www.nature.com/ncomms/2014/140919/ncomms5938/full/ncomms5938.html#auth-3) et al., “Epidermal photonic devices for quantitative imaging of temperature and thermal transport characteristics of the skin”, *Nature Communications* Volume:

   5, Article number: 4938 DOI:

   doi:10.1038/ncomms5938 [↑](#footnote-ref-5)
6. Previously called Fibrocaps [↑](#footnote-ref-6)
7. D. Moeckel, A. Nguyen; D. Abendschein,S.S. Jeong, R. Chen, X. Sun, S.C. Robson, X. Sun, M.J. Broekman, J.H.F. Drosopoulos, A.J. Marcus "Optimizing human apyrase to treat arterial thrombosis and limit reperfusion injury without increasing bleeding risk", in *Science Translational Medicine*, 6 August 2014 Vol. 6, Issue 248, p. 248ra105 Sci. Transl. Med. DOI: 10.1126/scitranslmed.3009246 [↑](#footnote-ref-7)
8. Zongxi Li, Emmanuel Roussakis, Pieter G. L. Koolen, Ahmed M. S. Ibrahim, Kuylhee Kim, Lloyd F. Rose, Jesse Wu, Alexander J. Nichols, Yunjung Baek, Reginald Birngruber, Gabriela Apiou-Sbirlea, Robina Matyal, Thomas Huang, Rodney Chan, Samuel J. Lin, and Conor L. Evans,   “Non-invasive transdermal two-dimensional mapping of cutaneous oxygenation with a rapid-drying liquid bandage”, *Biomedical Optics Express*, Vol. 5, Issue 11, pp. 3748-3764 (2014)  
   http://dx.doi.org/10.1364/BOE.5.003748 [↑](#footnote-ref-8)
9. Acquired hemophilia A is not a genetic disorder. It can be acquired by both males and females. [↑](#footnote-ref-9)
10. PCC is used for the treatment and prophylaxis prophylaxis of congenital and acquired deficiencies of clotting factor II, factor VII, factor IX or factor X deficiencies. PCC is also used for anticoagulant reversal and vitamin K deficiency [↑](#footnote-ref-10)
11. The notice to hospitals included the following:

    *Thromboembolic events can occur in patients using immunoglobulins regardless of dose or route of administration.*

    *Thromboembolic events can occur in patients in the absence of known risk factors, such as advanced age, obesity, diabetes, prolonged immobilization, a history of hypercoagulability or thrombotic events, use of estrogens, indwelling central vascular catheters, and hyperviscosity.*

    *Canadian Product Monographs for all non-hyperimmune immunoglobulins were updated to include thromboembolic events in the Serious Warnings and Precautions.*

    Amongst immunoglobulins whose use is authorised in Canada are GamaSTAN S/D, Gammagard liquid, Gammagard S/D, Gamunex, Hizentra, IGIVnex, Immune Serum Globulin (Human), Octagam (5% and 10%), and Privigen [↑](#footnote-ref-11)
12. The proprietary plasma fractionation platform is known as the Salt Diafiltration process [↑](#footnote-ref-12)
13. Lars B. Holst et al. **“**Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock”,*N Engl J Med* 2014; 371:1381-1391 [October 9, 2014](http://www.nejm.org/toc/nejm/371/15/) DOI: 10.1056/NEJMoa1406617 [↑](#footnote-ref-13)
14. such as re-operation for bleeding, ventilation longer than 24 hours, infection, renal failure and death [↑](#footnote-ref-14)
15. [Tuttle JR. J Arthroplasty. 2014. doi:10.1016/j.arth.2014.01.031.](http://www.arthroplastyjournal.org/article/S0883-5403(14)00073-4/abstract) [↑](#footnote-ref-15)
16. The findings were originally reported at the 2013 annual meeting of the American Society of Anesthesiologists (abstracts A2147 and A2146). [↑](#footnote-ref-16)
17. This was reported by the Center for Bloodless Medicine and Surgery in the journal Transfusion. [↑](#footnote-ref-17)
18. Joseph A.Garcia et al. “An acetate switch regulates stress erythropoiesis”, *Nature Medicine* 20, 1018–1026 (2014) [DOI: 10.1038/nm.3587](http://dx.doi.org/10.1038/nm.3587) [↑](#footnote-ref-18)
19. The FDA said in November 2013 that Pradaxa did not put patients at an increased risk for bleeding. The FDA then said with a study released recently that although Pradaxa did put patients at an increased risk for “major gastrointestinal haemorrhage, compared to warfarin in patients with non-valvular atrial fibrillation,” it also reduced the risk of ischemic stroke by 20 per cent, reduced the risk of intracranial haemorrhage by 66 per cent and showed no difference in major haemorrhage compared with warfarin. *JAMA Internal Medicine* published its own findings the same day, writing that it is “unclear” if Pradaxa “is associated with higher risk of bleeding than warfarin in real-world clinical practice,” while at the same time saying they found a higher bleeding risk compared with warfarin as a whole, and found the “risk of major bleeding among dabigatran users was especially high for African Americans and patients with chronic kidney disease.” [↑](#footnote-ref-19)
20. A Canadian study concluded that almost 40% of reported TRALI cases in that country occurred during the perioperative period. [↑](#footnote-ref-20)
21. Anesthesiologists at the Mayo Clinic found that the rate of TRALI decreased between 2004 and 2011. [↑](#footnote-ref-21)
22. R, Delgado FF, Manalis SR, Higgins JM (2014) In Vivo Volume and Hemoglobin Dynamics of Human Red Blood Cells. *PLoS Comput Biol* 10(10):e1003839. [DOI: 10.1371/journal.pcbi.1003839](http://dx.doi.org/10.1371/journal.pcbi.1003839) [↑](#footnote-ref-22)
23. Basanta Bhaduri et al., “Optical Assay of Erythrocyte Function in Banked Blood” in [Nature’s Scientific Reports](http://www.nature.com/srep/index.html), doi:10.1038/srep06211 [↑](#footnote-ref-23)
24. See Robert Lanza et al. at [http://www.cell.com/stem-cell-reports/abstract/S2213-6711(14)00295-1](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.cell.com%2Fstem-cell-reports%2Fabstract%2FS2213-6711%2814%2900295-1&esheet=50963856&newsitemid=20141017005032&lan=en-US&anchor=http%3A%2F%2Fwww.cell.com%2Fstem-cell-reports%2Fabstract%2FS2213-6711%2814%2900295-1&index=2&md5=33b27f93c8d089e7f50f6b0752065abf) [↑](#footnote-ref-24)
25. Genovese P, Schiroli G, Escobar G, Di Tomaso T, Firrito C, Calabria A, Moi D, Mazzieri R, Bonini C, Holmes MC, Gregory PD, van der Burg M, Gentner B, Montini E, Lombardo A, Naldini L., “[Targeted genome editing in human repopulating haematopoietic stem cells.](http://www.ncbi.nlm.nih.gov/pubmed/24870228)”,*Nature*. 2014 Jun 12;510(7504):235-40. doi: 10.1038/nature13420. Epub 2014 May 28. [↑](#footnote-ref-25)
26. . The results are published in the Proceedings of the National Academy of Sciences. The first author of the paper is research associate Yongzhi Qiu [↑](#footnote-ref-26)
27. Dr. Timothy Hla reported 24 September in [*Journal of Clinical Investigation*](https://www.facebook.com/jclininvest)*.* <http://bit.ly/1rnXrX4> [↑](#footnote-ref-27)
28. [Brice Gaudillière](http://stm.sciencemag.org/search?author1=Brice+Gaudilli%C3%A8re&sortspec=date&submit=Submit) et al. “Clinical recovery from surgery correlates with single-cell immune signatures”, *Sci Transl Med,* 24 September 2014*:* Vol. 6, Issue 255, p. 255ra131   
    Sci. Transl. Med. DOI: 10.1126/scitranslmed.3009701 [↑](#footnote-ref-28)
29. [Jiang J](http://www.ncbi.nlm.nih.gov/pubmed?term=Jiang%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24948658), [Woulfe DS](http://www.ncbi.nlm.nih.gov/pubmed?term=Woulfe%20DS%5BAuthor%5D&cauthor=true&cauthor_uid=24948658),, [Papoutsakis](http://www.ncbi.nlm.nih.gov/pubmed?term=Papoutsakis%20ET%5BAuthor%5D&cauthor=true&cauthor_uid=24948658) “Shear enhances thrombopoiesis and formation of microparticles that induce megakaryocytic differentiation of stem cells.” [Blood.](http://www.ncbi.nlm.nih.gov/pubmed/24948658) 2014 Sep 25;124(13):2094-103. doi: 10.1182/blood-2014-01-547927. Epub 2014 Jun 19. [↑](#footnote-ref-29)
30. Sumitran-Holgersson S, Olausson M, Kuna V, et al, “In vivo application of tissue-engineered veins using autologous peripheral whole blood: A proof of concept study”, *EBioMedicine*. 2014.  [↑](#footnote-ref-30)
31. The technology was described in “Platelet-like Nanoparticles: Mimicking Shape, Flexibility, and Surface Biology of Platelets To Target Vascular Injuries” in *ACS Nano* [↑](#footnote-ref-31)
32. See 19 October issue of *Nature Medicine* [↑](#footnote-ref-32)
33. On day 1, the plenary session was a *MERS-CoV Update* with a speaker from Saudi Arabia. The symposium topic was *MERS-CoV and Ebola*, with a speaker on the human perspective, a presentation entitle “Why did the camel kiss the bat” and a talk on “MERS-CoV: the Animal Human Interface”. The second plenary that day, led by a South African speaker, was *Challenges and Controversies in the 2014 West African Ebola Virus Outbreak Response.* [↑](#footnote-ref-33)
34. Including the role of biologic therapies, organ transplants and medical devices in infectious diseases [↑](#footnote-ref-34)
35. Ebola in West Africa, chinkingunya in the Americas, and the pandemic potential of avian influenza [↑](#footnote-ref-35)
36. On 11 November in Sierra Leone 111 new cases were registered, but the UN warned that cases in that country were being underestimated by 50 per cent. [↑](#footnote-ref-36)
37. Emotion over burial practices runs high. The government order ed that the bodies of all suspected Ebola victims in the capital be cremated. However, cremation violates values and cultural practice, so some of the sick are being kept at home, and when they die they are secretly buried thus increasing the risk of more infections. [↑](#footnote-ref-37)
38. <http://www.cdc.gov/media/releases/2014/fs1020-ebola-personal-protective-equipment.html> [↑](#footnote-ref-38)
39. Isaac I Bogoch et al., “Assessment of the potential for international dissemination of Ebola virus via commercial air travel during the 2014 west African outbreak”, *The Lancet,* Early Online Publication, 21 October 2014. doi:10.1016/S0140-6736(14)61828-6 [↑](#footnote-ref-39)
40. Dr CJ Peters of the University of Texas in Galveston said he would not rule out the possibility that Ebola spreads through air. Michael Osterholm of the University of Minnesota and a former member of the National Science Advisory Board for Biosecurity says no one knows whether an infected person without the virus could spread symptoms. [↑](#footnote-ref-40)
41. TKM-Ebola interferes with the Ebola virus’s replication process, allowing the body’s immune system to catch up with the virus and destroy it. Tekmira received a $US 140 million US Defense Department contract in 2010 to develop the drug. [↑](#footnote-ref-41)
42. Hybridoma technology forms hybrid cell lines (hybridomas) by fusing an antibody-producing cell with a cell that is selected for its capacity to grow in tissue culture and for its lack of antibody chain synthesis. [↑](#footnote-ref-42)
43. Results will be published in the November issue of the journal of the American Society for Microbiology. [↑](#footnote-ref-43)
44. See ACS Chemical Biology.     [↑](#footnote-ref-44)
45. In the *New England Journal of Medicine*. The full data of the Latin American study werealso presented at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting, 2-6 November 2014. [↑](#footnote-ref-45)
46. A.Roth et al.,”Concurrent outbreaks of dengue, chikungunya and zika virus unfections-an unprecedented epidemic wave of mosquito-borne viruses in the Pacific”, *Eurosurveillance*, Volume 19, Issue 41, 16 October 2014. http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20929 [↑](#footnote-ref-46)
47. Which included researchers from the University of Melbourne, CSIRO and Indonesian organisations. The research was funded by the Australian Centre for International Agricultural Research (ACIAR) and published in [PLOS ONE](http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0108420). [↑](#footnote-ref-47)
48. Mark J Mulligan et al.“Serological Responses to an Avian Influenza A/H7N9 Vaccine Mixed at the Point of-Use With MF59 Adjuvant:  A Randomized Clinical Trial”, *JAMA.* 2014;312(14):1409-1419. doi:10.1001/jama -.2014.12854 [↑](#footnote-ref-48)
49. Middle East Respiratory Syndrome Corona Virus (Mers-CoV) [↑](#footnote-ref-49)
50. in the Animal Reproduction and Biotechnology Laboratory, the camels could be cared for in a sealed Biosafety Level 3 Laboratory. [↑](#footnote-ref-50)
51. See “Enterovirus D68: the unexpected guest”,*The Lancet Infectious Diseases*, [Volume 14, Issue 11](http://www.thelancet.com/journals/laninf/issue/vol14no11/PIIS1473-3099(14)X7075-1), Page 1023, November 2014. doi:10.1016/S1473-3099(14)70968-5[http://www.thelancet.com/images/clear.gif](http://www.thelancet.com/popup?fileName=cite-using-doi) [↑](#footnote-ref-51)