Monitoring International Trends

**posted September 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:

* Baxter International announced that an extended-release version of Advate, BAX 855, met the main goal in a late-stage study (page 3).
* Bayer HealthCare and Dimension Therapeutics announced a collaboration to develop a “novel gene therapy” for patients with haemophilia A (page 3).
* [CSL Behring](http://www.cslbehring.com/) announced that the last patient has been treated in a Phase III study of fibrinogen concentrate to control bleeding during aortic aneurysm surgery (page 3).
* Researchers have developed a new class of synthetic platelet-like particles to augment natural blood clotting for the emergency treatment of traumatic injuries (page 4).
* Health Canada approved Biogen’s long-acting recombinant factor VIII (Eloctate) for the control and prevention of bleeding episodes and routine prophylaxis in adults and children aged 12 and older with haemophilia A (page 6).
* The US Food and Drug Administration (FDA) approved Baxter’s recombinant factor IX (Rixubis) for routine prophylactic treatment, control and prevention of bleeding episodes, and perioperative management in children with haemophilia B (page 6).
* [The FDA approve](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://seekingalpha.com/pr/11018715-fda-approves-baxter-s-hyqvia-for-treatment-of-adults-with-primary-immunodeficiency?source=email_rt_mc_body&app=n)d Baxter’s subcutaneous immunoglobulin ([Hyqvia](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://www.baxter.com/downloads/healthcare_professionals/products/HYQVIA_PI.pdf)) for the treatment of adult patients with primary immunodeficiency (page 6).
* [CSL](http://www.csl.com.au/) is building a new plant in Switzerland (page 7).
* Baxter named as Baxalta Incorporated the publicly traded biopharmaceutical company that it will hive off in mid-2015. Baxalta will provide therapeutic treatments in bleeding disorders, immunology, oncology and gene therapy. (page 8).
* Research from the Kirby Institute for Infection and Immunity in Society shows that more Australians were diagnosed with syphilis in 2013 than in any year since recording began (page 10).
* University of Illinois researchers have found that stored blood loses cell functionality within the FDA-recommended 42-day shelf life (page 12).
* A meta-analysis and systematic review has found that restrictive red blood cell transfusion thresholds are associated with a decreased risk of acquiring healthcare-associated infections compared with liberal transfusion thresholds (page 12).
* A US study found that severe combined immunodeficiency was much higher in newborns than previously suspected and that the survival rate was high for neonates who received early diagnosis and treatment (page 14).
* Ebola virus disease continues to spread in West Africa despite increased efforts from round the world to control it. Concern remains that it will spread to further countries. Belated efforts to develop vaccines and treatments have been stepped up (page 15).

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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.*

### Treating haemophilia

* 1. Baxter International announced that an extended-release version of Advate, BAX 855, met the main goal in a late-stage study. The drug was being tested as a prophylactic and an on-demand treatment in 138 previously treated adolescent and adult haemophilia A patients. The trial's main goal was to reduce bleeding rates compared with on-demand treatment. Patients in the twice-weekly prophylaxis arm of the trial experienced a 95 per cent reduction in median annual bleeding rates compared with those in the on-demand arm. Baxter will undertake another late-stage study to test BAX 855 in previously treated patients under the age of 12.
	2. Grifols has launched a 2000 IU/vial for Alphanate, used to prevent bleeding in patients with haemophilia A, and for adult and paediatric patients with von Willebrand disease (vWD) undergoing surgical and/or invasive procedures in whom desmopressin is either ineffective or contraindicated. It is not, however, indicated for patients with severe vWD undergoing major surgery.
	3. Bayer HealthCare presented data on haemophilia A research at the National Hemophilia Foundation's 66th Annual Meeting, September 18-20 in Washington, D.C.[[1]](#footnote-1)
	4. Bayer and Dimension Therapeutics announced a collaboration to develop a “novel gene therapy” for patients with haemophilia A. Thomas R. Beck, Dimension’s CEO said. “Currently available replacement therapies for hemophilia A are often administered intravenously multiple times a week and may be required for life…..Gene therapy offers the potential to transform the treatment of hemophilia by inserting a correct version of the faulty gene responsible for the disease.” The initial agreement gives a $US 20 million payment up front to Dimension. This could increase to as much as $232 million with development and commercialization milestone payments. Dimension will handle pre-clinical development activities and the Phase I/IIa clinical trials which Bayer will fund. Depending on the results, Bayer will conduct the Phase III trial, make regulatory submissions and have worldwide sales rights. Dimension will earn tiered royalties based on sales.

### Controlling bleeding from surgery or trauma

* 1. [CSL Behring](http://www.cslbehring.com/) announced that the last patient has been treated in a Phase III study of fibrinogen concentrate to control bleeding during aortic aneurysm surgery.[[2]](#footnote-2)
	2. Researchers[[3]](#footnote-3) have developed a new class of synthetic platelet-like particles to augment natural blood clotting for the emergency treatment of traumatic injuries. The clotting particles comprise soft deformable hydrogel materials. They have been tested in animal models, in a simulated circulatory system and with human blood, but have not yet been clinically trialled in humans.
	3. A gel that stops bleeding very rapidly has been approved for clinical veterinary trials in the United States[[4]](#footnote-4). 1600 veterinary clinics enrolled to use samples in a clinical trial. The gel uses plant polymers which replicate the tissue surrounding the application site.
	4. **In the US, Olympus** has released QuickClip following FDA clearance. The pro-haemostasis device is used in endoscopies for stopping bleeding and for closing various defects.

### Treating other conditions

* 1. Oxygen Biotherapeutics announced that the company has stopped the Phase IIb trial for its Oxycyte drug candidate in traumatic brain injury and will consider strategic alternatives for Oxycyte, while applying resources to its lead critical care product, levosimendan, a calcium sensitizer in Phase III development in the US for the reduction of morbidity and mortality in cardiac surgery patients at risk for developing Low Cardiac Output Syndrome (LCOS). The FDA has granted fast track status for levosimendan in this indication.
	2. Earlier this year, Kamada announced that in a PhaseII/III trial on 168 patients its inhaled treatment for alpha-1antitrypsin deficiency (AATD) failed to beat placebo in its primary goal of delaying flare-ups in lung conditions. The company has now confirmed the drug did not meet its secondary goals either. Kamada says the drug did prove safe and tolerable, and that it "showed concordance of a potential treatment effect" on lung function, particularly in a sub-group of the 168 who were most prone to exacerbations. The company intends to proceed with regulatory filings, its CEO David Tsur said in a statement: "Based on orphan designation of the drug, prior discussions held with the regulator, the strength of these data and the persistent unmet need in this orphan indication, we will advance our discussions with the European Medicines Agency (EMA) with the intent to submit for conditional approval in order to bring our inhaled AAT to patients with AATD in Europe, and will initiate discussion with the FDA to determine a US path for registration".
	3. Green Cross is developing an artificial immunoglobulin to treat hepatitis B. The Korean company has received approval for a phase II trial of Hepabig-Gene, in patients recovering from liver transplants. Ji Hyi-jeong, senior vice president of Green Cross, said: “If Hepabig-Gene is proven safe and effective, it will be the first recombinant hepatitis B immunoglobulin and an alternative treatment choice for physicians and their patients who undergo [the most common kind of] liver transplantation.” Both the EMA and the FDA granted orphan drug designation for Hepabig-Gene in 2013.
	4. At the South African Orthopaedic Association Congress in Cape Town in September, Dr. David North presented data from a clinical trial with REPAIR Bone Putty. The putty, based on blood plasma, was reported to reduce infections, speed bone healing, and promote more rapid wound closure of open tibia fractures. The putty was developed by Carnell Therapeutics.

### Devices and Services

* 1. Testing for sickle cell disease with gel electrophoresis is expensive, and not generally available in developing countries. Now Harvard University scientists have conducted a preliminary trial on a new and much cheaper test[[5]](#footnote-5) which can tell doctors the sickle cell status of a child in twelve minutes and may give them the benefit of more timely treatment. The test relies on the fact that sickle cells are heavier than healthy blood cells, using a centrifuge machine to spin the blood into layers.
	2. The World Economic Forum named Vaxxas a 2015 Technology Pioneer for its needle-free vaccine delivery technology. The patch technology was developed at the University of Queensland’s Australian Institute for Bioengineering and Nanotechnology.
	3. A new smartphone app, BiliCam, detects jaundice in newborns by taking their picture[[6]](#footnote-6).
	4. Claret Medical of California is trialling a cerebral protection device which filters potentially dangerous blood clots or tissue that may dislodge during transcatheter aortic valve implantation surgeries.
	5. Harvard University researchers have developed a portable device that can detect malarial antigens, measure blood glucose levels, trace heavy metals in water, and detect sodium in urine using a special electrochemical sensor. The device can transmit its readings via a cellphone to an online server[[7]](#footnote-7).
	6. Laboratory Corporation of America Holdings (LabCorp) announced the availability of the informaSeq Prenatal Test. This is an advanced, non-invasive, screening assay that can assess risk for multiple foetal chromosomal aneuploidies, or abnormalities in the number of chromosomes, from a single maternal blood draw.
	7. Researchers from Emory University and Georgia Tech University have developed an at-home testing device (using the same technology as blood glucose monitoring) for patients with anaemia. The test uses a single drop of blood to assess haemoglobin level, the readout of which can be paired with a smartphone app[[8]](#footnote-8). The device is yet to be approved by the FDA. Dr. Wilbur Lam (a professor in the department of pediatrics at Emory University School of Medicine) and several colleagues have launched a startup company, Sanguina, to commercialize the product as AnemoCheck. They hope it will be on sale by 2016.
	8. Harvard researchers led by bio-engineer Donald E. Ingber, are developing a device to mimic and enhance the functions of the human spleen. It filters pathogens from the blood. In their report[[9]](#footnote-9) Ingber's team said that of a cohort of rats infected with potentially fatal levels of E. coli or staphylococcus, 89 per cent of the ones whose blood had been filtered by the device survived, compared with 14 per cent who survived with no blood filter. The device removes blood from the body, filters it, then returns it. The innovation lies in a protein that naturally occurs in the human body that was genetically modified to maximize its pathogen-fighting abilities and minimize its side effects.

# 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. Health Canada approved Biogen’s recombinant factor VIII (Eloctate) for the control and prevention of bleeding episodes and routine prophylaxis in adults and children aged 12 and older with haemophilia, Eloctate offers patients with haemophilia A the potential to extend the interval between prophylactic infusions.
	2. The FDA approved Baxter’s recombinant factor IX (Rixubis) for routine prophylactic treatment, control and prevention of bleeding episodes, and perioperative management in children with haemophilia B. Rixubis was the first recombinant factor IX approved for routine prophylaxis and control of bleeding episodes in the US for adult haemophilia B patients.
	3. [The FDA approve](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://seekingalpha.com/pr/11018715-fda-approves-baxter-s-hyqvia-for-treatment-of-adults-with-primary-immunodeficiency?source=email_rt_mc_body&app=n)d Baxter’s [Hyqvia](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://www.baxter.com/downloads/healthcare_professionals/products/HYQVIA_PI.pdf) [Immune Globulin Infusion 10% (Human) with Recombinant Human [Hyaluronidase](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://en.wikipedia.org/wiki/Hyaluronidase)[[10]](#footnote-10)] for the treatment of adult patients with primary immunodeficiency (PI). Patients require only one infusion of Hyqvia every three of four weeks delivered subcutaneously via one injection site. The product uses Halozyme's [rHuPH20](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://www.halozyme.com/technology/enhanze-technology/default.aspx) platform[[11]](#footnote-11). The shares of Halozyme Therapeutics rose almost 7.5 per cent immediately following the news, but dropped back subsequently.

### Blood processing

* 1. Cerus Corporation submitted a clinical protocol to the FDA to make the Intercept Blood System for platelets available under an Expanded Access Investigational Device Exemption (IDE) to regions in the US experiencing chikungunya and dengue, which may be transfusion-transmitted. The Treatment Use provision permits the FDA to agree to early access to a medical treatment as yet unapproved if there is not a satisfactory alternative available to patients with serious or life-threatening conditions. The Intercept platelet system license application is currently under FDA review with a decision expected in 2015.

### Devices

* 1. Vital Connect received FDA clearance for use of its HealthPatchTM MD biosensor for monitoring patients in their homes: patients with chronic conditions, for short-term monitoring after a patient is discharged from a hospital or as part of the follow-up care provided after a non-critical emergency room visit. The device provides clinical-grade measurements of heart rate, heart rate variability, single lead electrocardiogram (ECG), respiratory rate, skin temperature, posture including fall detection and severity, and steps. The device is approved for distribution in EU, and is licensed and registered by Health Canada for distribution in Canada.
	2. Masimo announced CE Mark (European approval), clearance in Japan, and limited market release of the first non-invasive haemoglobin spot-check sensor for infants and small children (weight 3 to 30 kg). Previously, spot-check sensors were available only for patients weighing 10 kg or more.
	3. AliveCor received FDA clearance for its algorithm to detect atrial fibrillation, a common form of cardiac arrhythmia. AliveCor's automated analysis process (algorithm) instantly detects atrial fibrulation through real-time ECG recordings on the mobile phone based AliveCor Heart Monitor. Physicians can intervene before potentially life-threatening conditions, like strokes, occur.
	4. The FDA has approved the delivery of bioCSL’s Afluria flu vaccine in patients aged 18-64 with the PharmaJet Stratis 0.5mL Needle-Free Jet Injector. This delivers the vaccine by means of a narrow fluid stream that penetrates the skin in about one-tenth of a second.

### Other

* 1. Amyndas has received orphan drug status in Europe[[12]](#footnote-12) for its drug ANY-101 to treat paroxysmal nocturnal haemoglobinuria (PNH), a rare but potential fatal disease that causes anaemia due to destruction of red blood cells and thrombosis.
	2. The FDA approved GlaxoSmithKline’s supplemental New Drug Application (sNDA) for the once-daily use of Promacta (eltrombopag) in patients with severe aplastic anaemia who have had an inadequate response to immunosuppressive therapy.
	3. Bristol-Myers Squibb and Pfizer announced that the FDA had expanded approval of their blood thinner Eliquis to treat two types of dangerous blood clots. It cleared the drug for patients suffering from or at risk of deep vein thrombosis and pulmonary embolism. Eliquis (apixaban) was originally approved in 2012 to treat atrial fibrillation (a form of irregular heartbeat), in patients at risk for strokes or dangerous clots.

# 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.*

### Facilities

* 1. [CSL](http://www.csl.com.au/) is building their new plant in Switzerland, citing as compelling reasons a lower corporate tax rate and government assistance. Output from the new plant will be based on research and development performed in Australia.
	2. NovoNordisk has purchased a manufacturing facility in New Hampshire from Olympus Biotech.

### Agreements

* 1. Expression Therapeutics has agreed that ABL will perform cell line development studies to facilitate manufacture of its recombinant factor VIII replacement therapy. ABL will adapt the current cell line to grow in chemically defined, animal origin-free media, and determine optimum cell growth conditions to support large scale production in a bioreactor-based process.
	2. Cerus Corporation has entered into an agreement with Biomedica Foscama Group (BFG) to distribute the Intercept Blood System for plasma and platelets in Italy. BFG will be the exclusive distributor for the Intercept Blood System in Italy, Vatican City and San Marino. BFG’s responsibilities include the promotion, sale, deployment and support of Intercept. BFG has collaborated with Cerus for almost a decade through its manufacture and supply of a key component for Cerus’ Intercept System for red blood cells.
	3. Biogen Idec and Swedish Orphan Biovitrum (Sobi) collaborated to develop and commercialise Eloctate and Alprolix for haemophilia A and B respectively. Biogen leads development, holds the manufacturing rights, and holds commercialisation rights in North America and all other regions in the world apart from Sobi territory. Sobi has the right to opt in to assume final development and commercialisation in Europe, including Russia, the Middle East and North Africa. Now Sobi has agreed to add the preclinical rFVIIIFc-XTEN-vWF[[13]](#footnote-13) fusion molecule to its collaboration with Biogen[[14]](#footnote-14) with similar terms to those of Eloctate and Alprolix. Geoffrey McDonough, CEO and President of Sobi, said: "Although at an early stage, the XTEN technology has the potential to further extend FVIII half-life and could one day potentially become a next-generation long-acting factor for people with haemophilia A."

### Other

* 1. rEVO Biologics of Framingham, Massachusetts, plans to raise $US 50 million by offering 3.6 million shares at a price range of $US 13 to $US 15. [rEVO Biologics](http://revobiologics.com/)’ only commercial product at present is the recombinant human antithrombin [ATryn](http://www.atryn.com/) for the prevention of blood clots during or after surgery or childbirth in patients with the rare clotting disorder, [hereditary antithrombin deficiency](http://ghr.nlm.nih.gov/condition/hereditary-antithrombin-deficiency). The product has been available in the U.S. since 2009. Part of the proceeds from the public offering will fund the Phase III trial of Atryn to manage preeclampsia. In 2013 total revenue was $US 21.4 million and net loss was $US 23.4 million. The company, originally a subsidiary of Genzyme, was bought by France’s LFB Biotechnologies in 2010. LFB Biotechnologies intends to purchase some of the shares in this offering.
	2. Baxter International named as Baxalta Incorporated the publicly traded biopharmaceutical company that it will hive off in mid-2015. Baxalta will provide therapeutic treatments in bleeding disorders, immunology, oncology and gene therapy. It will trade on the New York Stock Exchange as BXLT. Baxter International will continue trading as BAX. The corporate headquarters of both companies will be located in northern Illinois.
	3. Grifols has bought 50 per cent [of](http://email.seekingalpha.com:80/track?type=click&mailingid=1991565&messageid=2900&databaseid=&serial=2900O1991565O1411128338.352ab61241e3df28b32fdb96878ff182&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://www.kiro-robotics.com/) Kiro Robotics for €21 million in cash. Kiro’s lead product is an oncology robot which automates the preparation of intravenous medication for chemotherapy treatment.
	4. Bayer plans a separate stock listing for its polymer division, part of a move to focus the group on health care and crop science. Analysts have valued the polymer division at about $US 10 billion.

# 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. The US Centers for Disease Control and Prevention (CDC) advised US colleges and universities to take precautions against Ebola being spread by people arriving from West Africa. Some said they were already questioning people known to have been in West Africa about possible symptoms. The CDC said anyone who has been in the region who develops a fever of 101.5 degrees or more, or has other possible signs of the disease, should seek immediate medical care and warn a hospital or doctor’s office in advance of their arrival. It advises steps to minimize proximity to others, like not taking public transport.
	2. Howard University Hospital in Washington,DC, has been granted $US 11 million in federal funds towards developing a drug to target a specific protein of the Ebola virus. It is also researching HIV resistance in people with sickle cell disease.
	3. The Boston Biomedical Innovation Center has awarded two grants to accelerate commercialization: to Seemantini Nadkarni, (Harvard Medical School and the Wellman Center for Photomedicine at Massachusetts General Hospital) for continued development of a low-cost, bed-side blood sensor; and Jonathan Thon and Joseph Italiano (both from Harvard Medical School and Brigham and Women’s Hospital) for continued development of an *in vitro* platelet bioreactor.
	4. Companies seeking drug approval in the US have historically avoided clinical studies involving children. Now Congress has passed the Best Pharmaceutical for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). These provide new exclusivity-based incentives to conduct studies (BPCA), and the capacity for the FDA to require companies to conduct paediatric studies as a condition of approval (PREA).
	5. Reports show that over 1,100 laboratory incidents involving potential bioterror germs were reported to federal regulators from 2008 to 2012 inclusive.
	6. The CDC has issued a hospital checklist for Ebola preparedness[[15]](#footnote-15).
	7. The National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), convened an expert panel to make recommendations relating to care for patients with sickle cell disease[[16]](#footnote-16). The panel recommended wider adoption of hydroxyurea in treatment, and also suggested that clinicians give periodic blood transfusions to children with the disease to reduce stroke risk. The panel said both treatments are underutilized at present.
	8. A national pandemic influenza vaccine manufacturing facility was dedicated in Bryan, Texas[[17]](#footnote-17). The facility will be completed by the end of 2015, with start-up and validation phases completed by early 2017. The plant will have the capacity to produce the bulk antigen needed for up to 50 million adjuvanted pandemic influenza vaccine doses within four months of a declared pandemic and release of satisfactory virus seeds.
	9. New York Blood Center's Laboratory of Viral Immunology has received an NIH grant to develop a mucosal universal influenza vaccine. A separate grant has been awarded for developing therapeutics for treating Middle East Respiratory Syndrome-novel coronavirus (MERS).
	10. A registry is being constructed with free testing for people in the US with haemophilia A and B. “My Life, Our Future,” is a partnership of the National Hemophilia Foundation, the Puget Sound Blood Center in Seattle, Biogen Idec and the American Thrombosis and Hemostasis Network. It offers free genotyping to patients receiving care at haemophilia treatment centres.

### India

* 1. Through a co-operative agreement between the UK and India, Oxford-based biotech firm Oxitec will assist India in developing genetically engineered mosquitoes which are sterile and unable to reproduce, thereby reducing the prevalence of mosquito-borne diseases.
	2. On a visit to Japan, the Indian Prime Minister discussed co-operation to combat sickle cell disease in his country. He discussed recent clinical interventions with stem cell pioneer Shinya Yamanaka.

### Australia

* 1. The Australian Infectious Diseases Research Centre Eureka Prize for Infectious Diseases Research was awarded to [CSIRO](http://www.csiro.au/)’s Hendra virus team for creating the first vaccine and effective human treatment against Hendra virus and developing skills and resources that are being applied against Ebola.
	2. Research from the University of New South Wales' Kirby Institute for Infection and Immunity in Society shows that more Australians were diagnosed with syphilis in 2013 than in any year since recording began. There were 1760 syphilis notifications, a 34 per cent increase since 2009. Diagnosis was highest in the 20 to 39 age group, almost all cases were gay men, and 600 occurred in NSW. The report showed an increase in notifications of gonorrhoea with 14,947 in 2013 compared with 13,842 in 2012. The past five years have seen an 80 per cent increase in gonorrhoea notifications. The most prevalent sexually transmitted infection was chlamydia, with 82,537 new diagnoses in 2013. An estimated 220 people in NSW died after contracting hepatitis C, more than double the number of fatalities recorded in 2003.

###  Other

* 1. The Hong Kong Red Cross Blood Transfusion Service is deferring blood donation by those who have lived in or visited countries with an Ebola virus outbreak. People who have been to Guinea, Sierra Leone, Liberia and Nigeria cannot give blood in Hong Kong for at least 28 days from the date they left those countries.
	2. The New Zealand Blood Service, in an appeal for donations at the beginning of September, said it was at its highest level of need for ten years. It was particularly seeking donations of O positive blood.
	3. Danish financial regulators fined Novo Nordisk $US 90,000 for its delay in announcing the FDA's February, 2013 demand for a new study for its insulin drug Tresiba. This setback wiped out some $US 14 billion of market value as investors moved out of Novo Nordisk.
	4. In the UK, Dr. Richard Tedder and his team reported in The Lancet that they had retrospectively screened for the hepatitis E virus nearly a quarter of a million blood donations from southeast England collected during 2012 and 2013[[18]](#footnote-18). About 1 in every 3,000 blood donors was viremic with hepatitis E. The team tracked 79 cases of infected blood donations which had been used to prepare 129 blood components, 62 of which were transfused before the virus was identified. Dr. Tedder described the symptoms in recipients who received the hepatitis E contaminated blood products: “We found 16 transmission events in 42 recipients. The outcome was only one mild case of jaundice, but nevertheless, infection in others who became viremic for quite some extended periods of time.” A commentary in The Lancet on this study said all blood donations in hepatitis E endemic areas such as the United Kingdom should be screened. Dr. Tedder commented: “How much money do you spend to save the very occasional case of jaundice? Are there other ways of containing the HEV infection risk in the immunosuppressed? And there is also reputational damage if you are found to be transmitting.”
	5. An ordinance adapting the use of voluntary blood donations to pay penalties for violations of traffic regulations has been approved in the Philippines. If blood examination shows that the blood is not fit for medical use, the traffic violator will be made to pay the mandated fine.
	6. Kuala Lumpur will host the World Federation of Hemophilia Congress in 2020.
	7. The latest (2012) data from the Marketing Research Bureau has Canada behind the US and Australia in immunoglobulin use, at 146.4 kilograms per million people, but ahead of 20 other countries considered, including the UK, Germany and Switzerland, where usage ranged from 53.5 to 74.6 kilograms per million people. The [*Canadian Blood Services 2012/13 annual report*](http://fundraising.blood.ca/page.aspx?pid=385)shows immunoglobulin accounted for $C 202 million, a quarter of annual expenses. Dr. Graham Sher, CEO of Canadian Blood Services, says that the use of plasma protein therapies (free to patients) has been extended to new conditions in the past two decades, sometimes without randomized controlled trials to show benefit. Less than one-third is used to treat primary immune deficiency disorders, for which it is the only treatment[[19]](#footnote-19).

# Safety and patient blood management

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

### Appropriate transfusion

* 1. The Institute for Patient Blood Management and Bloodless Medicine and Surgery in Englewood Hospital and Medical Center has shared eight years of experience in managing gastrointestinal bleeding in a population refusing blood transfusion[[20]](#footnote-20). The report concludes: “These results suggest that transfusion-free management of gastrointestinal hemorrhage can be effective with mortality comparable with the general population accepting medically indicated transfusion. Management of these patients is challenging and requires a dedicated multidisciplinary team approach knowledgeable in techniques of blood conservation.”
	2. A new analysis[[21]](#footnote-21) found that blood transfusion was linked to lower risk for in-hospital mortality among anaemic patients with acute [myocardial infarction](http://en.wikipedia.org/wiki/Myocardial_infarction) (MI). The researchers analysed 34,937 consecutive patients from 2000 to 2008 at 57 centres. **Adam C. Salisbury,** from the department of cardiology at Saint Luke’s Mid America Heart Institute, Kansas City, and colleagues wrote: “These findings suggest that previous observational reports of increased mortality with transfusion may have been influenced by selection bias, and they highlight the need for randomized trials to establish the role of transfusion during [acute] MI.” They noted that patients who did and did not receive a blood transfusion had markedly different clinical profiles, and most could not be included in their propensity-matched analysis[[22]](#footnote-22). The analysts commented that more research is required to determine the optimal threshold for blood transfusion during acute MI. **Robert W. Yeh,** from the cardiology division at Massachusetts General Hospital, and **Neil J. Wimmer, in their comment**[[23]](#footnote-23) **on the analysis said:** “We are no closer now to understanding the optimal way to treat anemia or bleeding in these patients than we were a decade ago.” They said that until a definitive randomized study is done, “the wide variation in transfusion practices across hospitals is likely to persist, as clinicians sift through the varied offerings of a growing number of observational comparisons”.
	3. A small study found that paediatric patients with sickle cell anaemia and asymptomatic neurologic injury were almost sixty per cent less likely to suffer a repeat cerebral infarction while undergoing regular blood transfusions[[24]](#footnote-24). An editorial comment[[25]](#footnote-25) emphasised that clinicians see children over a longer period during which the adverse effects of repeated transfusions could emerge, such as inability to maintain intravenous access, iron overload, and alloimmunization.
	4. University of Illinois researchers have found that stored blood loses cell functionality within the FDA-recommended 42-day shelf life. They found the microcapillaries have diminished oxygen-carrying capacity. The researchers employed spatial light interference microscopy (SLIM)[[26]](#footnote-26).
	5. A meta-analysis and systematic review has found that restrictive red blood cell transfusion thresholds are associated with a decreased risk of acquiring healthcare-associated infections compared with liberal transfusion thresholds[[27]](#footnote-27).

### Treating iron deficiency

* 1. The human body in response to inflammation increases secretion of the hormone hepcidin which reduces the amount of iron available in the bloodstream. With iron being required for the production of red blood cells in the bone marrow, patients with inflammation may develop anaemia. One hepcidin inhibitor, lexaptepid pegol (lexaptepid), showed efficacy in animal studies and has now been trialled in humans. Lead study author Lucas van Eijk, of Radboud University Medical Center in Nijmegen, Netherlands, said: "It is quite encouraging that lexaptepid helped maintain appropriate levels of iron in the bloodstream of healthy volunteers without compromising the immune response[[28]](#footnote-28).

### Other.

* 1. A study reports that aspirin after anticoagulation reduced the risk for recurrent venous thromboembolism (VTE) by more than one-third in patients with an initial unprovoked VTE[[29]](#footnote-29). **Professor John Simes from the University of Sydney, and** director of the National Health and Medical Research Council Trials Centre, and colleagues analyzed two trials[[30]](#footnote-30), to assess the effect of aspirin vs. placebo on recurrent VTE, major vascular events and bleeding in patients with a first unprovoked VTE who had completed initial treatment with heparin plus [warfarin](http://www.healio.com/search?q=warfarin&requiredfields=specialty:Cardiology) or equivalent. Simes said: “It is not recommended that aspirin be given instead of anticoagulant therapy, but rather to be given to patients who are stopping anticoagulant therapy or for whom such treatments are considered unsuitable……Although less effective, aspirin is inexpensive, easily obtainable, safe and familiar to patients and clinicians worldwide. If cost is the main consideration, aspirin is a particularly useful therapy. The costs of treating future thromboembolic events is greater than the cost of the preventive treatment.” Researchers found aspirin was not associated with increased risk for bleeding in this patient population.
	2. Janssen Research & Development and Bayer HealthCare, announced the expansion of the EXPLORER global cardiovascular research program for its factor Xa inhibitor, Xarelto (rivaroxaban) to include additional high-risk patient populations. The new trials will test the treatment of acute coronary syndrome, embolic stroke of undetermined source and peripheral artery disease.
	3. [Bristol-Myers Squibb](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.bms.com%2F&esheet=50927792&newsitemid=20140820005354&lan=en-US&anchor=Bristol-Myers+Squibb+Company&index=1&md5=51b373475f2c5cc054502570cdc27ad7) and Pfizer presented 14 abstracts (oral and poster presentations) at the European Society of Cardiology Congress 2014 in Barcelona. The new clinical trial data and analyses assessing cost effectiveness and real-world use underlined the companies’ intention to develop markets for Eliquis in a variety of patient populations[[31]](#footnote-31).
	4. A review[[32]](#footnote-32) of the use of recombinant factor VIIa for rapid INR[[33]](#footnote-33) normalization in life-threatening haemorrhage in anticoagulated patients concluded that recombinant factor VIIa appeared to lower INR without significant thromboembolic complications.
	5. Ascendia Pharmaceuticals applied its nano-emulsion technology platform to a novel injectable formulation of blood-thinner clopidogrel. The company has filed for US and global patents.
	6. Researchers have found that the naturally occurring protein fibronectin plasma can switch its function from stopping bleeding to stopping overactive blood clots[[34]](#footnote-34).

# 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. Chimerix, presented new data on its investigational broad-spectrum antiviral brincidofovir at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held in September in Washington, DC. Two oral presentations reviewed new *in vitro* and *in vivo* studies that advance the understanding of brincidofovir's resistance profile specific for two important viral pathogens: cytomegalovirus (CMV) and adenovirus (AdV). Chimerix is also working with the US Biomedical Advanced Research and Devlopment Authority (BARDA) to develop brincidofovir as a medical countermeasure against smallpox[[35]](#footnote-35).
	2. A new study[[36]](#footnote-36) suggests that synthetic erythropoietin (EPO), which stimulates red blood cell production, may prevent brain damage when used shortly after preterm birth, reported researcher Dr. Petra Huppi, a professor of paediatrics and newborn medicine at the University of Geneva, in Switzerland[[37]](#footnote-37). "The real test of whether EPO protects the brains of these children will be when they are evaluated when they are older," she said. Dr. David Mendez, a neonatologist at Miami Children's Hospital, commented: "This study raises more questions than it answers." He said that although EPO had been used to reduce the need for blood transfusions in preemies, it was falling out of favour. "There has been some concern that EPO reduces white blood cell counts and there is some concern that EPO may predispose the baby to have an eye condition called 'retinopathy of prematurity' that can lead to blindness," he said. "A lot of neonatologists don't even use EPO anymore."
	3. A US study[[38]](#footnote-38) found that severe combined immunodeficiency was much higher in newborns than previously suspected and that the survival rate was high for neonates who received early diagnosis and treatment.
	4. In early October, a team at Stanford School of Medicine will give a transfusion of blood plasma donated by people under 30 to older volunteers with mild to moderate Alzheimer's disease to see if there is improvement in cognition.
	5. Researchers led by Dr Sidney (Wally) Whiteheart, of the University of Kentucky have examined how a gene STXBP5 (known to regulate the protein von Willebrand factor) influences blood clotting as a whole. Whiteheart said. "What we found has the potential for profound impact down the road in identifying genetic risk factors for cardiovascular disease"[[39]](#footnote-39). Researchers led by Dr Charles Lowenstein, of the University of Rochester, examined the function of STXBP5 in the endothelial cells that line the walls of blood vessel walls and release von Willebrand factor when damaged[[40]](#footnote-40).

# Legal actions and enquiries

*The NBA is interested in the implications for Australia of any proceedings against companies, governments and professional practitioners in relation to blood and blood products; or of relevant public enquiries.*

* 1. In California a federal judge denied partial summary judgment sought by CSL Limited, CSL Behring, CSL Plasma, Baxter International, and the Plasma Protein Therapeutics Association, rejecting their claim that plaintiff San Mateo County "may not seek damages from defendants for blood plasma products purchased from rival non-conspirators at prices that were inflated by defendants' anti-competitive conduct."

# 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).*

### Ebola virus disease-incidence and logistics

* 1. The World Health Organisation (WHO) estimated that by 14 September Ebola virus had sickened at least 5335 people and killed 2622 of them in Sierra Leone, Guinea, Liberia, and Nigeria, although this was known to be a significant underestimate of those affected. Up to ten per cent of cases figures are healthcare workers. Almost 50 per cent of cases had occurred in the previous 21 days. A separate outbreak–supposedly not related to the outbreak in West Africa–was laboratory-confirmed on 26 August in the Democratic Republic of Congo.
	2. CDC Director Dr Tom Frieden visited West Africa and reported that the Ebola epidemic was outpacing the current response. He called for speed, flexibility and work on the front lines. The US is sending 3000 military personnel to Africa to assist in the fight. The Pentagon will send engineers to set up 17 treatment centres in Liberia—each with a 100-bed capacity—as well as medical personnel to train up to 500 health-care workers per week. The CDC is running safety training courses for healthcare volunteers going to West Africa. The Pentagon is sending a 25-bed hospital to Liberia for health-care workers who become ill. The US will manage and staff the hospital.
	3. Army engineers from Britain are building a 200 bed hospital in Sierra Leone, and a number of other countries are also contributing to the effort against Ebola.
	4. Experts emphasise that to stop the spread of Ebola the sick must be identified and isolated and their contacts must be monitored. Strict infection control in healthcare settings and in funeral practices is also essential. Infected people are able to spread the virus to others only after they have symptoms. A person usually has no symptoms for the incubation period which can be anywhere between 2 and 21 days.
	5. The heads of WHO, the International Civil Aviation Organization (ICAO), the World Tourism Organization (UNWTO), Airports Council International (ACI), the International Air Transport Association (IATA) and the World Travel and Tourism Council (WTTC) activated a Travel and Transport Task Force. Affected countries have been requested to conduct exit screening of all persons at international airports, seaports and major land crossings for unexplained febrile illness consistent with potential Ebola infection. Any person so affected should not be allowed to travel unless the travel is part of an appropriate medical evacuation.
	6. Aid groups including Doctors Without Borders (MSF) and the European Commission have criticized WHO for a lack of leadership in coordinating the fight against Ebola. “Clearly WHO didn’t foresee this outbreak and while the Ebola crisis was clear in March, it didn’t act until August to declare an emergency,” said Barry Bloom, a public health professor at Harvard University. J. Stephen Morrison, director of the global health policy centre at Washington’s Center for Strategic and International Studies said: “The scale of the disease’s devastation goes far beyond what health officials had seen previously”. He said it’s not “a question of incompetence or complacency. It’s the fact we’re catching up with the unknown, and it’s way ahead of us.”
	7. The Bill & Melinda Gates Foundation donated $US 50 million in September to buy supplies and scale up the emergency response to Ebola.

### Ebola virus disease-understanding the virus

* 1. The UK government and the Wellcome Trust have launched a £6.5 million research fund to ease the Ebola epidemic in West Africa. Wellcome Trust director Jeremy Farrar said the gravity of the Ebola epidemic “demands an urgent response and we believe rapid research into humanitarian interventions and therapeutics can have an impact on treatment and containment during the present outbreak” and that “what we learn could also change the way we approach future outbreaks, providing us with tested tools and techniques that were not available to public health authorities this time”.
	2. There are five known ebolaviruses. The current epidemic is of EBOV, the Zaire strain. The Sudan ebolavirus (SUDV) is also deadly, and a research team which has been developing a therapy has given a progress report[[41]](#footnote-41).
	3. Scientists have identified 300 genetic changes that distinguish the 2014 Ebola virus genomes from the viral genomes tied to previous Ebola outbreaks. These multiple mutations alter protein sequences, potential targets for future diagnosis, vaccination and treatment. They found the current EVD outbreak followed single introduction into humans[[42]](#footnote-42) and then sequential spread over a number of months.
	4. A collaborative study[[43]](#footnote-43) has shown how Ebola disables the body’s ability to halt infected cell reproduction[[44]](#footnote-44).
	5. Researchers at the La Jolla Institute for Allergy and Immunology (La Jolla Institute) and the San Diego Supercomputer Center (SDSC) at the University of California, San Diego are running high-speed online publications of analysis of EBOV-related epitope data being curated in the Immune Epitope Data Base (IEDB), and predicting epitopes using the IEDB Analysis Resource. Sebastian Maurer-Stroh of Bioinformatics Institute, A\*STAR, Singapore is also assisting with analysis of the latest outbreak sequences of Ebola proteins. The aim is to produce an overview of the molecular targets of the immune responses to Ebola virus.
	6. A Namibian farmer died of Crimean-Congo haemorrhagic fever (CCHF) in Bloemfontein in September**.** Like Ebola, CCHF is a viral haemorrhagic fever and the [symptoms are similar](http://www.health24.com/Medical/infectious-diseases/Ebola/Signs-and-symptoms-of-Ebola-20140729). However, according to the WHO Crimean-Congo haemorrhagic fever is primarily transmitted to people from [ticks](http://www.health24.com/Lifestyle/Man/Your-life/Tick-bites-20120721) and livestock. Marburg haemorrhagic fever is also similar to that caused by the genetically related Ebola virus. The Marburg virus is carried by bats[[45]](#footnote-45).

### Ebola virus disease-vaccine development

* 1. A number of Ebola vaccines are being trialled. The US NIH has accelerated human clinical trials of the vaccine in which GlaxoSmithKline has a joint interest. It has already shown encouraging results in non-human primates. Safety trials will be run in parallel in the UK by an Oxford team. GlaxoSmithKline will begin manufacturing up to 10 000 additional doses of the vaccine while clinical trials are conducted, these doses to be made available if WHO decides to permit emergency immunizations in high-risk communities.
	2. The Canadian Government announced it would donate to WHO up to 1000 doses of an experimental vaccine. In animal studies the vaccine was effective at preventing infection when given in advance, and also at improving chances of survival when administered soon after infection. The vaccine was developed by the Public Health Agency of Canada and licensed to NewLink Genetics of Iowa.
	3. Immunovaccine announced positive results for a vaccine formulated in its DepoVax technology in an Ebola virus challenge study performed by the National Institute of Allergy and Infectious Diseases (NIAID) of NIH. In a study using cynomolgus macaque monkeys all vaccinated subjects survived while all unvaccinated subjects did not. Testing DepoVax for Ebola followed earlier positive results with an anthrax vaccine under the same preclinical services program offered by NIAID.
	4. [Johnson & Johnson](http://quotes.wsj.com/JNJ) is accelerating the development of a vaccine, with two components, from Crucell NV and Denmark-based biotech company [Bavarian Nordic](http://quotes.wsj.com/DK/BAVA), both of which are developing vaccines against filoviruses, including Ebola. Clinical trials in humans are expected early in 2015.
	5. Bavarian Nordic has accelerated its collaboration with NIAID on Ebola vaccine. First human trials are expected in 2015.

### Ebola virus disease-developing potential treatments

* 1. Chimerix announced *in vitro* activity of its investigational antiviral brincidofovir (BCV) against the Ebola virus following testing at the Viral Special Pathogens Branch of the CDC and NIH. Further assessments in animal models are being conducted. BioCryst Pharmaceuticals also put forward its broad spectrum antiviral [BCX4430](http://www.globenewswire.com/newsroom/ctr?d=10097079&l=3&a=BCX4430&u=http%3A%2F%2Fwww.biocryst.com%2Fbcx_4430) as a drug candidate for the treatment of Ebola virus disease and other haemorrhagic fever virus diseases.
	2. A WHO ethics committee declared it ethical in particular circumstances to use experimental treatments that have been shown to combat infection in animal studies. These included ZMapp a cocktail of antibodies which had already been given to two US healthcare workers who recovered[[46]](#footnote-46). Three Liberian healthcare workers, and one British nurse evacuated to London also received the drug and three of the four recovered. These doses were reported to have exhausted the supply, with more supplies not available for some months. In the US, [BARDA](http://www.phe.gov/about/barda/Pages/default.aspx) will provide funding as well as technical support for manufacturing, regulatory, and nonclinical activities through a $US 24.9 million, 18-month contract with Mapp Biopharmaceutical, of San Diego. The contract can be extended to a total of $US 42.3 million. Work under the contract supports the development and manufacturing ZMapp toward FDA approval. Since Marburg virus and Ebola virus are similar, there is an expectation that a treatment for Marburg virus could be successful against Ebola[[47]](#footnote-47).
	3. WHO has been reconsidering using the blood of people who have recovered from Ebola to treat those who are ill. Convalescent serum was first used for Ebola in 1976, during the first documented outbreak. “The jury is still out” on this treatment according to Ebola expert Daniel Bausch of Tulane University, New Orleans. However he said “I feel we have a moral imperative to push forward with all the scientifically plausible modalities.”
	4. A nurse from the UK who was airlifted home from West Africa with Ebola, and treated with ZMapp, travelled to the US to donate blood to help an American with the disease.
	5. Japan has offered WHO favipiravir, an anti-influenza drug developed by Fujifilm subsidiary Toyama Chemical Co for treatment of Ebola. The drug was approved by Japan’s health Ministry in March. Favipiravir inhibits viral gene replication within infected cells to prevent propagation. Ebola and influenza viruses are of the same general type[[48]](#footnote-48). The company has enough of the drug for 20,000 patients.
	6. Hemispherx Biopharma and the US Army Medical Research Institute of Infectious Diseases (USAMRIID) have agreed to test Alferon (the only multi-species, natural alpha interferon commercially approved in the US) and Ampligen (an experimental drug) against the Ebola virus. Ebola is a major focus of USAMRIID, a unit of the US Department of Defense responsible for medical biological defence research.
	7. NanoViricides reported progress in developing its anti-Ebola drug. It has designed broad-spectrum drug candidates that should continue to work in spite of mutations, and has commenced synthesising them. The company’s CEO, Dr. Eugene Seymour, presented on the current Ebola outbreak in West Africa, at the Rodman and Renshaw Investment Conference in New York City on 9 September[[49]](#footnote-49).

### Mosquito-borne diseases-dengue

* 1. Sanofi announced that, in its final clinical trial for its dengue vaccine, the product reduced disease cases by 60.8 per cent. The trial was conducted in over 20,000 children aged 9-16 in Latin America[[50]](#footnote-50). The vaccine was 42.3 per cent efficient against serotype 2, compared with 35 per cent in a previous trial on some 10,000 children in Asia. Trial results will be presented at the American Society of Tropical Medicine and Hygiene's annual meeting in November.
	2. Japan's Takeda Pharmaceutical will commence its final dengue vaccine trials in 2015 and hopes DENVax[[51]](#footnote-51) may gain regulatory approval in 2016. While Sanofi Pasteur's CYD-TDV is administered as three injections over 12 months, DENVax is administered as two injections given over 90 days. Both products are live-attenuated vaccines, whereas the pipeline products of Merck and GlaxoSmithKline are a subunit vaccine and an inactivated virus vaccine respectively.
	3. Visterra presented new preclinical data for VIS513 at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Washington, D.C[[52]](#footnote-52). Brian J. G. Pereira, President and Chief Executive Officer of Visterra, said: “We are very encouraged by these new data which show the potential of VIS513 to broadly neutralize all four dengue virus serotypes”.
	4. Japan’s Biomedical Research Institute Co has developed a dengue detecting kit (RapiDeng Ag). It has a test strip containing dengue antibody. The announcement came as the number of locally acquired dengue cases in Japan this year reached 144. This is Japan’s first experience of locally contracted dengue since 1945. A Tokyo park was closed down in an attempt to prevent further cases.
	5. A report by researchers from the University of East Anglia says that European holiday destinations such as Spain and Italy could become dengue hotspots. Professor Paul Hunter, from the University’s Norwich Medical School, said: "Our study has shown that the risk of dengue fever is likely to increase in Europe under climate change, but that almost all of the excess risk will fall on the coastal areas of the Mediterranean and Adriatic seas and the North Eastern part of Italy, particularly the Po Valley". Public Health England said that in 2013 there were 541 cases reported in returning travellers compared with 343 in 2012. Most cases were reported in travellers to India and Thailand, with an increase in cases contracted in Barbados during 2013.
	6. WHO and Singapore have held the fourth Asia-Pacific Dengue Workshop.
	7. Experts have cautioned that vaccines (such as a forthcoming dengue vaccine) will probably cause temporary but significant spikes in the disease after they are first used[[53]](#footnote-53). They say this is just the natural result of complex interactions between imperfect vaccine protection and routine fluctuations in the populations of insects who carry the diseases. "Our analysis suggests that if we develop and widely use a vaccine for [dengue fever](http://medicalxpress.com/tags/dengue%2Bfever/), there may later be spikes in the incidence of the [disease](http://medicalxpress.com/tags/disease/) that are two to three times higher than its normal level," said Jan Medlock, an assistant professor in the Department of Biomedical Sciences at Oregon State University, and expert on the evolution and epidemiology of infectious disease. "We can explain why this will happen and show how, in the long run, vaccine use will clearly result in fewer cases of disease," Medlock said. "Our concern is to warn people in advance about this issue, so that policy makers and the public don't freak out and lose faith in the vaccination programs.

### Mosquito-borne diseases-chikungunya

* 1. DARPA, offered a prize of $US 150,000 for the best model predicting how the mosquito-borne chikungunya virus could spread across countries in the Americas. The predictions are to cover a six-month period beginning in September.
	2. Lee-Jah Chang, from NIH and colleagues examined the safety, tolerability, and immunogenicity of a chikungunya virus-like particle (VLP)vaccine in a phase 1, dose-escalation trial involving 25 healthy adults aged 18 to 50 years. They found no evidence of serious adverse events. Neutralizing antibodies were detected in all dose groups after the second vaccination, and a significant boost was seen after the third vaccination[[54]](#footnote-54).
	3. Researchers at the Medical Research Council (MRC) – University of Glasgow Centre for Virus Research, in collaboration with colleagues at the Institut Pasteur, France, have identified a potential new pathway-the RNA interference (RNAi) pathway in the mosquito-to prevent transmission of chikungunya.
	4. Samoa has been experiencing a significant chikungunya outbreak. In mid-September the CDC issued a travel notice for chikungunya in American Samoa, as the case total reached 700.
	5. New Zealand has been experiencing a significant number of ZIka cases returning from the Cook Islands. Chikungunya has been coming in from Tonga.

### Mosquito-borne diseases-malaria

* 1. Researchers from the Singapore-MIT Alliance for Research and Technology have developed a fast, reliable and inexpensive method to diagnose malaria that uses [magnetic fields](file:///%5C%5Ccbrintfs01%5Ctopic%5Cmagnetic-fields) to detect the parasite's [waste products](file:///%5C%5Ccbrintfs01%5Ctopic%5Cwaste-products) in the blood of infected patients[[55]](#footnote-55). “The new technique uses a significantly smaller blood sample to traditional blood-smear methods, and is more sensitive and less error-prone,” says Donhee Ham, professor of electrical engineering at Harvard University.
	2. Scientists have used laser optical tweezers to study interactions between the malaria-causing parasite and red blood cells, hopefully facilitating the development of more effective drugs or vaccines[[56]](#footnote-56).

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

* 1. Human cases of H7N9 continue to be reported from China in small numbers. China’s agriculture ministry detected the virus in fourteen samples in July and the first third of August, nine from live bird markets in Guangdong, and five from Shandong, three from layer farms and two from breeder farms.
	2. Northeast China's Heilongjiang Province reported an outbreak of the H5N6 bird flu virus in poultry at the beginning of September. 69,000 birds were culled.
	3. Vietnam’s Ministry of Agriculture and Rural Development in August issued an emergency dispatch asking cities and provinces to prevent spreading of the new avian flu virus A/H5N6.
	4. Hong Kong’s Centre for Food Safety in early September banned the import of poultry meat and products from Salem County, New Jersey, following an outbreak of avian influenza.
	5. A study[[57]](#footnote-57) has found that the avian influenza A H3N8 virus that killed harbour seals along the New England coast can spread to humans through respiratory droplets.
	6. BARDA has awarded InDevr a contract to support the development of FluChip-8G, a microarray-based test that quickly distinguishes strains of influenza virus such as H5N1 or H7N9.
	7. Russian scientists from Microgen[[58]](#footnote-58) have patented new technology to create a split-virus flu vaccine. This type of vaccine chemically disrupts the flu virus.
	8. Researchers from the Emory Vaccine Center found that giving people a flu vaccine targeting an unfamiliar flu strain may generate antibodies targeting the stem of the flu virus's hemagglutinin (HA) protein. This is the structure where efforts to develop a "universal" flu vaccine are directed[[59]](#footnote-59).
	9. Immune Targeting Systems (ITS) is working on a Tcell vaccine (Flunisyn) to protect humans from all flu strains, both seasonal and pandemic.
	10. Hemispherx Bipharma announced its drug Ampligen plus intranasal seasonal influenza vaccine induces cross-reactive antibody formation against avian H5N1 and H7N9 influenza hemagglutinins (HA) in humans**[[60]](#footnote-60)**
	11. A mouse study suggests that proteins from intestinal microbes may enhance the effectiveness of the seasonal flu vaccine[[61]](#footnote-61).

### Middle East Respiratory Syndrome-novel coronavirus (MERS-CoV)

* 1. As at 20 September, the number of laboratory confirmed cases of MERS in Saudi Arabia had been 749, with 317 deaths.
	2. An international team led by virologists from the University of Bonn has concluded that the rate of human transmission of MERS is low[[62]](#footnote-62). Nevertheless, one-third of infected persons with symptoms die.
	3. Researchers from the NIAID facility in Hamilton, Montana, have found that marmosets are a good animal model for MERS, suffering from the same symptoms humans do[[63]](#footnote-63), and being small enough to work with in a containment laboratory. MERS infects camels, but they do not become as ill as humans, and they are too large for the lab. However, the researchers suggest that where the aim is to develop MERS vaccines, scientists should probably work with rhesus monkeys as repeated blood analyses will not be easier in the somewhat larger animal.
	4. Bats are thought to be a native reservoir for MERS, even if it seems certain that recent human infection has been associated with camels. Work continues on the nature of the species jump involved[[64]](#footnote-64).
	5. Oman's Ministry of Health (MoH) has urged the people planning to visit Saudi Arabia to perform Haj and Umrah to postpone their pilgrimage plan this year.
	6. Researchers from the University of Illinois, Chicago, have identified a compound that inhibits an enzyme crucial to the viruses that cause MERS and SARS, although the method of inhibition differs[[65]](#footnote-65).
	7. A vaccine developed by a team led from the University of Pittsburgh School of Medicine have developed a vaccine that protects mice against MERS. They say the vaccine is suited to camels, thought to be a source of infection for humans.

### Other diseases: occurrence, prevention and treatment

* 1. HIV is controlled using antiretroviral drugs, taken for life because previously dormant viruses become activated when the drug is stopped. Now a study published in the journal *Cell* indicates that a “shock-and-kill” approach using drugs called inducers with virus-fighting antibodies to active dormant cells may help to eliminate the latent virus from the body[[66]](#footnote-66).
	2. A multi-university study has identified a protein that appears to play a key role in protecting people infected with *Mycobacterium tuberculosis* from developing the active form of TB. Interleukin-32 was found to be one biomarker of adequate host defence[[67]](#footnote-67).
	3. Most new cases of leprosy occurring round the world occur in areas where TB is endemic. Now research led from UCLA[[68]](#footnote-68) may have found a stronger weapon against both diseases than the partially protective century-old vaccine Bacille Calmette-Guerin, or BCG. “This is the first study demonstrating that an improved vaccine against tuberculosis also offers cross-protection against Mycobacterium leprae, the causative agent of leprosy,” said Dr. Marcus Horwitz, professor of medicine and microbiology, immunology and molecular genetics, and the study’s senior author. “That means that this vaccine has promise for better protecting against both major diseases at the same time….It is also the first study demonstrating that boosting a recombinant BCG vaccine further improves cross-protection against leprosy”.
	4. NSW Health has urged thorough cooking of pork products, particularly pork livers, after three recent notifications of Hepatitis E in the state in people who have not travelled overseas.
	5. Western Australia has had growing concerns about the frequency of Ross River virus infections.
	6. Residents of the Northern Territory have been advised to keep clear of flying foxes after the deadly Australian bat lyssavirus was detected in an animal located in Katherine. The last detection of the virus in the Territory was in 1997
	7. Europe has been experiencing an increase in Lyme disease as climate factors have led to ticks spreading more widely.
1. Its poster presentations were *Joint Function and health-related quality of life in adults using prophylaxis after treatment with Bayer's sucrose formulated recombinant factor VIII.*; *Joint outcomes by magnetic resonance imaging after treatment with Bayer's sucrose formulated recombinant factor VIII; Results at the three-year evaluation time point with Bayer's sucrose formulated recombinant factor VIII; Analysis of the prevalence of cardiovascular comorbidities in a US patient population with hemophilia A; confirmation of findings; Changes in healthcare resource utilization and healthcare-related events in patients diagnosed with hemophilia A; Prevalence of depression in US patients with hemophilia A compared to a general medical population; a retrospective database analysis* [↑](#footnote-ref-1)
2. the REPLACE (**R**andomized **E**valuation of fibrinogen versus **PLACE**bo in complex cardiovascular surgery) Phase III clinical trial. REPLACE is the first randomized, double blinded, placebo-controlled, multicenter study in a large population of patients evaluating fibrinogen concentrate (Human) (FCH) in controlling bleeding during aortic aneurysm surgery. [↑](#footnote-ref-2)
3. from the Georgia Institute of Technology, Emory University, Children’s Healthcare of Atlanta and Arizona State University. They were supported by the National Institutes of Health, the US Department of Defense, and the American Heart Association. See Ashley Brown, et al., “Ultrasoft microgels displaying emergent platelet-like behaviours,” *Nature Materials*, 7 September 2014. [dx.doi.org/10.1038/nmat4066](http://dx.doi.org/10.1038/nmat4066) [↑](#footnote-ref-3)
4. Veti-Gel , developed by Joe Landolina [↑](#footnote-ref-4)
5. Reported in *Proceedings of the National Academy of Sciences* [↑](#footnote-ref-5)
6. Jaundice is the result of insufficient elimination of bilirubin. Not all jaundiced babies will appear yellow to the naked eye. [↑](#footnote-ref-6)
7. Alex Nemiroski, “Universal mobile electrochemical detector designed for use in resource-limited applications”, *Proceedings of the National Academy of Sciences,* 19 August 2014, Volume 111,Number 33, pp11984-11989. doi: 10.1073/pnas.1405679111 [↑](#footnote-ref-7)
8. Tyburski E, Gillespie S, Stoy W, et al. “Disposable platform provides visual and color-based point-of-care anemia self-testing”. The Journal of Clinical Investigation. 2014. [↑](#footnote-ref-8)
9. Published in the journal *Nature Medicine* [↑](#footnote-ref-9)
10. The recombinant human hyaluronidase increases the dispersion and absorption of the immunoglobulin, which is made from pooled plasma. Law firm [Hyman Phelps & McNamara PC](file:///C%3A%5Cfirms%5Chyman-phelps) in a citizen petition released in September urged the FDA to place significant restrictions on HyQvia. The petition concerning the ingredient recombinant human hyaluronidase called for strict labelling and monitoring. The petition reportedly said the labelling should warn against unknown effects on fertility associated with the ingredient, and that Baxter should be required to establish a registry for patients of reproductive age. Hyman Phelps did not disclose its client. [↑](#footnote-ref-10)
11. In 2013 it received European approval for the treatment of PI syndromes and myeloma or chronic lymphocytic leukaemia with severe secondary [hypogammaglobulinemia](http://email.seekingalpha.com:80/track?type=click&mailingid=1981345&messageid=2900&databaseid=&serial=2900O1981345O1410629179.4f772885e6c0df2ce38caa54101a933a&emailid=susan.bambrick%40nba.gov.au&userid=2550971&extra=&&&3000&&&http://ccjm.org/content/73/2/133.full.pdf) and recurrent infections. [↑](#footnote-ref-11)
12. Orphan status carries tax incentives, market exclusivity for 10 years, possibilities for additional research funding, and additional guidance from the European Medicines Agency during clinical development. [↑](#footnote-ref-12)
13. rFVIII=recombinant factor VIII, vWF=von Willebrand factor [↑](#footnote-ref-13)
14. The XTEN technology belongs to Amunix Operating, Inc.. Amunix and Biogen Idec signed a global licence agreement in April this year. [↑](#footnote-ref-14)
15. <http://www.cdc.gov/vhf/ebola/pdf/hospital-checklisk-ebola-preparedness.pdf> [↑](#footnote-ref-15)
16. *Evidence-Based Management of Sickle Cell Disease*, Expert Panel Report, 2014, [↑](#footnote-ref-16)
17. by GlaxoSnithKline, the Department of Health and Human Services, the Governor of Texas, the Texas A&M University System Chancellor and the CEO of the Texas A&M Health Science Center. [↑](#footnote-ref-17)
18. Hepatitis E virus tends to be transmitted through either fecally contaminated food and water or poorly cooked meat—particularly pork. There are four genotypes of varying virulence. Acute infections are generally mild and self-limiting but some patients have a higher risk of complications. The hepatitis E virus has been detected in blood donors in Europe, Japan and China; and transfusion-transmitted infections have been documented. The frequency, however, of transmission and outcome of the transfusion recipients has been unknown. [↑](#footnote-ref-18)
19. See the *Canadian Medical Association Journal*, DOI:10.1503/cmaj.109-4861. This refers to the guidelines for use adopeted in British Columbia, Ontario and the Atlantic provinces. [↑](#footnote-ref-19)
20. [Sharma P](http://www.ncbi.nlm.nih.gov/pubmed?term=Sharma%20P%5BAuthor%5D&cauthor=true&cauthor_uid=25144897), [Barajas FJ](http://www.ncbi.nlm.nih.gov/pubmed?term=Barajas%20FJ%5BAuthor%5D&cauthor=true&cauthor_uid=25144897), [Krishnamoorthy P](http://www.ncbi.nlm.nih.gov/pubmed?term=Krishnamoorthy%20P%5BAuthor%5D&cauthor=true&cauthor_uid=25144897), [Campo LM](http://www.ncbi.nlm.nih.gov/pubmed?term=Campo%20LM%5BAuthor%5D&cauthor=true&cauthor_uid=25144897), [Blumenthal E](http://www.ncbi.nlm.nih.gov/pubmed?term=Blumenthal%20E%5BAuthor%5D&cauthor=true&cauthor_uid=25144897), [Spinnell M](http://www.ncbi.nlm.nih.gov/pubmed?term=Spinnell%20M%5BAuthor%5D&cauthor=true&cauthor_uid=25144897)., ‘Transfusion-free Management of Gastrointestinal Bleeding: The Experience of a Bloodless Institute.’ [J Clin Gastroenterol.](http://www.ncbi.nlm.nih.gov/pubmed/25144897) 2014 Aug 20., published online ahead of print. [↑](#footnote-ref-20)
21. Salisbury AC.et al., “Blood Transfusion During Acute Myocardial Infarction: Association With Mortality and Variability Across Hospitals”, [J Am Coll Cardiol, August 26 2014, Volume 64, Issue 8, pp.811-819.](http://content.onlinejacc.org/article.aspx?articleID=1898527) doi:10.1016/j.jacc.2014.05.040 [↑](#footnote-ref-21)
22. The analysts compared in-hospital mortality rates for patients who received at least one packed red blood cell transfusion with rates for those who did not. In an unadjusted analysis, transfusion was associated with higher in-hospital mortality. However, there was a significant baseline difference in clinical characteristics between the two group so the analysts also conducted a propensity-matched analysis. Only 3,108 patients (1,121 transfused, 1,987 not transfused) could be included. All the rest had nonoverlapping propensity scores and incomparable clinical profiles. Among the propensity-matched patients, [blood transfusion](http://www.healio.com/search?q=blood%20transfusion) was associated with a decreased risk for in-hospital mortality. [↑](#footnote-ref-22)
23. Robert W. Yeh, and Neil J. Wimmer” Blood Transfusion in Myocardial Infarction: Opening Old Wounds for Comparative-Effectiveness Research∗”,J Am Coll Cardiol. , August 26, 2014; Volume 64, Issue 8 pp.:820-822. doi:10.1016/j.jacc.2014.05.041 [↑](#footnote-ref-23)
24. The study by Michael R. DeBaun (from the Vanderbilt-Meharry Center of Excellence in Sickle Cell Disease, Vanderbilt University School of Medicine, Nashville) and colleagues appeared in the 21 August issue of the *New England Journal of Medicine*. [↑](#footnote-ref-24)
25. By Martin H. Steinberg, Boston University School of Medicine [↑](#footnote-ref-25)
26. Kandel M, Brugnara C, Tangella K, Bhaduri B, Popescu G. Optical Assay of Erythrocyte Function in Banked Blood, *Scientific Reports*.2014. [↑](#footnote-ref-26)
27. Rohde JM, Dimcheff DE, Blumberg N, et al. “Health care-associated infection after red blood cell transfusion: A systematic review and meta-analysis”. *JAMA*. 2014;311(13):1317-1326. [↑](#footnote-ref-27)
28. The study appeared in *Blood*, the Journal of the American Society of Hematology. [↑](#footnote-ref-28)
29. [John Simes](http://circ.ahajournals.org/search?author1=John++Simes&sortspec=date&submit=Submit), [Cecilia Becattini](http://circ.ahajournals.org/search?author1=Cecilia++Becattini&sortspec=date&submit=Submit), [Giancarlo Agnelli](http://circ.ahajournals.org/search?author1=Giancarlo++Agnelli&sortspec=date&submit=Submit), [John W. Eikelboom](http://circ.ahajournals.org/search?author1=John+W.+Eikelboom&sortspec=date&submit=Submit), [Adrienne C. Kirby](http://circ.ahajournals.org/search?author1=Adrienne+C.+Kirby&sortspec=date&submit=Submit), [Rebecca Mister](http://circ.ahajournals.org/search?author1=Rebecca++Mister&sortspec=date&submit=Submit), [Paolo Prandoni](http://circ.ahajournals.org/search?author1=Paolo++Prandoni&sortspec=date&submit=Submit), [Timothy A. Brighton](http://circ.ahajournals.org/search?author1=Timothy+A.+Brighton&sortspec=date&submit=Submit), for the INSPIRE (International Collaboration of Aspirin Trials for Recurrent Venous Thromboembolism) Study Investigators, “Aspirin for the Prevention of Recurrent Venous Thromboembolism: The INSPIRE Collaboration” in *Circulation,* the Journal of the American Heart Association, published online before print August 2014, doi: 10.1161/CIRCULATIONAHA.114.008828 [↑](#footnote-ref-29)
30. ASPIRE and WARFASA with a combined enrolment of 1224. The ASPIRE study was funded by National Health and Medical Research Council, the New Zealand Health Research Council, New South Wales Health and the Australian Society of Thrombosis and Haemostasis. The WARFASA study was funded by the University of Perugia and Bayer HealthCare. Bayer HealthCare provided all study drugs for both trials. [↑](#footnote-ref-30)
31. Abstracts can be accessed on the [ESC Congress 2014 website](http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fspo.escardio.org%2Fdefault.aspx%3Feevtid%3D69&esheet=50927792&newsitemid=20140820005354&lan=en-US&anchor=ESC+Congress+2014+website&index=3&md5=75aa02f4133d21de063798a1c8c514e7). [↑](#footnote-ref-31)
32. Natalie Yampolsky,Douglas Stofko,Erol Veznedaroglu, Kenneth Liebman,Mandy J Binning, “Recombinant factor VIIa use in patients presenting with intracranial haemorrhage” SpringerPlus 2014, 3:471, doi:10.1186/2193-1801-3-471 [↑](#footnote-ref-32)
33. International normalized ratio, a measure used in determining the clotting tendency of blood [↑](#footnote-ref-33)
34. The research, carried out in injured mice, was reported 2 September 2014 in Yiming Wang1, Adili Reheman, Christopher M. Spring, Jalil Kalantari, Alexandra H. Marshall, Alisa S. Wolberg, Peter L. Gross, Jeffrey I. Weitz, Margaret L. Rand, Deane F. Mosher, John Freedmanand Heyu Ni, “Plasma fibronectin supports hemostasis and regulates thrombosis”, *J Clin Invest.* doi:10.1172/JCI74630. [↑](#footnote-ref-34)
35. For further information, please visit Chimerix's website, [www.chimerix.com](http://www.globenewswire.com/newsroom/ctr?d=10096879&l=6&a=www.chimerix.com&u=http%3A%2F%2Fwww.chimerix.com%2F). [↑](#footnote-ref-35)
36. published 27 August in the *Journal of the American Medical Association* [↑](#footnote-ref-36)
37. MRI scans when the babies were the equivalent age of a full-term birth found that the brains of those who received EPO showed less damage than the brains of infants who did not. [↑](#footnote-ref-37)
38. By Antonia Kwan (University of California, San Francisco, and UCSF Benioff Children’s Hospital) and colleagues. The study was published 19 August in the *Journal of the American Medical Association*. [↑](#footnote-ref-38)
39. See the *Journal of Clinical Investigation,* October 2014. [↑](#footnote-ref-39)
40. *Ibid.* [↑](#footnote-ref-40)
41. Chen, Gang; Koellhoffer, Jayne F.; Zak, Samantha E.; Frei, Julia C.; Liu, Nina; Long, Hua; Ye, Wei; Nagar, Kaajal; Pan, Guohua; Chandran, Kartik; Dye, John M.; Sidhu, Sachdev S.; Lai, Jonathan R., “[Synthetic Antibodies with a Human Framework That Protect Mice from Lethal Sudan Ebolavirus Challenge](http://pubs.acs.org/doi/abs/10.1021/cb5006454).” *ACS Chemical Biology* (2014), DOI: 10.1021/cb5006454, [↑](#footnote-ref-41)
42. Fruit bats are currently considered the host of the Ebola virus and there is concern that the confirmation of Ebola in fruit bats in South Asia extends the potential range of the disease to mainland Asia. [↑](#footnote-ref-42)
43. led by scientists from Washington University School of Medicine in St. Louis in collaboration with researchers from the Icahn School of Medicine at Mount Sinai and the University of Texas Southwestern Medical Center [↑](#footnote-ref-43)
44. Wei Xu, Megan R. Edwards, Dominika M. Borek, Alicia R. Feagins, Anuradha Mittal, Joshua B. Alinger, Kayla N. Berry, Benjamin Yen, Jennifer Hamilton, Tom J. Brett, Rohit V. Pappu, Daisy W. Leung, Christopher F. Basler, Gaya K. Amarasinghe, “Ebola Virus VP24 Targets a Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1”, Cell Host and Microbe [Volume 16, Issue 2](http://www.cell.com/cell-host-microbe/issue?pii=S1931-3128%2814%29X0009-0), p187–200, 13 August 2014

DOI: <http://dx.doi.org/10.1016/j.chom.2014.07.008> [↑](#footnote-ref-44)
45. See **“Marburgvirus Resurgence in Kitaka Mine Bat Population after Extermination Attempts, Uganda”,** Emerging Infectious Diseases**, Vol. 20, No. 10, October 2014** [↑](#footnote-ref-45)
46. One had earlier received a blood transfusion from one of his patients who recovered. [↑](#footnote-ref-46)
47. E P Thi, C E Mire, R Ursic-Bedoya, J B Geisbert, A C H Lee, K N Agans, M Robbins, D J Deer, K A Fenton, I MacLachlan, T W Geisbert, Marburg virus infection in nonhuman primates: Therapeutic treatment by lipid-encapsulated siRNA.*Sci. Transl. Med.* 6, 250ra116 (2014). [↑](#footnote-ref-47)
48. They are both single-stranded negative-sense RNA (ribonucleic acid) viruses. [↑](#footnote-ref-48)
49. The Company had previously developed anti-Ebola drug candidates that demonstrated the validity and potential of the Company’s approach, based on cell culture and animal testing conducted at US Army Medical Research Institute of Infectious Diseases (USAMRIID) in a BSL-4 facility. [↑](#footnote-ref-49)
50. In Brazil, Colombia, Mexico, Honduras and Puerto Rico. [↑](#footnote-ref-50)
51. Japan’s Takeda acquired DENVax in 2013 when in bought Inviragen. [↑](#footnote-ref-51)
52. “Design of a Broadly Neutralizing Antibody Targeting Dengue Virus E Protein Domain III” [V-1819]” [↑](#footnote-ref-52)
53. The research was published in *Epidemiology and Infection* [↑](#footnote-ref-53)
54. The study report was published in the 15 August issue of *The Lancet*. [↑](#footnote-ref-54)
55. The research was published in *Nature Medicine.* [↑](#footnote-ref-55)
56. Crick A, Theron M, Tiffert T, Lew V, Cicuta P et al. "Quantitation of malaria parasite-erythrocyte cell-cell interactions using optical tweezers." Biophysical Journal. 19 August 2014. [↑](#footnote-ref-56)
57. Reported in *Nature Communications* [↑](#footnote-ref-57)
58. Federal state scientific-industrial company Microgen is the largest company in the Russian medical industry [↑](#footnote-ref-58)
59. Proceedings of the National Academy of Sciences, 25 August [↑](#footnote-ref-59)
60. "Intranasal Seasonal Influenza Vaccine and a TLR-3 Agonist, Rintatolimod, Induced Cross-Reactive IgA Antibody Formation Against Avian H5N1 and H7N9 Influenza HA in Humans" (*Vaccine* (2014), [http://dx.doi.org/10.1016/j.vaccine.2014.07.078](http://www.globenewswire.com/newsroom/ctr?d=10098536&l=1&u=http%3A%2F%2Fdx.doi.org%2F10.1016%2Fj.vaccine.2014.07.078)) [↑](#footnote-ref-60)
61. **J.Z. Oh et al., “TLR5-mediated sensing of gut microbiota is necessary for antibody responses to seasonal influenza vaccination,”** Immunity**,11 September. doi:10.1016/j.immuni.2014.08.009, 2014.** [↑](#footnote-ref-61)
62. “Transmission of MERS-Coronavirus in Household Contacts”, *The New England Journal of Medicine*, DOI: 10.1056/NEJMoa1405858. [↑](#footnote-ref-62)
63. The researchers reported in August in the journal *PLoS Pathogens*. [↑](#footnote-ref-63)
64. eg research led by Fang Li, associate professor of Pharmacology at the University of Minnesota Medical School appeared in the Proceedings of the National Academy of Sciences. The paper was titled “Receptor usage and cell entry of bat coronavirus HKU4 provide insight into bat-to-human transmission of MERS coronavirus.” [↑](#footnote-ref-64)
65. They presented their research at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) an infectious disease meeting of the American Society for Microbiology (ASM). [↑](#footnote-ref-65)
66. Ariel Halper-Stromberg et al.,”Broadly Neutralizing Antibodies and Viral Inducers Decrease Rebound from HIV-1 Latent Reservoirs in Humanized Mice”, August 14, 2014.<http://dx.doi.org/10.1016/j.cell.2014.07.043> [↑](#footnote-ref-66)
67. See the 20 August online edition of *Science Translational Medicine* [↑](#footnote-ref-67)
68. and reported in *Infection and Immunity* [↑](#footnote-ref-68)