**Monitoring International Trends**

**Posted August 2019**

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 put financial or other pressures on the Australian sector.

**Summary**

Some recent matters of interest appear on pages 7 to 18. Highlights are listed below:

**Safety and Patient Blood Management (begins page 7)**

## Appropriate transfusion; bleeding risk (p7)

* + Studies have concluded that:
		1. in simultaneous bilateral total knee arthroplasty tranexamic acid could reduce blood loss with no apparent increase in the incidence of complications;
		2. “perioperative TXA (tranexamic acid) administration was associated with reduced postoperative drain output and surgical time”;
		3. the administration of tranexamic acid in the pre-hospital environment was associated with “significantly lower rates of massive transfusion protocol activation when compared to the control group”;
		4. the risk of transfusion reactions was twice as high for women requiring blood to treat postpartum hemorrhage as it was for nonpregnant women;
		5. elective surgery patients whose anaemia was managed in advance had a much lower transfusion risk and a shorter hospital stay than anaemic patients not assessed through patient blood management;
		6. a four-factor prothrombin complex concentrate was “effective as adjuvant treatment with an acceptable safety profile, not only for the emergent reversal of vitamin K antagonists but also for refractory coagulopathy associated with major bleeding”;
		7. “time to hemostasis should be considered as an endpoint in trauma studies and as a potential quality indicator”; and that
		8. “patients with solid malignancies are at risk for multi-transfusion and iron overload even when adhering to restrictive red blood cell transfusion policies”.
	+ Noting that whole blood is regaining popularity for use in massive bleeding, researchers have turned their attention to the haemostatic potential of platelets in cold-stored whole blood.
	+ A South Australian study found that only 56 per cent of patients presenting with upper gastrointestinal bleeding met the criteria for consideration of restrictive transfusion practice as described in a well-accepted European trial.

## Other (p8)

* + An Australian study has examined the detrimental effects of donor adverse events, and the differences in factors associated with return for plasma donors compared with whole blood donors.
	+ Researchers have:
		1. suggested “that blood collection services could safely use shorter donation intervals and more intensive reminders to meet shortages, for donors who maintain adequate haemoglobin concentrations and iron stores”;
		2. developed a quality improvement toolkit for use in obstetric clinics, which led to increased rates of ferritin testing and decreased rates of anaemia; and
		3. genetically engineered an antithrombotic drug which binds only to activated platelets at the site of a thrombus.

#### **Products and Treatments (begins page 9)**

## Treating haemophilia (p9)

* + European data has shown that switching to [extended half-life](https://hemophilianewstoday.com/hemophilia-treatments/extended-half-life-ehl-products/) haemophilia treatments has reduced both the number of infusions and the number of bleeding events compared with standard treatments, especially in haemophilia B.
	+ The FDA has granted orphan drug designation to Sigilon Therapeutics’ SIG-001, currently under evaluation for haemophilia A.
	+ A study has found that, in patients with severe hemophilia A, genetic variations in certain immune-related genes, are linked with an increased risk for developing inhibitors against factor VIII replacement therapies.
	+ Takeda unveiled new data reinforcing the potential benefit for personalized prophylaxis with Adynovate in severe Haemophilia A.

## Treating beta thalassemia and sickle cell disease (p10)

* + A study has suggested a new way to monitor blood cells that doesn’t require microscopic imaging or biochemical markers and that may allow for better management of sickle cell disease.

## Treating other conditions (p10)

* + Researchers have reported that:
		1. acquired thrombotic thrombocytopenic purpura can be effectively treated with adjuvant low-dose rituximab together with plasma exchange and steroids;
		2. in evaluating children with potential Kawasaki Disease, earlier use of echocardiograms was advisable; and that
		3. patients over 65 with hereditary angioedema types 1 or 2 can as safely be treated for an acute attack with Firazyr (icatibant) as younger patients.
	+ Kedrion Biopharma announced the first patient had been enrolled in a Phase III, multi-centre study to assess a 10 per cent intravenous immunoglobulin in adults with Primary Immunodeficiency Disease.

**Regulatory matters (begins page 10)**

* + The US Food and Drug Administration (FDA) accepted for review a marketing application from Rockwell Medical for an intravenous formulation of ferric pyrophosphate citrate, approved in 2015 as a haemodialysate (mixed with bicarbonate) for the maintenance of haemoglobin in dialysis patients.

**Market structure and company news (begins page 11)**

* + Pfizer plans to invest $US 500 million to expand its manufacturing plant in Stanford, North Carolina, which focuses on gene therapy development.
	+ Gene therapy developer uniQure N.V. will report data in September.
	+ CSL full-year profit rose, reflecting strong growth in immunoglobulin and albumin therapies and in its flu-vaccine. The company is establishing new corporate headquarters and laboratories on the edge of the Melbourne CBD.
	+ In 2018 Sanofi completed its $US 11.6 billion buyout of hemophilia specialist Bioverativ. It has now had to revise its sales projections.

**Specific country events (begins p 12)**

* + Mitsubishi Tanabe Pharma and Jichi Medical University launched a program in Japan focussed on developing gene therapy to treat haemophilia B.
	+ The American Society of Health-System Pharmacists outlined a shortage across a number of IgG drugs.
	+ In the US, a bipartisan group of congressional leaders asked FDA Acting Commissioner Norman Sharpless at the end of July to give an assurance that the national heparin supply was not threatened by the African swine fever which has been sweeping pig herds in China, the primary source of crude heparin.
	+ Research on dangerous pathogens was suspended at the US Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick in Maryland after the Centers for Disease Control and Prevention (CDC) found biosafety lapses.
	+ The second US National Conference for Women with Hemophilia will be held in November.
	+ In the UK, the National Health Service (NHS) has warned that a no-deal Brexit would make a delay in flu vaccine supply this year “likely”.
	+ In England, patients with severe congenital hemophilia A without factor VIII inhibitors will receive Roche’s Hemlibra (emicizumab) on the NHS.
	+ Swiss health authorities introduced a waiting period for potential donors who have recently returned from a country where West Nile virus has been reported.
	+ Canadian Blood Services has announced three new proof-of-concept plasma collection sites in Sudbury (Ontario), Lethbridge (Alberta) and Kelowna (British Columbia).
	+ Elk meat from herds with chronic wasting disease has been released into Canada's food supply over the last five years.
	+ The inaugural meeting of an International Commission on the Clinical Use of Human Germline Genome Editing was held in Washington, DC.

**Research not included elsewhere (begins page 13)**

* + Researchers have:
		1. suggested that abnormally low platelet counts in developing and newborn babies could result in weakened blood vessels in the brain and lead to stroke and cerebral palsy;
		2. examined “the long-term association of haemoglobin levels and anaemia with risk of dementia”;
		3. shown a consistent underestimation of the incidence of central line-associated bloodstream infections; and
		4. reported that a non-invasive prenatal test to diagnose a risk of sickle cell disease in a baby is possible.

**Infectious diseases (begins page 14)**

## Mosquito-borne diseases (p14)

* + Studies of the Zika virus have:
		1. identified an asymptomatic infection in a blood donor in Puerto Rico occurring before those previously recognized by blood donation screening;
		2. found that in 200 toddlers exposed to the virus in the womb nearly a third suffered developmental delays and other problems;
		3. linked the microcephaly risk in newborns to features of maternal antibodies; and
		4. focussed on how to target vaccination to eliminate the transmission of the virus by mosquitoes and by sex.
	+ The US Food and Drug Administration (FDA) has given Fast Track Status to two Zika virus vaccines.
	+ The *Aedes aegypti* mosquito has been found in Sacramento, California.
	+ In malaria research:
		1. scientists have developed a new drug which could be used in treatment and prevention; and
		2. vaccination has been shown to increase levels of antibodies that recognize *P. falciparum*' antigens that are not included in the vaccine.

## Influenza (p15)

* + Seqirus offered data on its adjuvant and cell-based vaccines for seasonal and pandemic influenza at the Options for the Control of Influenza Conference.
	+ Vaxart, a company developing oral recombinant vaccines administered by tablet, has signed a research agreement with Janssen Vaccines & Prevention to evaluate Vaxart’s oral vaccine platform for the Janssen universal influenza vaccine program.

## Ebola virus disease (p17)

* + In Uganda, a two-year trial has begun of vaccination involving a two -dose regimen of Ad26.ZEBOV and MVA-BN-Filo.
	+ By the end of August, the number of vaccinations in the Democratic Republic of Congo with Merck’s VSV-EBOV vaccine had reached 206, 774. Case numbers totalled 3,004 with 2,006 deaths.
	+ The US National Institute of Allergy and Infectious Diseases announced that a comparative trial of four Ebola drugs had ended early after preliminary data indicated higher survival rates with two of the drugs.
	+ GlaxoSmithKline is transferring its work on three vaccine candidates to the Sabin Vaccine Institute in Washington, DC.

## MERS-CoV (p18)

* + World Health Organisation (WHO) officials are still deeply concerned about transmission in hospitals. They said: "Much more emphasis on improving standard infection prevention and control practices in all health care facilities is required."
	+ GeneOne Life Science, after conducting a trial in collaboration with the Walter Reed Army Institute for Research, said the GLS-5300 DNA vaccine targeted “MERS-CoV’s outer spike glycoprotein was well-tolerated and generated strong antibody and T-cell responses in healthy adult volunteers.”

## Other diseases (p18)

* + WHO said 365,000 cases of measles were reported globally between January and July this year, the highest number since 2006. The number of suspected cases was 6.7 million. In the US there had in 2019 been 1,172 measles cases up to 1 August.
	+ A two-dose course of recombinant zoster vaccine decreased the incidence of herpes zoster in adults who had undergone recent autologous hematopoietic stem cell transplantation during a median follow-up of 21 months.
	+ A number of domestic dogs in Sydney have contracted leptospirosis.
	+ In the US, the incidence of West Nile virus neuroinvasive disease was approximately 25 per cent higher in 2018 than the median annual incidence during the previous decade.

**Detailed Report**

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# Safety and patient blood management

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

## Appropriate Transfusion; Bleeding Risk

* + A study[[1]](#footnote-1) has concluded that in simultaneous bilateral total knee arthroplasty tranexamic acid could reduce blood loss with no apparent increase in the incidence of complications.
	+ A Swedish retrospective study[[2]](#footnote-2) found that the risk of transfusion reactions was twice as high for women requiring blood to treat postpartum hemorrhage compared with nonpregnant women who also required a blood transfusion during the same time period.
	+ A research study[[3]](#footnote-3) found that “perioperative TXA (tranexamic acid) administration was associated with reduced postoperative drain output and surgical time”. Researchers recommended further higher-level studies “to investigate the safety and utility of TXA’s routine use in 1 and 2-level posterior lumbar fusion operations performed for degenerative indications”.
	+ Another study[[4]](#footnote-4) has found that elective surgery patients whose anaemia was assessed and managed in advance had a much lower transfusion risk and a shorter hospital stay than anaemic patients not assessed through patient blood management.
	+ Researchers[[5]](#footnote-5) pronounced a four-factor prothrombin complex concentrate “effective as adjuvant treatment with an acceptable safety profile, not only for the emergent reversal of VKAs (vitamin K antagonists) but also for refractory coagulopathy associated with major bleeding”.
	+ Researchers[[6]](#footnote-6) found that earlier time to haemostasis was independently associated with decreased incidence of 30-day mortality, acute kidney injury, acute respiratory distress syndrome, multiple organ failure and sepsis in bleeding trauma patients. They recommended that “time to hemostasis should be considered as an endpoint in trauma studies and as a potential quality indicator”.
	+ A study[[7]](#footnote-7) has found that the administration of tranexamic acid in the pre-hospital environment was associated with “significantly lower rates of massive transfusion protocol activation when compared to the control group” and “significantly lower rates of massive blood transfusion”. No statistically significant relationship could be reported with respect to mortality or thromboembolic events.
	+ Researchers[[8]](#footnote-8) found that “patients with solid malignancies are at risk for multi-transfusion and iron overload even when adhering to restrictive RBC (red blood cell) transfusion policies”. They commented that “with improved long-term cancer survivorship, increased awareness of iatrogenic side effects of supportive therapy and development of evidence-based guidelines are essential”.
	+ Researchers, noting that whole blood is regaining popularity for use in massive bleeding, have turned their attention to the haemostatic potential of platelets in cold-stored whole blood[[9]](#footnote-9). They concluded that “*in vitro* tests of platelet functionality in whole blood uniformly demonstrate that within commonly used storage and time constraints, platelets are highly functional……..but we do not know how long platelet haemostatic functionality is preserved in the clinical setting.….we still need to find out whether whole blood improves outcome in a hospital setting compared to a well‐balanced component transfusion practice”. They say this evidence will emerge as emphasis increases on cold-stored whole blood in both the pre-hospital and in-hospital protocols for massive transfusion.
	+ A South Australian study[[10]](#footnote-10) found that only 56 per cent of patients presenting with upper gastrointestinal bleeding met the criteria for consideration of restrictive transfusion practice as described in a well-accepted European trial[[11]](#footnote-11).

## Other

* + An Australian study[[12]](#footnote-12) has examined the detrimental effects of donor adverse events, particularly vasovagal reactions, and the differences in factors associated with return for plasma donors compared with whole blood donors. The authors said more research is required “to understand the mechanisms underlying the decision to return following a donor adverse event”.
	+ A study[[13]](#footnote-13) has suggested “that blood collection services could safely use shorter donation intervals and more intensive reminders to meet shortages, for donors who maintain adequate haemoglobin concentrations and iron stores”.
	+ Researchers at St. Michael's Hospital in Toronto developed a quality improvement toolkit, called IRON MOM. Its implementation in the hospital’s obstetric clinics led to increased rates of ferritin testing and decreased rates of anaemia[[14]](#footnote-14).
	+ Researchers have genetically engineered an antithrombotic drug which binds only to activated platelets at the site of a thrombus. Speaking at the ISTH Congress in Melbourne, the Baker Institute’s Dr Xiaowei Wang said the specific binding affinity of Targ-TAP to activated platelets had been shown in both mouse and human blood[[15]](#footnote-15).

# Products and treatments

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

## Treating haemophilia

* + European data has shown[[16]](#footnote-16) that switching to [extended half-life](https://hemophilianewstoday.com/hemophilia-treatments/extended-half-life-ehl-products/) haemophilia treatments has reduced both the number of infusions and the number of bleeding events compared with standard treatments, especially in haemophilia B.
	+ The FDA has granted orphan drug designation[[17]](#footnote-17) to Sigilon Therapeutics’ SIG-001, currently under evaluation for haemophilia A. The treatment uses Sigilon’s Shielded Living Therapeutics platform to implant cells that are engineered to produce stable blood plasma levels of factor VIII. Clinical trials are expected begin in the first half of next year.
	+ A study[[18]](#footnote-18) has found that, in patients with severe hemophilia A, genetic variations in certain immune-related genes, the HLA and IL-10 genes, are linked with an increased risk for developing inhibitors against factor VIII replacement therapies.
	+ At the ISTH Congress in Melbourne, Takeda unveiled new data reinforcing the potential benefit for personalized prophylaxis with Adynovate in severe Haemophilia A[[19]](#footnote-19). Pharmacokinetic -driven dosing may be used to achieve FVIII target trough levels of 8–12 per cent. Choosing a patient-appropriate target FVIII level, plus adjusting a dosing regimen to that patient’s pharmacokinetic characteristics, can enhance the overall pharmacokinetic profile and may improve outcomes, with no adverse event profile change –emphasising the potential benefit of personalized prophylaxis with Adynovate.

## Treating beta thalassemia and sickle cell disease

* + A study[[20]](#footnote-20) has suggested a new way to monitor blood cells that doesn’t require microscopic imaging or biochemical markers and that may allow for better .management of sickle cell disease.

## Treating other conditions

* + Researchers have reported that acquired thrombotic thrombocytopenic purpura can be effectively treated with adjuvant low-dose rituximab together with plasma exchange and steroids[[21]](#footnote-21).
	+ A US study[[22]](#footnote-22) found that in evaluating children with potential Kawasaki Disease, earlier use of echocardiograms was advisable. The authors said their data suggested “superiority in the use of infliximab or steroids in second-line therapy over intravenous immunoglobulin in terms of reducing additional therapy needs”. They noted that prospective, controlled studies would be required to verify this finding.
	+ A study[[23]](#footnote-23) has found that patients over 65 with [hereditary angioedema](https://ghr.nlm.nih.gov/condition/hereditary-angioedema) types 1 or 2 can as safely be treated for an acute attack with Firazyr (icatibant) as younger patients, even though they may metabolize medicines differently and are being treated for multiple disorders.
	+ Kedrion Biopharma announced the first patient had been enrolled in CARES10, a Phase III, multi-centre study to assess a 10 per cent intravenous immunoglobulin in adults with Primary Immunodeficiency Disease.

# Regulatory

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

* + The US Food and Drug Administration (FDA) has accepted for review a marketing application from Rockwell Medical for an intravenous formulation of TRIFERIC (ferric pyrophosphate citrate), first approved in the US in January 2015 as a haemodialysate (mixed with bicarbonate) for the maintenance of haemoglobin in dialysis patients. The IV formulation would allow dialysis centres to administer TRIFERIC to patients regardless of how bicarbonate is delivered. The FDA’s action date is 28 March, 2020.

# 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.*

* + Pfizer plans to invest $US 500 million to expand its manufacturing plant in Stanford, North Carolina, which focuses on gene therapy development.
	+ Gene therapy developer [uniQure N.V.](https://www.globenewswire.com/Tracker?data=bT2R-fSJKVs-lQmjyDHGz-_W-hHaxi9lZCeA4YxvI9jgLm6uj2-H1GwOUGwmOI5lg8BT6wtGf72Ma59iSfjvDg==) announced its participation in several conferences in September[[24]](#footnote-24).
	+ CSL is establishing new corporate headquarters and laboratories within a research and education project being developed on the edge of the Melbourne CBD. The move will take around 800 employees to a 16-storey building at the top of Elizabeth Street, close to the existing Parkville biomedical precinct which includes the University of Melbourne, several hospitals and research facilities such as the Doherty Institute for Infectious Disease. CSL will maintain its presence at the Bio21 Institute nearby, home to 130 researchers, while its flu vaccine and anti-venom manufacturing will remain at the Poplar Road site.
	+ CSL full-year profit rose, reflecting strong growth in immunoglobulin and albumin therapies and in its flu-vaccine business. CSL reported net profit of $ US 1.92 billion for the year through to 30 June, an increase of 11 per cent from the year before. The company said the immunoglobulin portfolio is performing well, with Privigen sales up 23 per cent and Hizentra up 22 per cent in constant currency. Seasonal flu-vaccine sales in its Seqirus unit rose 19 per cent. CSL Chief Executive Paul Perreault said the company planned to open about 40 new plasma-collection centres in the current fiscal year.
	+ In 2018 Sanofi closed its $US 11.6 billion buyout of hemophilia specialist Bioverativ. But the company has had to revise its sales projections for one of Bioverativ’s key products. Sanofi recorded a $US 2 billion write-down “mainly related to Eloctate,” a long-acting treatment that starred in the takeover deal. It has found itself competing against Roche’s Hemlibra.

# Specific country events

* + [Mitsubishi Tanabe Pharma](https://www.mt-pharma.co.jp/e/) announced it is working with researchers from [Jichi Medical University](https://www.jichi.ac.jp/english/) to launch a program in Japan focussed on developing a gene therapy product to treat patients with haemophilia B. The project was selected by the Japan Agency for Medical Research and Development to receive financial support thought the agency’s [Cyclic Innovation for Clinical Empowerment](https://www.amed.go.jp/en/program/list/07/01/001.html) program.
	+ A July report from the American Society of Health-System Pharmacists outlined a shortage across a number of IgG drugs.
	+ In the US, a bipartisan group of congressional leaders asked FDA Acting Commissioner Norman Sharpless at the end of July to give an assurance that the national heparin supply was not threatened by the African swine fever which has been sweeping pig herds in China, the primary source of crude heparin.
	+ Research on dangerous pathogens was suspended at the US Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick in Maryland after the Centers for Disease Control and Prevention (CDC) found biosafety lapses there**[[25]](#footnote-25)**.
	+ In the US, the second [National Conference for Women with Hemophilia](https://hfmich.org/national-conference-for-women-with-hemophilia/) will be held 1-3 November in Detroit.
	+ In the UK, the NHS has warned that a no-deal Brexit would make a delay in flu vaccine supply this year “likely”,
	+ In England, patients with severe congenital hemophilia A without factor VIII inhibitors will receive Roche’s Hemlibra (emicizumab) on the National Health Service (NHS).
	+ Swiss health authorities have introduced a 30-day waiting period for potential donors who have recently returned from a country where West Nile virus has been reported. The virus spreads via migratory birds and local mosquitoes. The incubation period is ten days. Beat Frey, of [Zurich’s Red Cross blood centre](https://www.blutspendezurich.ch/), told [Swiss public television, SRF](https://www.srf.ch/news/schweiz/west-nil-virus-blutspenden-wird-fuer-reisende-aus-suedeuropa-eingeschraenkt): “The blood donor can be symptom-free, but still be carrying the virus and pass it on through the blood donation. This can cause illness and serious complications for the recipient”. There have been no reports of West Nile virus in Switzerland so far this year, but if five cases are reported, the [Federal Office of Public Health](https://www.bag.admin.ch/bag/en/home.html) will require that every blood donor be tested. West Nile virus has been recorded in neighbouring France and Italy as well as south eastern European countries.
	+ Canadian Blood Services has announced three new proof-of-concept plasma collection sites in Sudbury (Ontario), Lethbridge (Alberta) and Kelowna (British Columbia). They will be dedicated to the collection of source plasma. These three provinces in 2018 banned paying for plasma donations. Results of an opinion poll by the Consumer Choice Centre suggest that 63 per cent of Canadians surveyed endorsed payment for plasma as "morally appropriate" with support strongest, at 75 per cent, among respondents between the ages of 18-34.
	+ Elk meat from 21 herds where chronic wasting disease was discovered has been released into Canada's food supply over the last five years. Both the Canadian Food Inspection Agency (CFIA) and Health Canada say that animals known to be infected with the disease are prohibited from entering the food supply. However, there is no national requirement to have animals tested for the disease. A national non-profit advocacy group BloodWatch is calling for the government to take stronger action against the spread of the disease.

# Research not included elsewhere

*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.*

* + The inaugural meeting of an International Commission on the Clinical Use of Human Germline Genome Editing was held on 13 August at the National Academy of Sciences in Washington, DC, to discuss establishing a framework to guide applications of the controversial technology[[26]](#footnote-26). Attendees came from the US, the UK, China, South Africa, Canada, Sweden, Japan, Malaysia, and India.
	+ A study, funded by the [Cerebral Palsy Alliance Research Foundation](https://cerebralpalsy.org.au/our-research/), suggested that abnormally low platelet counts in developing and newborn babies could result in weakened blood vessels in the brain and lead to stroke and cerebral palsy. Researchers were from the [Walter and Eliza Hall Institute (WEHI)](https://www.wehi.edu.au/), Melbourne[[27]](#footnote-27).
	+ A study[[28]](#footnote-28) has examined “the long-term association of haemoglobin levels and anaemia with risk of dementia”, exploring “underlying substrates on brain MRI in the general population”. It found that both high and low levels of haemoglobin are associated with a greater long-term risk for dementia, including Alzheimer’s disease. Authors suggested this may “relate to differences in white matter integrity and cerebral perfusion”.
	+ A systematic review, conducted by the Alliance for Vascular Access Teaching and Research and Griffith University, showed a consistent underestimation of the incidence of central line-associated bloodstream infections, or CLABSIs, within publicly reported rates[[29]](#footnote-29).
	+ UK researchers reported[[30]](#footnote-30) that a non-invasive prenatal test to diagnose a risk of sickle cell disease in a baby is possible and may soon be available in clinics, if further testing confirms its efficacy.
	+ Researchers have found[[31]](#footnote-31) that patients with chronic anemia demonstrated a decrease in brain white matter volume proportional to anemia severity regardless of patients’ sickle cell disease status. The severity of anemia, not disease state, predicts white matter volume.

# 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, Zika virus and the tick-borne babesiosis and Lyme disease).*

## Mosquito-borne diseases

* + A study[[32]](#footnote-32) has identified an asymptomatic Zika infection in a blood donor in Puerto Rico occurring before those previously recognized by blood donation screening. The authors concluded that while nucleic acid testing and pathogen reduction “continue to be used as acceptable strategies to prevent transfusion‐transmitted arboviral infections worldwide, repeated arboviral outbreaks warrant consideration of pathogen reduction as a more proactive approach”.
	+ A study[[33]](#footnote-33) of 200 toddlers exposed to the Zika virus in the womb found that nearly a third suffered developmental delays and other problems — even if they were born without the abnormally small heads and underdeveloped brains often associated with the virus. A very small number of children born with congenital microcephaly had their symptoms improve while a very small number of the children born without symptoms of microcephaly went on to develop it.
	+ An international team of researchers [[34]](#footnote-34)has linked the risk of microcephaly in newborns to features of maternal antibodies, offering a possible explanation of why a Zika infection results in birth defects in some babies but not others.
	+ The US Food and Drug Administration (FDA) has given Fast Track Status to two Zika virus vaccines, Moderna mRNA-1893 (currently in Phase I studies) and TAK426.
	+ A new study[[35]](#footnote-35) has focussed on ‘how best to eliminate the mosquito and sexual transmission of the Zika virus with a preventive vaccine. Researchers said that “while vaccinating everyone naturally averted the most possible Zika cases, targeting women of childbearing age, children and young adults with a preventive vaccine was found to be the most cost-effective.”
	+ The *Aedes aegypti* mosquito which can carry and transmit Zika, chikungunya and dengue, has been found in Sacramento, California.
	+ An international team of scientists, led from the University of Glasgow, has developed a new drug which could be used to treat people suffering with malaria and help prevent it from being spread. The drug can kill the parasite at all three stages of its life cycle - when it is in the liver and red blood cells, as well as preventing sexual development of the parasite. Lead researcher Andrew Tobin, professor of molecular pharmacology at the University of Glasgow, said: "We are tremendously excited about these new findings and hope they pave the way for the first step in the eradication of malaria. Our work has shown that by killing the parasites at the various stages of parasite development, we have not only discovered a potential cure for malaria but also a way of stopping the spread of malaria from person to mosquito, which can then infect other people."
	+ A study[[36]](#footnote-36) has shown for the first time that vaccination increases levels of antibodies that recognize *P. falciparum*' antigens that are not included in the vaccine.

## Influenza

* + The US National Institute of Allergy and Infectious Diseases (NIAID) is funding a Phase I clinical trial evaluating two seasonal influenza vaccines, with or without novel adjuvants, for their safety and ability to generate an immune response[[37]](#footnote-37).
	+ Seqirus featured data in three presentations and 24 posters on the company's adjuvant and cell-based vaccines for seasonal[[38]](#footnote-38) and pandemic[[39]](#footnote-39) influenza at the Options for the Control of Influenza (OPTIONS X) Conference in Singapore.
	+ The US Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP) emphasised two changes in the 2019-2020 recommendations for flu vaccine composition and regulatory actions[[40]](#footnote-40). The trivalent influenza vaccines administered will contain hemagglutinin (HA) derived from an A/Brisbane/02/2018 (H1N1) pdm09–like virus, an A/Kansas/14/2017 (H3N2)–like virus, and a B/Colorado/06/2017–like virus (Victoria lineage). The quadrivalent influenza vaccines will contain HA derived from these three viruses and from an additional influenza B vaccine virus, a B/Phuket/3073/2013–like virus (Yamagata lineage).  Afluria Quadrivalent is licensed by the Food and Drug Administration (FDA) for individuals aged 6 months or older[[41]](#footnote-41). The FDA has approved a change in dose volume for Fluzone Quadrivalent[[42]](#footnote-42).
	+ Vaxart, a company developing oral recombinant vaccines administered by tablet, has entered into a research collaboration agreement with Janssen Vaccines & Prevention to evaluate Vaxart’s proprietary oral vaccine platform for the Janssen universal influenza vaccine program. Vaxart will produce an oral vaccine containing proprietary antigens from Janssen, and then test the result in a pre-clinical challenge model. Next, Janssen will have an exclusive option to negotiate a sole worldwide license to the Vaxart technology encompassing the Janssen antigens.

## Ebola virus disease

* + In Uganda, a two-year trial of an Ebola vaccine has begun, involving 800 people including core health workers. The trial is backed by the London School of Hygiene and Tropical Medicine. The vaccination involved is a two -dose regimen of Ad26.ZEBOV and MVA-BN-Filo. Manufacturer is Belgium-based Janssen Pharmaceutica which is owned by Johnson & Johnson[[43]](#footnote-43).
	+ By the end of August, the number of vaccinations in the Democratic Republic of Congo with Merck’s VSV-EBOV vaccine had reached 206, 774. Case numbers had reached 3,004 with 2,006 deaths.
	+ The World Health Organisation (WHO) announced mid- August that Burundi had started vaccinating its health workers against Ebola, beginning with those near the border with the Democratic Republic of Congo. The vaccine being used is Merck's rVSV-ZEBOV. The campaign is receiving financial support from the Vaccines Alliance[[44]](#footnote-44) GAVI.
	+ The US National Institute of Allergy and Infectious Diseases (NIAID) announced that a comparative trial of four Ebola drugs had ended early after preliminary data indicated higher survival rates with two of the drugs. The open-label randomized trial[[45]](#footnote-45) has been testing the safety and efficacy of ZMapp, remdesivir, mAb114, and Regeneron EB-3 (REGN-EB3) for treating Ebola in two Congo provinces since November 2018. The control was the monoclonal antibody drug ZMapp, previously shown to result in better outcomes than supportive care alone. The nucleotide analog antiviral remdesivir and monoclonal antibodies mAb114 and REGN-EB3 had not previously been used to treat Ebola. Interim analysis of data from 499 participants showed overall mortality of 29 per cent with REGN-EB3, 34 per cent with mAb114, 49 per cent with ZMapp and 53 per cent with remdesivir[[46]](#footnote-46). Final data analysis from the trial is expected by early October.
	+ GlaxoSmithKline is transferring its work on three vaccine candidates (two against Ebola and one against the Marburg virus) to the Sabin Vaccine Institute in Washington, DC. There is no financial element involved. Sabin will continue to develop the vaccines, one of which - a potential Ebola shot known as ChAd3 - has been through mid-stage, Phase II, trials in Africa[[47]](#footnote-47).
	+ The US Department of Health and Human Services (HHS) [announced](https://www.hhs.gov/about/news/2019/08/21/hhs-funds-an-additional-year-of-ebola-vaccine-manufacturing.html) financial support to continue the manufacturing of the investigational Ebola vaccine from Merck for another year. The Biomedical Advanced Research and Development Authority (BARDA), a component of the HHS Office of the Assistant Secretary for Preparedness and Response, will contribute $US 23 million to Merck for production of the vaccine over the next 12 months.
	+ A research study[[48]](#footnote-48) has reported on the “unprecedented challenge” of hospitals around the world in preparing to “identify, isolate and treat” patients with Ebola and ensure the safety of their staff in the event of a case.

## MERS-CoV

* + In its annual global [risk assessment](https://apps.who.int/iris/bitstream/handle/10665/326126/WHO-MERS-RA-19.1-eng.pdf?ua=1) of MERS-CoV, the World Health Organisation (WHO) said officials are still deeply concerned about transmission in hospitals. Since its last update in June 2018, 97 secondary cases were reported to the WHO, 52 of which were linked to transmission in hospitals, including 23 infections in healthcare workers. It said: "Much more emphasis on improving standard IPC [infection prevention and control] practices in all health care facilities is required[[49]](#footnote-49)."
	+ **Christine C. Roberts,** director of clinical laboratory development at GeneOne Life Science, said[[50]](#footnote-50) the company has conducted a trial in collaboration with the Walter Reed Army Institute for Research, and “it showed that the GLS-5300 DNA vaccine targeting MERS-CoV’s outer spike glycoprotein was well-tolerated and generated strong antibody and T-cell responses in healthy adult volunteers.” A scientific journal report[[51]](#footnote-51) which detailed this first human trial of the GLS-5300 MERS-CoV DNA vaccine candidate said the vaccine was well-tolerated and induced a strong immune response with no serious adverse events.

## Other diseases

* + As at 1 August there had been 1172 measles cases in the US so far this year. Researchers have reported that vaccination levels in parts of Texas are low enough to permit measles outbreaks in hundreds of people[[52]](#footnote-52).
	+ WHO said 365,000 cases of measles were reported globally between January and July this year, the highest number since 2006. The number of suspected cases was 6.7 million.
	+ A study[[53]](#footnote-53) has shown that a two-dose course of recombinant zoster vaccine[[54]](#footnote-54) decreased the incidence of herpes zoster in adults who had undergone recent autologous hematopoietic stem cell transplantation (HSCT) during a median follow-up of 21 months.
	+ A number of domestic dogs in inner Sydney and its inner west have contracted leptospirosis. Construction activity is thought to have increased exposure to rats. "The recent outbreak of leptospirosis poses not only a risk to unvaccinated dogs but also to their owners," said Dr Christine Griebsch, Senior Lecturer in Small Animal Medicine, from the University of Sydney’s School of Veterinary Science.
	+ In the US, the incidence of West Nile virus neuroinvasive disease was approximately 25 per cent higher in 2018 than the median annual incidence during the previous decade.
1. #  G Cao et al., The efficacy and safety of tranexamic acid for reducing blood loss following simultaneous bilateral total knee arthroplasty: a multicenter retrospective study [*BMC Musculoskelet Disord.*](https://www.ncbi.nlm.nih.gov/pubmed/31299945) 2019 Jul 12;20(1):325. doi: 10.1186/s12891-019-2692-z. <https://www.ncbi.nlm.nih.gov/pubmed/31299945>

 [↑](#footnote-ref-1)
2. Lars Thurn et al., “Incidence and risk factors of transfusion reactions in postpartum blood transfusions”, [Blood Advances](http://www.bloodadvances.org/content/3/15/2298), 2019 3:2298-2306; doi: <https://doi.org/10.1182/bloodadvances.2019000074> [↑](#footnote-ref-2)
3. Larson, Evan et al., “Does prophylactic administration of TXA reduce mean operative time and postoperative blood loss in posterior approach lumbar spinal fusion surgery performed for degenerative spinal disease?” 31 July 2019 Clinical Spine Surgery: [August 2019 - Volume 32 - Issue 7 - p E353–E358](https://journals.lww.com/jspinaldisorders/pages/currenttoc.aspx) doi: 10.1097/BSD.0000000000000770 [↑](#footnote-ref-3)
4. J Faulds, et al., “Transfusion requirement and length of stay of anaemic surgical patients associated with a patient blood management service: a single‐Centre retrospective study”, *Transfusion Medicine,*

July 2019 DOI: [10.1111/tme.12617](http://dx.doi.org/10.1111/tme.12617) [↑](#footnote-ref-4)
5. Marcos-Jubilar M et al., “Safety and effectiveness of a prothrombin complex concentrate in approved and off‐label indications”, [*Transfus Med.*](https://www.ncbi.nlm.nih.gov/pubmed/31347218) 2019 Aug;29(4):268-274. Published online 25 July 2019. PMID: 31347218 DOI: [10.1111/tme.12621](https://doi.org/10.1111/tme.12621) [↑](#footnote-ref-5)
6. #  Chang R et al., “Earlier time to hemostasis is associated with decreased mortality and rate of complications: Results from the Pragmatic Randomized Optimal Platelet and Plasma Ratio trial”, *The Journal of Trauma and Acute Care Surgery*; 87(2). 342-3491 August 2019. PMID: [31349348 [PubMed]](https://www.ncbi.nlm.nih.gov/pubmed/%2031349348).

 [↑](#footnote-ref-6)
7. Ayman El-Menyar et al*., “*Prehospital Administration of Tranexamic Acid in Trauma Patients: A 1:1 Matched Comparative Study from a Level 1 Trauma Center”, [The American Journal of Emergency Medicine](https://www.sciencedirect.com/science/journal/07356757), <https://doi.org/10.1016/j.ajem.2019.04.051> [↑](#footnote-ref-7)
8. #  FJ Sherida Woel-A-Jin et al., “Lifetime Transfusion Burden and Transfusion‐Related Iron Overload in Adult Survivors of Solid Malignancies”, *The Oncologist,* online 27 August 2019. doi: 10.1634/theoncologist.2019-0222 <http://theoncologist.alphamedpress.org/content/early/2019/08/27/theoncologist.2019-0222.short>

 [↑](#footnote-ref-8)
9. Einar K. Kristoffersen et al., “Platelet functionality in cold‐stored whole blood”, *ISBT Science Series,* first published 23 July 2019, <https://doi.org/10.1111/voxs.12501> [↑](#footnote-ref-9)
10. Zaki Hamarneh et al., “Transfusion Strategies in Upper Gastrointestinal Bleeding Management ‐ A Review of South Australian Hospital Practice” published 23 July 2019, *Internal Medicine Journal*, <https://doi.org/10.1111/imj.14440> [↑](#footnote-ref-10)
11. Càndid Villanueva et al., “Transfusion Strategies for Acute Upper Gastrointestinal Bleeding”, 3 January 2013, N Engl J Med 2013; 368:11-21 <https://www.nejm.org/doi/full/10.1056/NEJMoa1211801> [↑](#footnote-ref-11)
12. Amanda Thijsen et al., Trends in return behavior after an adverse event in Australian whole blood and plasma donors, Transfusion, 12 August 2019. <https://doi.org/10.1111/trf.15475> [↑](#footnote-ref-12)
13. Stephen Kaptoge et al., “Longer-term efficiency and safety of increasing the frequency of whole blood donation (INTERVAL): extension study of a randomised trial of 20 757 blood donors”, The Lancet, 2 August, 2019 DOI: [https://doi.org/10.1016/S2352-3026(19)30106-1](https://doi.org/10.1016/S2352-3026%2819%2930106-1) [↑](#footnote-ref-13)
14. Jameel Abdulrehman et al., “Development and implementation of a quality improvement toolkit, iron deficiency in pregnancy with maternal iron optimization (IRON MOM): A before-and-after study”, *PLOS* *Medicine,* 20 August 2019. <https://doi.org/10.1371/journal.pmed.1002867> [↑](#footnote-ref-14)
15. Donny Hanjaya-Putra et al., “Platelet-targeted dual pathway antithrombotic inhibits thrombosis with preserved hemostasis”, 9 August 2019, *Journal of Clinical Investigation,*

<https://doi.org/10.1172/jci.insight.99329>. [↑](#footnote-ref-15)
16. Flora Peyvandi et al., “[Real‐life experience in switching to new extended half‐life products at European haemophilia centres](https://onlinelibrary.wiley.com/doi/abs/10.1111/hae.13834),” 16 August 2019, *Haemophilia* <https://doi.org/10.1111/hae.13834> [↑](#footnote-ref-16)
17. Orphan drug designation can be awarded to emerging drugs and biologics that are intended for the safe and effective treatment, diagnosis or prevention of diseases or disorders that affect fewer than 200,000 people in the US. Manufacturers can qualify for tax credits for clinical trials and —following regulatory approval — 7 years of market exclusivity. [↑](#footnote-ref-17)
18. Delphine Bachelet, , “[Risk stratification integrating genetic data for factor VIII inhibitor development in patients with severe hemophilia A](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0218258),” [PLOS One](file:///C%3A%5CUsers%5C77462457%5CAppData%5CLocal%5CMicrosoft%5CWindows%5CTemporary%20Internet%20Files%5CContent.Outlook%5CHKQHKJNO%5CPLOS%20One). <https://doi.org/10.1371/journal.pone.0218258> [↑](#footnote-ref-18)
19. Klamroth R, Windyga J, Radulescu V, et al., *PK-guided rurioctocog alfa pegol prophylaxis in patients with severe hemophilia* *A targeting two FVIII trough levels: results from the phase 3 PROPEL Study*. Presented at ISTH 2019 (International Society on Thrombosis and Haemostasis (ISTH) Biennial Congress. July 6-10, 2019. Abstract #A-1052-0038-01311 [↑](#footnote-ref-19)
20. Jia Liu et al, “[Electrical Impedance Characterization of Erythrocyte Response to Cyclic Hypoxia in Sickle Cell Disease](https://pubs.acs.org/doi/10.1021/acssensors.9b00263),” [*ACS Sensors*](https://pubs.acs.org/journal/ascefj). 2019, 4, 7, 1783-1790 <https://doi.org/10.1021/acssensors.9b00263> [↑](#footnote-ref-20)
21. Results of a prospective, single-arm Phase II study were published online 22 July 2019 in [Zwicker JI, et al *Blood*. 2019;doi:10.1182/blood.2019000795.](http://www.bloodjournal.org/content/early/2019/07/22/blood.2019000795?sso-checked=true) [↑](#footnote-ref-21)
22. Dominguez, Samuel R et al., “Diagnostic and treatment trends in children with Kawasaki disease in the United States, 2006–2015”, *The Pediatric Infectious* *Disease Journal*: [October 2019 - Volume 38 - Issue 10 - p 1010–1014](https://journals.lww.com/pidj/pages/currenttoc.aspx) doi: 0.1097/INF.0000000000002422 [↑](#footnote-ref-22)
23. Anette Bygum et al., “[Elderly versus younger patients with hereditary angioedema type I/II: patient characteristics and safety analysis from the Icatibant Outcome Survey](https://ctajournal.biomedcentral.com/articles/10.1186/s13601-019-0272-9),” 19 July 2019 in *Clinical and Translational Allergy.* <https://ctajournal.biomedcentral.com/articles/10.1186/s13601-019-0272-9> [↑](#footnote-ref-23)
24. **Citi 14th Annual Biotech Conference, September 4 – 5, Boston.** [Matt Kapusta](http://uniqure.com/about/management-team-matt-kapusta.php), chief executive officer at uniQure, will participate in the panel discussion “Peering Into the Gene Therapy Crystal Ball - What Does the Future Look Like?”  **Wells Fargo 2019 Healthcare Conference, September 4 – 5, Boston.**Matt Kapusta will present a corporate update. **Morgan Stanley 17th Annual Global Healthcare Conference, September 9 – 11, New York City.** Matt Kapusta will host investor meetings and participate in a fireside chat.  **National Hemophilia Foundation (NHF) 15thWorkshop on Novel Technologies and Gene Transfer for Hemophilia, September 13 – 14, Washington, DC.** Eileen Sawyer, vice president of medical affairs, will present “Recent Progress in the Development Program of AMT-061 for Persons with Severe or Moderately Severe Hemophilia B.” Sander van Deventer, executive vice president research and product development, will present “Overcoming pre-existing immunity”. **The 5th Animal Models of Neurodegenerative Diseases, September 15 – 18, Chateau Liblice, CZ.** Melvin Evers, associate director research at uniQure, will present “The development of microRNA-based gene therapy for Huntington’s disease.”  Astrid Valles-Sanchez, senior scientist at uniQure, will present “Translational efficacy measures of huntingtin lowering in small and large animal models of Huntington’s disease”.  **International Congress of Parkinson’s Disease and Movement Disorders – MDS 2019, September 22 -26, 2019, Nice, FR.**uniQure will deliver the following presentations on the development of AMT-130 for Huntington’s disease: MRI, Clinical, and Neuropathological Findings after Bilateral Intra-striatal Administration of rAAV5-miHTT in Non-human Primates; Translating Preclinical Data to a Human Equivalent Dose for AMT-130 AAV Gene Therapy for Early Manifest Huntington’s Disease Patients;Sustained Mutant Huntingtin Lowering in the Brain and Cerebrospinal Fluid of Huntington’s Disease Minipigs Mediated by AAV5-miHTT Gene Therapy; and Exploring the Effects of Intrastriatal AAV5-miHTT Lowering Therapy on MRS Signal and Mutant Huntingtin Levels in the Q175FDN Mouse Model of Huntington’s Disease [↑](#footnote-ref-24)
25. USAMRIID has worked on medical biological defence research since 1969. It is reported to have both level 3 and level 4 biosafety labs and has worked on pathogens such as Ebola, Yersinia pestis (plague), and Francisella tularensis (tularemia). [The New York Times](https://www.nytimes.com/2019/08/05/health/germs-fort-detrick-biohazard.html) reported that the lab received the cease and desist order in part because the (CDC) found it did not have “sufficient systems in place to decontaminate wastewater” from its highest-security labs. A USAMRIID spokesperson reportedly told the Times that the facility’s steam sterilization plant had been damaged in a flood in May 2018, and that it had since been using chemical decontamination.  [↑](#footnote-ref-25)
26. See <https://www.medscape.com/viewarticle/916884> [↑](#footnote-ref-26)
27. See [press release](https://www.wehi.edu.au/news/tiny-blood-cells-could-protect-against-cerebral-palsy). The research was led by Dr Alison Farley and Dr Samir Taoudi [↑](#footnote-ref-27)
28. Frank J Wolters et al., “Hemoglobin and anemia in relation to dementia risk and accompanying changes on brain MRI”, *Neurology,* 27 August 2019; 93(9). DOI: <https://doi.org/10.1212/WNL.0000000000008003> [↑](#footnote-ref-28)
29. Emily N Larsen et al., “A systematic review of central-line–associated bloodstream infection (CLABSI) diagnostic reliability and error”, Published online 31 July 2019 in *Infection Control and Hospital Epidemiology.* (DOI: <https://doi.org/10.1017/ice.2019.205> [↑](#footnote-ref-29)
30. Julia van Campen presented the first results in the presentation “[Non-invasive prenatal diagnosis of sickle cell disease by next generation sequencing of cell-free DNA](https://www.abstractsonline.com/pp8/#!/7874/presentation/160)” at the recent [2019 European Human Genetics Conference](https://2019.eshg.org/) in Gothenburg, Sweden. [↑](#footnote-ref-30)
31. Choi S, O’Neil SH, Joshi AA, et al. [Anemia predicts lower white matter volume and cognitive performance in sickle and non‐sickle cell anemia syndrome](https://onlinelibrary.wiley.com/doi/10.1002/ajh.25570) [published online 1 July 2019 ]. Am J Hematol. <https://doi.org/10.1002/ajh.25570> [↑](#footnote-ref-31)
32. Paula Saa et al., “Acute Zika virus infection in an asymptomatic blood donor at the onset of the Puerto Rico epidemic”, *Transfusion,* 13 August 2019 <https://doi.org/10.1111/trf.15484> [↑](#footnote-ref-32)
33. Karen Nielsen-Saines et al.,” Delayed childhood neurodevelopment and neurosensory alterations in the second year of life in a prospective cohort of ZIKV-exposed children”, 8 July 2019 [*Nature Medicine*](https://www.nature.com/nm)volume 25, pages1213–1217 (2019) <https://www.nature.com/articles/s41591-019-0496-1> [↑](#footnote-ref-33)
34. Davide F Robbiani et al., “[Risk of Zika microcephaly correlates with features of maternal antibodies](http://jem.rupress.org/content/early/2019/08/13/jem.20191061?rss=1)” in [*Journal of Experimental Medicine*](http://jem.rupress.org/) 14 August 2019, DOI: 10.1084/jem.20191061 [↑](#footnote-ref-34)
35. Sarah M Bartsch et al., “What Is the Value of Different Zika Vaccination Strategies to Prevent and Mitigate Zika Outbreaks?”, The Journal of Infectious Diseases, Volume 220, Issue 6, 15 September 2019, Pages 920–931, <https://doi.org/10.1093/infdis/jiy688> [↑](#footnote-ref-35)
36. Dobaño C, Ubillos I, Jairoce C, et al. “RTS,S/AS01E immunization increases antibody responses to vaccine unrelated Plasmodium falciparum antigens associated with protection against clinical malaria in African children: a case-control study”. 14 August 2019. [*BMC Medicine*](https://bmcmedicine.biomedcentral.com/)  **17**, Article number: 157 (2019) | <https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-019-1378-6> [↑](#footnote-ref-36)
37. The trial will enrol 240 healthy volunteers who will be randomly assigned to receive a single dose of either the [Fluzone®](https://www.precisionvaccinations.com/vaccines/fluzone-high-dose-influenza-vaccine) Quadrivalent Influenza Vaccine or [Flublok®](https://www.precisionvaccinations.com/vaccines/flublok-quadrivalent-influenza-vaccine) Quadrivalent Influenza Vaccine, both made by Sanofi Pasteur and reformulated annually to best match the anticipated seasonal influenza strains selected by the World Health Organisation. Fluzone is manufactured from inactivated influenza viruses grown in chicken eggs. Flublok is an egg-free recombinant vaccine consisting of a surface protein of influenza virus, hemagglutinin, specifically engineered to achieve an exact genetic match to the WHO-selected influenza strains each year. The Flublok proteins are manufactured in insect cells using a genetically engineered baculovirus. Vaccine will be given alone or in combination with either the AF03 or the Advax-CpG55.2™ adjuvant. These have both shown promise in animal models at enhancing the immune response to influenza vaccines. The trial is expected to last approximately 18 months. [↑](#footnote-ref-37)
38. Seasonal Influenza : *MF59®-Adjuvanted Quadrivalent Influenza Vaccine Provides Consistent Benefit Upon Revaccination in Young Children* (I. Smolenov, J. Oberyé); *Adjuvanted Vaccine Induced Higher Strain Cross-Reactive Antibody Response than Non-Adjuvanted Vaccine* (E. Settembre, Y. Wen); *Retrospective Evaluation of Antigenic Similarity Between Egg-Derived Versus Cell-Derived Influenza Vaccine Reference Strains and Circulating Influenza B-Victoria and Yamagata Viruses* (S. Rajaram); *Reduced Vaccine Effectiveness Resulting from Candidate Influenza Virus Variation During Egg-Based Manufacture: Literature Review and Expert Survey* (S. Rajaram); *Prevention of Influenza during Mismatched Seasons in Older Adults: A Randomized Efficacy Study of an MF59®-Adjuvanted Quadrivalent Influenza* (I. Smolenov, C. Fierro); *MF59®-Adjuvanted Quadrivalent Subunit Influenza Vaccine is Non-Inferior to the Licensed MF59-Adjuvanted Trivalent Vaccine and Well-Tolerated in Older Adults* (I. Smolenov, C. Fierro); *The Economic Advantages of a Cell-Based Quadrivalent Influenza Vaccine in the Adult Population in Europe. The Cost-Effectiveness Evidence in United Kingdom and Spain* (V. H. Nguyen, S. Márquez-Peláez, J. Ruiz-Aragón); *Effectiveness of Risk Minimisation Activities for Afluria® Quad Through an Online Survey - A Quantitative Research Study* (H. Shetty); *Effectiveness of an Independent, Online Educational Program for Australian Healthcare Professionals on Seasonal Influenza Immunisation Strategies in Older Adults in 2018* (M. Tham); *Afluria® Quadrivalent Influenza Vaccine for Adults and Paediatric Use* (F. R. Albano); *Assessing Factors Influencing Influenza Vaccine Choice in U.S. Nursing Homes* (J. Mansi, S. Gravenstein); *Evaluation of Influenza Case Definitions in a Primary Care Database for Use in Real World Evidence Research* (J. Mansi, T. Boikos); *Influenza Vaccine Programs with the Cell-Based Quadrivalent Influenza Vaccine are Highly Effective in Canada* (J. Mansi, T. Boikos); *Strengthening Pediatric Influenza Vaccination Offering and Acceptance: Findings from the Pediatric Influenza Vaccination Optimization Trial (PIVOT)* (J. Mansi, T. Boikos); *Real World Outcomes of Adjuvanted Trivalent Influenza Vaccine Compared to Egg-Based Trivalent High-Dose, Egg-Based Quadrivalent and Trivalent Vaccines Among the U.S. Elderly During 2016-2018 Flu Seasons Using Claims Data* (V. Divino, M. Jiang, M. DeKoven); *Hospitalization Encounters Following Vaccination with Adjuvanted Trivalent Influenza Vaccine Compared to Egg-Based Trivalent High-Dose, Egg-Based Quadrivalent and Trivalent Vaccines Among the U.S. Elderly Using Claims Data* (V. Divino, M. Jiang, M. DeKoven); *Method for Determining Percentage Split Virion by Nanosight* (C. Ong); *EIA Hemagglutinin Potency Assay: An Alternative to* SRID (J. Bodle, S. Rockman); *Use of a Biological Assay to Mitigate Vaccine Pyrogenicity* (C. Ong); *First International Workshop on Reassortment of Influenza Candidate Vaccine Viruses* (C. Wadey); *Practical Implementation of Cell Isolated Candidate Vaccine Viruses for Large Scale, Cell-Based Influenza Vaccine Manufacture* (K. Kulowiec); *Microneutralization Assay Titers as Estimates of Protective Efficacy Against Influenza Infection in Children* (M. Heeringa); *Improved Pyrogenicity (Fever) Profile of Quadrivalent Inactivated Influenza Vaccine* (D. Sawlwin)  [↑](#footnote-ref-38)
39. Pandemic Influenza: *Antibody Responses Against Heterologous H5N1 Strains for an MF59®-Adjuvanted Cell Culture-Derived H5N1 (aH5N1c) Influenza Vaccine in Healthy Pediatric Subjects* (E. Versage, M. Hohenboken); *Antibody Responses Against Heterologous H5N1 Strains for an MF59®-Adjuvanted Cell Culture-Derived H5N1 (aH5N1c) Influenza Vaccine in Adults and the Elderly* (E. Versage, M. Hohenboken); *Immunogenicity, Lot-To-Lot Consistency, and Safety of an MF59®-Adjuvanted Cell Culture-Derived H5N1 (aH5N1c) Influenza Vaccine in Healthy Adults* (E. Versage, M. Hohenboken); *Reference Antigen-Free and Antibody-Free LTD-IDMS Quantifies A(H5N1) Vaccine Potency* (E. Settembre, Y. Wen) [↑](#footnote-ref-39)
40. Grohskopf LA, Alyanak E, Broder KR, Walter EB, Fry AM, Jernigan DB; Advisory Committee on Immunization Practices. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices — United States, 2019–20 influenza season. *MMWR Recomm Rep*. 2019;68(No. RR-3):1-21. doi:[10.15585/mmwr.rr6803a1](https://www.cdc.gov/mmwr/volumes/68/rr/rr6803a1.htm?s_cid=rr6803a1_e&deliveryName=USCDC_921-DM7382). [↑](#footnote-ref-40)
41. The dose volume is 0.25 mL per dose (containing 7.5 *µ*g of HA per vaccine virus) for children aged 6 through 35 months and 0.5 mL per dose (containing 15 *µ*g of HA per vaccine virus) for all persons aged 36 months [or older]. [↑](#footnote-ref-41)
42. Children aged 6 through 35 months who receive Fluzone Quadrivalent may now receive either 0.25 mL (containing 7.5 *µ*g of HA per vaccine virus) or 0.5 mL (containing 15 *µ*g of HA per vaccine virus) per dose. Children aged 36 months or older, as well as adults, should receive 0.5 mL per dose. [↑](#footnote-ref-42)
43. J and J acquired Ad26.ZEBOV in its takeover of Crucell. It is designed to provide protection against Ebola Zaire. MVA-BN-Filo, a multivalent vaccine developed by Bavarian Nordic, is designed to protect against Ebola and Marburg. When giving the vaccines in a prime-boost regimen showed promise, J&J and Bavarian Nordic formed a global license and supply agreement. [↑](#footnote-ref-43)
44. Previously the GAVI Alliance, and before that the Global Alliance for Vaccines and Immunization. [↑](#footnote-ref-44)
45. [ClinicalTrials.gov: NCT03719586](http://clinicaltrials.gov/ct2/show/NCT03719586?term=REGN-EB3&rank=1) [↑](#footnote-ref-45)
46. Where patients had low viral load (that is, were treated early) the mortality rates were 6 per cent for REGN-EB3, 11 per cent for mAb114, 24 per cent for ZMapp, and 33 per cent for remdesivir. [↑](#footnote-ref-46)
47. GSK said Sabin had agreed a collaboration deal with the Vaccine Research Center at the US National Institute of Allergy and Infectious Diseases (NIAID) to further develop the vaccine candidates. ChAd3 was originally developed by NIAID in collaboration with the Swiss-based firm Okairos, which was bought by GSK in 2013. All three experimental vaccines have shown promise in safety trials after being administered to more than 5,000 adults and 600 children, GSK said. [↑](#footnote-ref-47)
48. “Perceived Benefits and Challenges of Ebola Preparation Among Hospitals in Developed Countries: a systematic literature review”, [Puig-Asensio M, et al. Clin Infect Dis. 2019;doi:10.1093/cid/ciz757.](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciz757/5549092) [↑](#footnote-ref-48)
49. See also Aug 8, 2018, CIDRAP News story "[WHO highlights ongoing hospital MERS risk](http://www.cidrap.umn.edu/news-perspective/2018/08/who-highlights-ongoing-hospital-mers-outbreak-threat)" [↑](#footnote-ref-49)
50. See Infectious Disease News. [↑](#footnote-ref-50)
51. Kayvon Modjarrod et al, “Safety and immunogenicity of an anti-Middle East respiratory syndrome coronavirus DNA vaccine; a phase 1, open-label, single-arm, dose-escalation trial“ in [*The Lancet Infectious Diseases*](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2819%2930266-X/fulltext#%20), volume 19, Issue 9, pp1013-1022 1 September, 2019. [↑](#footnote-ref-51)
52. **D.R. Sinclair et al., “Forecasted size of measles outbreaks associated with vaccination exemptions for schoolchildren,”** [JAMA Network Open](https://jama.jamanetwork.com/article.aspx?doi=10.1001/jamanetworkopen.2019.9768)**, doi:10.1001/jamanetworkopen.2019.9768, 2019.** [↑](#footnote-ref-52)
53. Bastidas A, de la Serna J, El Idrissi M, et al; ZOE-HSCT Study Group Collaborators. [Effect of recombinant zoster vaccine on incidence of herpes zoster after autologous stem cell transplantation: a randomized clinical trial](https://jamanetwork.com/journals/jama/article-abstract/2737683). JAMA. 2019;322(2):123-133. [↑](#footnote-ref-53)
54. Shingrix from GlaxoSmithKline [↑](#footnote-ref-54)