

# Monitoring International Trends

## October – December 2022

The NBA monitors international developments that may influence the management of blood and blood products in Australia including but not limited to:

- potential new product developments and applications
- global regulatory and blood practice trends
- events that may have an impact on global supply, demand and pricing
- emerging risks and relevant issues.

The following key topics have appeared in news media, online publications, industry, and research updates and have been included in this report:

**Blood supply:** During the COVID-19 pandemic, Australian donors aged 70 and over were advised to temporarily stop donating. Research looked at the number of donors that heeded the advice and the reasons some donors continued to donate. Researchers also suggest that stay at home advice should be accompanied by strategies to encourage donors to return once the health advice changed.

**Blood disorders:** A team of doctors and scientists at Great Ormond Street Hospital in London used base editing technology to engineer a new type of T-cell capable of hunting down and killing the cancerous cells in a 13-year-old girl. Scientists were able to zoom to a precise part of the genetic code and then alter the molecular structure to change its genetic instructions. The technology was successful after chemotherapy and a bone marrow transplant failed. The girls T-cell acute lymphoblastic leukemia is now in remission.

**Transfusion:** Researchers surveyed liver transplant centres in the US to assess blood utilisation and identify opportunities for standardisation to optimise blood use. Using responses from two surveys, researchers found that more blood products were issued during surgery than were transfused. They suggested future studies focus on how to better predict patient blood needs to improve efficiency.

**Product Management:** Octopharma have released a new freeze-dried form of its plasma product OctaplasLG. OctaplasLG and the new product OctaplasLG Lyo are used for treating complex coagulation factor deficiencies. Octopharma have stated that the new product offers quicker reconstitution, enabling more flexible storage conditions and utilisation.

**Immunoglobulin:** Researchers conducted a retrospective study of adult patients with sepsis or autoimmune diseases who received intravenous immunoglobulin (IVIg)s. They found that septic patients had a shorter ICU stay, received IVIg early, and had reduced mortality if treated with high dose IVIg. Patients with autoimmune diseases did not have a favourable outcome despite IVIg treatment, however, IVIg was administered later than in the sepsis group.

**Gene therapy:** The US FDA has approved CSL's gene therapy etranacogene dezaparvovec (Hemgenix) for the treatment of haemophilia B. Hemgenix is an adeno-associated virus vector-based gene therapy which consists of a viral vector carrying a gene for clotting Factor IX.

The Australian Haemophilia Centre Directors' Organisation (AHCDO) developed the Gene Therapy Roadmap to provide a Clinical Implementation Plan that sets out AHCDO's position on the preferred approach to implementation of gene therapy for haemophilia in Australia. It focuses on patient need, informed by clinical experience.

**Other items of interest:** Scientists have transfused ex-vivo grown blood cells for the first time. A clinical trial in the United Kingdom is studying the lifespan of the lab grown cells compared with infusions of standard red blood cells from the same donor. Two people have been transfused with the lab grown red cells and are being closely monitored with no untoward side effects reported. Grown blood cells could improve treatment for sufferers of rare blood diseases while reducing demand on blood supplies.



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# 1 Blood supply

This section contains news articles and government agency statements on blood supply in Australia and around the world.

## 1.1 Blood supply – Australia

The Lismore Blood Donor Centre finally reopened in December following inundation during the February 2022 flood event. The new Lismore Donor Centre offers donors a welcoming space, designed with donors in mind. Lifeblood delayed rebuilding to free up trades and let the community get back on their feet, using a mobile blood truck to maintain donations in the meantime.

- [Lismore Blood Donor Centre reopens Monday as Lifeblood Launches New Gifts Program](#)
- [MP Bridget Archer has spoken out against blood donation policies which ban most gay men](#)
- [There are only 100 Anti-D plasma donors in Australia, but their antibodies save thousands of babies each year](#)
- [Kalgoorlie MP Ali Kent continues to push for the return of blood donation service](#)
- [Aussie plasma donors needed for 'medical miracle'](#)
- [Tattoo artists illustrate tats are no barrier to blood donation](#)

## 1.2 Blood supply – United States

The American Red Cross' in Michigan hosted a blood drive as part of the Red Cross' Sickle Cell Initiative in November 2022. The blood drive sought to increase the diversity of the donor pool and boost access to matching blood products for sickle cell disease (SCD) patients. There are more than 100,000 SCD patients in the US, most of whom are of African descent.

- [Blood donations sought in Flint to diversify donor pool, combat Sickle Cell Disease](#)
- [LifeServe Blood Centre celebrates 75 years of saving lives](#)
- [Blood donations needed following mass shooting at Colorado Springs LGBTQ nightclub](#)
- [Northern California Community Blood Bank using new tech to address donation shortages](#)
- [CSL Plasma Expands in California with New Donation Centres to Collect Life-Saving Plasma](#)

## 1.3 Blood supply - World news

- [New Zealand - New \\$2m blood bank at Waikato Hospital a 'vital link' in life-saving chain](#)
- [Ireland - New 'fairer' risk assessment for blood donors](#)
- [UK - Female friendly' machines boost Birmingham plasma donors](#)
- [Iran: Over 1.3m Iranians donate blood in 7 months](#)
- [UK: Public responds to NHS amber alert over donor blood stocks](#)

## 1.4 Regulatory and donation criteria

[Risk of a blood donation contaminated with hepatitis E virus entering the blood supply before the implementation of universal RNA screening in France](#)

In early 2023, France will introduce hepatitis E-virus (HEV) RNA screening for all whole blood donations. HEV is mainly acquired by eating raw or undercooked meat that is contaminated, but it can also be transmitted by transfusion. Since 2012, HEV nucleic acid testing (HEV-NAT) has been conducted in France to screen and track the transmission risks. This study looked at data from 2018-2020 and estimated the risk of a whole blood donation being positive for HEV-RNA was 1 in 1682.



## 1.5 Blood donor characteristics and donation effects

### [Donor and non-donor perspectives on receiving information from routine genomic testing of donor blood](#)

Genomic testing is already used to identify rare blood types and match blood between donors and recipients, but there is scope to use genomic testing for other applications such as identifying genetic markers. Study participants were presented with hypothetical scenarios about how genomic testing could be used now and into the future. Participants felt that genomic testing to identify rare blood types was appropriate, while identifying markers associated with iron metabolism and cancer were only partially supported. Participants raised concerns about the boundaries of testing and the implications of testing for privacy, data security, and health insurance.

### [Donor variation in stored platelets: Higher metabolic rates of platelets are associated with mean platelet volume, activation and donor health](#)

Researchers investigated why platelet (PLT) glycolysis rates vary between platelet donors and how the rate of glycolytic activity affects subsequent storage performance. They found that high glucose-consuming platelet concentrates developed higher activation levels, displayed enhanced mitochondrial activity but were also found to contain larger PLTs. Storage performance of PLTs was associated with donor health, not with donor age.

### [Syphilis infections among volunteer blood donors](#)

This study analysed volunteer blood donors in a Chinese blood centre to determine the likelihood of syphilis infection amongst select donor groups. A total of 700,757 blood samples were collected from 2007 to 2021, with 2290 samples testing positive. A range of factors were identified as associated with high risk of infection, with the most significant being first time donors.

### [Beyond fear: A longitudinal investigation of emotions and risk of a vasovagal reaction in first-time whole-blood donors](#)

This study investigated the emotions experienced in blood donation centres to predict onsite vasovagal reactions (fainting due to stress) in Australia. First-time whole-blood donors completed surveys at multiple points during their time at the donor centre. Researchers found that donors often experienced negative emotional states in the waiting room which gradually increased to the moment before venepuncture. The occurrence of vasovagal reactions was significantly associated with negative emotional states suggesting that blood collection agencies need to address a broader range of emotions at different points during the donation process.

### [A pilot study of the metabolic profiles of apheresis platelets modified by donor age and sex and in vitro short-term incubation with sex hormones](#)

Researchers investigated the effect of sex on platelet biology to determine if platelets from males and females have different metabolic profiles at different life stages. Apheresis platelets were drawn from five pre-menopausal younger females, five post-menopausal older females, five younger males (under 45) and four older males (45 and above). Researchers found that platelets from older males are metabolically distinct from other donors, implying increased energy metabolism, more free fatty acids, acylcarnitines, and amino acids, and increased breakdown of purines and deamination products. Only platelets from older males were affected by sex hormones in vitro.

### [How do we decide how representative our donors are for public health surveillance?](#)

Researchers evaluated the Canadian donor base to understand which subset of the general population they represent. They found that donors are an ideal convenience population for the surveillance of infectious agents for which many people may be asymptomatic, as well as for the surveillance of vaccination serology.



### [‘Stay at home and limit contact’: The impact of stay-at-home advice on the behaviour of Australian donors aged 70 and over in the first year of the pandemic](#)

Early in the COVID-19 pandemic, Australian donors aged 70 and over were advised to temporarily stop donating. Researchers used survey data collected during the first 6 months of the pandemic to analyse the number of donors aged 70 and over who continued to donate despite stay-at-home advice. The study found that stay at home advice was partially successful in preventing older donors from donating however, that a more tailored approach may have prevented more donors from donating. Researchers also suggest that stay at home advice should be accompanied by strategies to encourage donors to return once advice has changed.

### [West Nile virus transfusion-transmission risk in Australia associated with a seasonal outbreak in the United States](#)

This study estimated the monthly West Nile virus (WNV) transfusion transmission (TT) risk in Australia associated with donors returning from the US where WNV is endemic and a potentially transfusion-transmissible virus. The highest monthly cumulative transfusion risk in Australia occurred in August 2018 when 746 West Nile neuroinvasive disease cases were reported in the US. However, researchers found that the risk in Australia associated with seasonal outbreaks in the US was extremely small.

### [Transfusion-transmitted arboviruses: Update and systematic review](#)

This study reviewed the published cases of arbovirus transmission through transfusion of blood or blood components worldwide. Researchers identified 74 cases of transfusion-transmitted arbovirus infections to November 2021. Most infections were West Nile virus (42) or dengue virus (18). The blood component most commonly involved was red blood cells and transmission resulted in death in 14 cases.

### [Explainable haemoglobin deferral predictions using machine learning models: Interpretation and consequences for the blood supply](#)

This research presents a novel, machine learning haemoglobin deferral prediction model based on donor characteristics and donation history. The model was developed to predict haemoglobin deferral for whole blood donors with the aim of reducing deferrals, while increasing efficiency and donor motivation. Researchers suggest using the prediction model could assist timing of when invites are sent to donors to match when their haemoglobin levels are safe for donation. The results concluded that by using the model, the number of blood bank visits would increase by 15%, while deferral rates would decrease by 60%.

### [Scientists find new set of blood types](#)

Scientists have described the different mutations of the Er blood group antigen, including two previously unknown versions.

## **2 Blood disorders and treatments**

This section includes published new media, research and industry statements on the progress of blood disorder treatments across various conditions.

### **2.1 Haemophilia**

#### [Drug associated acquired haemophilia A: an analysis based on 185 cases from the WHO pharmacovigilance database](#)

This study identified and characterised the drugs associated with acquired haemophilia A using the WHO global database of reported potential effects of medicinal products. Researchers analysed all adverse drug reactions associated with acquired haemophilia between 2004 and 2021. Researchers were able to identify 14 drugs associated with a total of 185 cases.



[Emicizumab assays evaluations with four different reagents in severe haemophilia A patients: Concentration from baseline to maintenance therapy](#)

Biological monitoring of patients treated with emicizumab (Hemlibra) presents challenges as the treatment can interfere with some coagulation assays. Evaluation of several reagents and assays used to measure emicizumab plasma concentrations in hemophilia A patients showed that in real life conditions, the four reagents tested seem to be acceptable for the measurement of emicizumab concentration. However, one of the assays (aPTT-based FVIII:C OSA) is influenced by the presence of exogenous FVIII and should be interpreted with caution in patients having received such therapeutic agents in combination with emicizumab.

[Clinical outcomes of low-dose pharmacokinetic-guided extended half-life versus low-dose standard half-life factor VIII concentrate prophylaxis in haemophilia A patients](#)

This Thai study aimed to compare clinical outcomes when switching haemophilia A (HA) patients from low-dose standard half-life FVIII prophylaxis to pharmacokinetic guided extended half-life FVIII concentrates. Over a 6-month period the switch improved annual bleeding rates, joint bleeding rates, joint health scores and quality of life in patients with severe or moderate HA but it did result in an overall increase in FVIII consumption. While cost effectiveness was not analysed as part of this study, the results do suggest that PK guided dosing is worth considering due to improved patient outcomes, even if there are budget constraints.

[Modulating the microenvironment during FVIII uptake influences the nature of FVIII-peptides presented by antigen-presenting cells](#)

In this study, researchers sought to understand the risk factors of haemophilia A patients developing inhibitors following Factor VIII (FVIII) replacement therapy. They looked at the FVIII peptide repertoire presented by antigen-presenting cells (APCs) under different microenvironment conditions, and how these microenvironments altered the uptake of FVIII by APCs.

[Haemophilia patients treated with marstacimab see fewer bleeds](#)

Treatment with marstacimab, an experimental antibody-based therapy developed by Pfizer, reduced the number of bleeds in patients with severe haemophilia who took part in a phase 1b/2 clinical study. The result was the same for patients with haemophilia A or haemophilia B, regardless of inhibitors.

[Association of factor expression levels with annual bleeding rate in people with haemophilia B](#)

This cross-sectional study evaluated the association between steady-state clotting factor expression level (FEL) and annual bleeding rate (ABR) in people with haemophilia B. The study included 407 participants with haemophilia B and no inhibitors who were receiving on-demand treatment. The results found a significant relationship between FEL and ABR. After adjusting for covariates, the model showed that for every 1% increase in FEL, the average ABR decreased by 0.08 ( $p < .001$ ).

[Prophylaxis use of clotting factor replacement products in people with non-severe haemophilia: A review of the literature](#)

This study investigated whether people with non-severe haemophilia A and B are receiving less treatment due to their lower severity of symptoms. A review of the literature identified large information gaps relating to the best treatment for people with non-severe haemophilia and suggested that best treatment for non-severe cases should be similar to the strategies employed for severe haemophilia.

[Increased acute care utilisation, comorbidities and mortality in adults with haemophilia: A population-based cohort study from 2012 to 2019](#)

A population-based study in Canada was conducted to understand the health outcomes of haemophilia patients. Men with haemophilia were identified in Alberta, Canada (2012–2019) with a validated case definition and were age-matched with male population controls. Researchers showed that patients had a significantly higher prevalence of hypertension, liver diseases and malignancies than the rest of the population. Moderately severe haemophilia was associated with significantly higher rates of hospitalisations, emergency department visits and intensive care admissions.



### [Emicizumab dose up-titration in case of suboptimal bleeding control in people with haemophilia A](#)

This study investigated the effect of increasing the dose of prophylactic drug emicizumab (Hemlibra) for people with haemophilia A who had suboptimal bleeding control after receiving the treatment. Researchers compiled data from seven completed or ongoing phase III studies and evaluated patient results before and after their dose of emicizumab was increased by 3mg/kg per week. They found that bleed control improved in most participants whose bleeding tendency was inadequately controlled during clinical trials.

### [Safety of FEIBA and emicizumab \(SAFE\): Dose escalation study evaluating the safety of in vivo administration of activated prothrombin complex concentrate in haemophilia A patients on emicizumab](#)

Researchers studied the effect of infusing various doses of activated prothrombin complex concentrate (aPCC) to patients on emicizumab when they experienced breakthrough bleeding events. Nine patients with severe haemophilia A with inhibitors were infused with varying doses of aPCC. Researchers found that clinically relevant concentrations of aPCC resulted in excessive thrombin generation when tested on tissue samples, however, in vivo administration of aPCC to the same patients demonstrated that most patients had normal thrombin generation at the approved dose.

### [Comprehensive analysis and prediction of long-term durability of factor IX activity following etranacogene dezaparvovec gene therapy in the treatment of haemophilia B](#)

The gene therapy etranacogene dezaparvovec (Hemgenix) for haemophilia B was assessed to determine the durability of the treatment. Only 10% of the current trial participants for Hemgenix would have durability of FIX activity levels up to 25 years post-infusion but suggested that future patients may have more than an 80% chance they would be free from prophylactic FIX replacement products 25 years post-infusion.

### [Peri-operative haemostatic management of tooth extraction in patients with haemophilia A, with and without inhibitors, receiving emicizumab prophylaxis](#)

Researchers investigated the effect of emicizumab (Hemlibra) treatment for people with haemophilia A who underwent tooth extraction and evaluated the outcomes of people with and without inhibitors to assess bleeding risk. Twenty-nine extractions were performed at a single institution, with researchers finding that while there was some risk of additional bleeding, planning, clamping and mouth splints achieved effective and safe haemostatic management in Hemlibra treated patients.

### [FDA clears trial of TI-168 therapy to eliminate haemophilia A inhibitors](#)

The U.S. Food and Drug Administration (FDA) has granted investigational new drug (IND) clearance for TI-168, a regulatory T-cell therapy designed to eliminate inhibitors in people with haemophilia A. The biotech company, Teralmmune, will launch a Phase 1/2a clinical trial to assess the safety and efficacy of TI-168 in up to eighteen congenital haemophilia A patients with refractory inhibitors.

### [Emicizumab for the treatment of acquired haemophilia A](#)

This study reviewed the results of 11 acquired haemophilia A patients treated with emicizumab (Hemlibra), in conjunction with rituximab (Rituxan) for four weeks at a single US institute. After an average follow-up period of 14 months, eight patients had achieved complete remission, two patients achieved a partial remission and one patient experienced a recurrence of the disease.

### [Factor IX inhibitors in haemophilia B: A report of National Haemophilia Registry in China](#)

Researchers analysed haemophilia B (HB) inhibitor patients' characteristics, factor IX (FIX) genotypes, treatment strategies and outcomes to explore the risk factors for FIX inhibitor development. The study looked retrospectively at patients registered on the Chinese National Registry and Patient Organisation Registry. It was found that large deletions and missense mutations of the FIX gene were most significantly associated with inhibitor development and that low-dose immune tolerance induction (ITI) therapy might be feasible for FIX inhibitor eradication.



### [Clinical experience of switching patients with severe haemophilia to rVIII-SingleChain or rIX-FP](#)

This report summarises the clinical experience of different haemophilia treatment centres in managing the switch to rVIII-SingleChain or rIX-FP in haemophilia patients. Researchers found that the physician plays an important role in the motivation of patients to switch based on their individual needs and expectations.

## 2.2 Von Willebrand disease (VWD)

### [ADAMTS13 inhibition to treat acquired von Willebrand syndrome during mechanical circulatory support device implantation](#)

Acquired von Willebrand syndrome (aVWS) is common in patients with mechanical circulatory support (MCS) devices. In these patients, the high shear stress in the device leads to increased shear-induced proteolysis of von Willebrand factor (VWF), by [ADAMTS13](#). As a result, VWF function was decreased and haemostasis impaired. Researchers developed a novel targeted therapy, using an anti-ADAMTS13 monoclonal antibody that inhibits the shear-induced proteolysis of VWF by ADAMTS13.

### [Patients with von Willebrand disease in China: Results of an online survey](#)

Researchers investigated the clinical characteristics of a group of von Willebrand disease (VWD) patients in China, the impact of Covid-19 on them and their genetic mutation. They found a high rate of type 3 patients and experiences of misdiagnosis reported which suggested that VWD may be significantly under-diagnosed in China.

## 2.3 Thrombocytopenia

### [NICE recommends Sobi's Doptelet to treat thrombocytopenia](#)

The National Institute for Health and Care Excellence (NICE) has issued the Final Appraisal Document in England and Wales recommending the use of Doptelet (avatrombopag) as a treatment for adults with primary chronic immune thrombocytopenia (ITP) who are resistant to other treatments such as corticosteroids or immunoglobulins. Among the 49 patients who participated in the study, Doptelet was superior to placebo for the cumulative number of weeks of platelet response.

## 2.4 Thalassemia

### [Long-term safety and erythroid response with luspatercept treatment in patients with \$\beta\$ -thalassemia](#)

This study reports on the long-term safety and efficacy results of the first clinical study of luspatercept in beta thalassemia. The study was initiated in 2013, enrolling adults with both nontransfusion-dependent (NTD) and transfusion-dependent (TD) beta-thalassemia. Researchers reviewed up to 5 years of treatment for 64 patients with NTD or TD beta-thalassemia, and long-term efficacy data for a subset of 63 patients with beta-thalassemia who received high-dose luspatercept. Long-term assessment of patients with beta-thalassemia showed luspatercept was associated with sustained increases in haemoglobin levels in NTD patients and sustained transfusion burden reductions in TD patients.

## 2.5 Myeloma

### [New Technique Can Detect and Analyse Tumor Cells of Multiple Myeloma and Precursor Conditions from Blood Sample](#)

A new technique developed by researchers at the Dana-Farber Cancer Institute in Boston can use a small blood sample to detect tumour cells in people at heightened risk for multiple myeloma, assess risk of progression in patients with myeloma, and track genetic changes in tumour cells over time. The approach, known as MinimuMM-seq, has the potential to replace a bone marrow biopsy by using whole-genome sequencing to probe the entirety of myeloma cells' DNA. Researchers found that MinimuMM-seq was able to detect the same genetic abnormalities in circulating tumour cells that existed in bone marrow biopsy samples, including hallmark features of myeloma.



### [Elranatamab receives breakthrough therapy designation for advanced multiple myeloma](#)

The FDA has granted breakthrough therapy designation to elranatamab for treatment of relapsed or refractory multiple myeloma. Elranatamab is a B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody designed to bind to BCMA on the surface of multiple myeloma cells and the CD3 receptor found on the surface of T cells.

## 2.6 Leukaemia

### [Acute myeloid leukemia resistant to venetoclax-based therapy: What does the future hold?](#)

Venetoclax is a highly selective B-cell lymphoma-2 (BCL-2) inhibitor. When combined with a DNA hypomethylating agent or low dose cytarabine, it results in high rates of initial responses in patients with acute myeloid leukemia (AML). However, the disease relapses in most patients. Understanding the mechanisms associated with resistance to venetoclax-based therapy is important and relevant to designing therapeutic strategies to mitigate or overcome resistance. Future studies should focus on identifying predictive biomarkers of response to venetoclax-based therapy and incorporating immunotherapeutic approaches to improve outcomes for patients with AML.

### [FDA approves olutasidenib for relapsed or refractory acute myeloid leukemia with a susceptible IDH1 mutation](#)

The FDA approved oral olutasidenib for treating patients with relapsed or refractory acute myeloid leukemia susceptible to harbouring an IDH1 mutation. It has also approved the Abbott RealTime IDH1 Assay, which is used to select patients suitable for receiving olutasidenib.

### [Electrostatic anti-CD33-antibody–protamine nanocarriers as platform for a targeted treatment of acute myeloid leukemia](#)

This research presents, personalised and targeted treatment options for acute myeloid leukemia (AML). The AML-targeting system consists of an antibody-based siRNA carrier able to silence leukaemia-related oncogenes, DNMT3A and FLT3.

### [The prognostic significance of hematogones in childhood B-cell acute lymphoblastic leukemia](#)

In this prospective cohort study, a total of 122 subjects with definitive diagnosis of precursor B lymphoblastic leukaemia were evaluated to assess the prognostic value of hematogones (HG) on relapse-free survival and overall survival in childhood acute lymphoblastic leukemia (ALL). The researchers found that HGs could be a significant independent prognostic factor which could be beneficial in assessing the risk stratification and treatment options for paediatric ALL patients.

### [CAR-T therapy effective in youngest kids with ALL](#)

Researchers examined the real-world outcome of treatment with tisagenlecleucel (Kymriah) in younger children and infants with acute lymphoblastic leukaemia (ALL) at 15 different hospitals in Europe. Patients received a single intravenous infusion of tisagenlecleucel with overall survival at 6 and 12 months after infusion being 88% and 84%, respectively, while event-free survival was 75% and 69%.

## 2.7 Myelodysplastic Syndrome

### [A sex-informed approach to improve the personalised decision-making process in myelodysplastic syndromes: a multicentre, observational cohort study](#)

Myelodysplastic syndromes (MDS) are extremely heterogeneous and therefore a risk-adapted approach is mandatory in their treatment. This study aimed to describe sex diversity in myelodysplastic syndromes in terms of disease genotype, phenotype, and clinical outcome. Research results suggest that a sex-informed approach can help make personalised treatment decisions for MDS patients and should be considered in the design of future clinical trials.



### [Luspatercept improves RBC transfusion independence in patients with MDS](#)

This phase 3 trial evaluated luspatercept-aamt (Reblozyl) as a frontline treatment, for patients with very low or intermediate-risk myelodysplastic syndromes (MDS) who required red blood cell transfusions. Researchers found that treatment with Reblozyl resulted in red blood cell transfusion independence with concurrent haemoglobin increase.

## 2.8 Sickle cell disease (SCD)

### [Trailing rivals, Editas shares first study data for sickle cell treatment](#)

Biotechnology company Editas have announced its experimental gene editing treatment for sickle cell disease has shown promise in the first two patients treated. This is an early step in the company's efforts to catch up, with some of their rivals already looking at seeking regulatory approval for their products.

### [Impact of Red Blood Cell Antigen Matching on Alloimmunization and Transfusion Complications in Blood transfusion vs. hydroxyurea for stroke prevention in children with sickle cell anemia: A systematic review and meta-analysis](#)

This systematic review compared the use of blood transfusions versus oral hydroxyurea (HU) therapy in preventing strokes in children with sickle cell anaemia (SCA). The study used transcranial Doppler (TCD) to determine a patient's risk of stroke. Results showed that both chronic blood transfusions and HU can effectively prevent primary strokes in children with SCA, however it is unclear if HU may prevent a second stroke.

### [Pulmonary hypertension screening in children with sickle cell disease](#)

This study examined the utility of screening for pulmonary hypertension (PHT) by using multiple methods to determine the best approach for discovery. Children aged 8-18 were screened but found that PHT symptoms were not consistent with current suggested screening methods.

### [Patients with Sickle Cell Disease: A Systematic Review](#)

Red blood cell transfusions are important to effectively manage sickle cell disease. However, patients often experience complications such as alloimmunisation, iron overload, transfusion reactions and infections. To prevent this, guidelines recommend genomic testing to ensure blood is properly matched to patients. This systematic review found low-quality evidence from observational cohort studies supported that alloimmunisation prevalence can be decreased by extending serological red blood cell antigen matching. It also found that transfusion reactions were generally poorly and inconsistently reported. Multicentre prospective randomised clinical trials are needed to determine best strategies for reducing the rate of alloimmunisation using serologic and genotypic matching in the future.

### [Impact of magnetic resonance angiography parameters on stroke prevention therapy in paediatric patients with sickle cell anaemia](#)

The primary objective of this study was to document if implementing a standardised magnetic resonance angiography (MRA) scanning protocol would affect stroke prevention treatment plans for patients with sickle cell anaemia. In a group of 10 paediatric patients receiving chronic blood transfusion for stroke prevention, 6 had their degree of stenosis reduced, and 5 of those had their transfusions discontinued. The authors concluded that this scanning protocol improved the accurate interpretation of cerebrovascular disease, ensuring appropriate treatments plans were in place for patients.



### [Hypoxic storage of donor red cells preserves deformability after exposure to plasma from adults with sickle cell disease](#)

Researchers investigated whether donor red blood cells (RBCs) exposed to the plasma of patients with sickle cell disease during vaso-occlusive crisis would have lower deformability and higher haemolysis than those exposed to non-crisis plasma. The aim of this research was to determine if low oxygen (hypoxic) storage could preserve deformability and reduce haemolysis. Hypoxic storage significantly influenced red blood cell deformability, while patient condition significantly influenced haemolysis.

### [A link between hypoxia and foetal haemoglobin provides hope for sickle cell disease: Scientists linked a well-known oxygen sensing pathway to foetal haemoglobin production](#)

This study found foetal haemoglobin (HbF) expression after birth can alleviate the symptoms of sickle cell disease and beta-thalassaemia. Scientists discovered that a protein responsible for adapting to low oxygen conditions (hypoxia), also causes increased expression of foetal HbF in adults. The finding suggests a pathway to treating sickle cell disease and beta-thalassaemia through treatments with proline hydroxylase inhibitor with cause hypoxia inducible factor 1 (HIF1) to accumulate.

### [Ferriprox safely, effectively lowers iron load in SCD patients](#)

Researchers have confirmed that long term treatment with deferiprone (Ferriprox) is safe and effectively reduced iron load in sickle cell disease (SCD) patients experiencing transfusion induced iron overload.

## **2.9 Pyruvate kinase (PK) deficiency**

### [PYRUKYND \(mitapivat\) approved in the EU for the treatment of pyruvate kinase \(PK\) deficiency in adult patients](#)

The European Commission (EC) has granted marketing authorisation for mitapivat (Pyrukynd) for the treatment of pyruvate kinase (PK) deficiency in adult patients. Mitapivat is an oral PK activator that treats haemolytic anaemia in adults with PK deficiency. It was approved for medical use by the US FDA in February 2022.

## **2.10 Cold agglutinin disease (CAD)**

### [Enjaymo gets EC marketing authorization for haemolytic anemia](#)

The European Commission (EC) granted marketing authorisation for the Sanofi product Enjaymo in September. Enjaymo is the only drug approved to treat haemolytic anaemia in adult patients with cold agglutinin disease (CAD), a rare autoimmune disorder where the body's immune system mistakenly attacks healthy red blood cells and destroys them.

## **2.11 Postpartum haemorrhage (PPH)**

### [Risk factors and recurrence of cause-specific postpartum haemorrhage: A population-based study](#)

Norwegian researchers performed a population-based cohort study, using records from 1967 -2017, to determine risk factors and recurrence of postpartum haemorrhage (PPH). They found that maternal, foetal, and obstetric characteristics had differential effects on types of PPH, while recurrence differed considerably between PPH types. Retained placenta was a significant risk factor associated with severe PPH, as was sex of the delivered child, with boys associated with lower risk of PPH.

### [Association of maternal perfluoroalkyl substance exposure with postpartum haemorrhage in China](#)

Prenatal exposure to perfluoroalkyl substances (PFASs) in women has been linked to pregnancy disorders and adverse birth outcomes. This study aimed to explore the associations of maternal PFAS exposure with the risk of postpartum haemorrhage and found that the risk increased with increased exposure to a PFAS mixture.



## 2.12 Hereditary angioedema

### [HAE patients see benefits following 1-year of treatment with Takhzyro](#)

In this study researchers found that half of the participants with hereditary angioedema (HAE) treated with lanadelumab (Takhzyro) for at least a year, prolonged their dosing interval and used significantly less on-demand treatments.

### [HAE attacks safely prevented by NTLA-2002 gene therapy](#)

The phase 1 trial of Intellia Therapeutics gene therapy for hereditary angioedema (HAE) 'NTLA-2002' has confirmed that the drug is well tolerated at two different doses and reduced the number of swelling attacks in patients. Phase 2 is expected to begin in the first half of 2023.

## 2.13 Venous thromboembolism

### [Achieving higher efficacy without compromising safety with Factor XI inhibitors versus low-molecular-weight heparin for the prevention of venous thromboembolism in major orthopaedic surgery](#)

Researchers reviewed the current evidence for use of factor XI inhibitors for thromboprophylaxis in major orthopaedic surgery. Evidence from four trials were included in the study, with a total of 2269 patients. Factor XI inhibitors were associated with a significant reduction in the incidence of venous thromboembolism (VTE) events and reduced major or clinically non-major bleeding events.

## 2.14 Immune system and immunotherapy

### [Base editing: Revolutionary therapy clears girl's incurable cancer](#)

A team of doctors and scientists at Great Ormond Street Hospital in London used base editing technology to engineer a new type of T-cell capable of hunting down and killing the cancerous cells in a 13 year old girl. Scientists were able to zoom to a precise part of the genetic code and then alter the molecular structure to change its genetic instructions. The technology was successful after chemotherapy and a bone marrow transplant failed. The girls T-cell acute lymphoblastic leukemia is now in remission.

### [Low-Dose lenalidomide lowers risk of transfusion dependency, provides other benefits in myelodysplastic syndrome](#)

This phase 3, double-blind, randomised SINTRA-REV trial evaluated lenalidomide (Revlimid) at low doses on 60 patients with low-risk myelodysplastic syndrome (MDS). The results show significant clinical benefit. This included prolonged time to, and decreased risk of, transfusion dependency (TD), high erythroid and cytogenetic responses, an acceptable safety profile, and no progression or clonal evolution, even in patients with TP53 mutations.

# 3 Transfusion

This section includes published research on transfusion procedures to improve patient outcomes.

## 3.1 Paediatrics

### [Blood component ratios in children with non-traumatic life-threatening bleeding](#)

This study's objective was to evaluate whether high blood product ratios or low deficits of platelets and plasma had an impact on mortality in children with non-traumatic, life-threatening bleeding. It found that while massive transfusions in children with non-traumatic bleeds are rare, they are often associated with high mortality. The authors concluded that more research is needed to identify the best blood product ratios to maximise survival rates in these children.



### [Transfusion-associated hyperkalemia in paediatric population: Analyses for risk factors and recommendations](#)

Transfusion-associated hyperkalemia (TAH) is a potentially life-threatening complication of red blood cell (RBC) transfusion. In this study, researchers compared RBC transfusions of 35 paediatric patients who had TAH with a control group to identify the factors associated with TAH occurrence. Researchers found that the total transfused volume within 12 hours per kg and per estimated total blood volume, age of RBC units, and kidney dysfunction were the most important factors in the development of TAH.

### [Blood transfusion is associated with increased mortality for neonates with congenital diaphragmatic hernia on extracorporeal membrane oxygenation support](#)

A single centre retrospective chart review of all neonates with congenital diaphragmatic hernia (CDH) undergoing surgical repair with extracorporeal membrane oxygenation (ECMO) was conducted, to determine the impact of platelet transfusion on patient outcomes. Researchers found that major bleeding and platelet transfusions in the post-operative period were associated with increased mortality for neonates on ECMO for CDH repair.

## **3.2 Clinical Practice**

### [Generating real-world evidence compatible with evidence from randomized controlled trials: a novel observational study design applicable to surgical transfusion research](#)

Numerous observational studies have revealed an increased risk of death and complications with transfusion, but this observation has not been confirmed in randomised controlled trials (RCTs). This study proposes a new design to address this long-term existing issue, which if left unresolved, will be damaging to the healthy generation of evidence that supports optimised transfusion practice.

### [Blood utilization in liver transplantation \(BUILT\): A multidisciplinary survey of transfusion practices](#)

This study surveyed liver transplant centres in the United States to assess baseline practices in blood utilisation and identify opportunities for standardisation to optimise blood use. Using responses from two surveys, sent to either transfusion physicians or anaesthesiologists, researchers found that more blood products were issued during surgery than were transfused. They suggest that future studies should focus on how to better predict blood needs for patients to improve efficiency and optimise blood usage.

### [The complexities of transfusion reactions: Coexistence of a delayed haemolytic transfusion reaction and post-transfusion purpura](#)

Researchers presented a case of a previously transfused and recently post-partum female who developed both delayed haemolytic transfusion reaction (DHTR) and post-transfusion purpura (PTP). To the author's knowledge, this is only the third reported instance of DHTR and PTP occurring in a single patient since 1980. The parallel development of these reactions suggests a hyperimmune response, assumed to occur in combination with an underlying autoimmune disease.

### [Association of anaemia, co-morbidities and red blood cell transfusion according to age groups](#)

This study examined the likelihood of transfusion based on health and age status to identify patient groups at risk when undergoing surgery. Over one million patients were included in this German population-based study. Researchers found that increasing age and co-morbidities were associated with an increased incidence of preoperative anaemia. Complications, length of hospital stay, and in-hospital mortality increased with age and was higher in patients with preoperative anaemia, with these patients more likely to require red blood cell transfusion.



### [The association of venous thromboembolism with blood transfusion in kidney transplant patients](#)

This Canadian study aimed to determine the risk factors for thrombotic events in adult kidney transplant recipients who received red blood cell transfusion (RBCT) after transplant. Researchers found that the risk of developing venous thromboembolism, deep vein thrombosis or pulmonary embolism was significantly increased in kidney transplant patients receiving RBCT after transplant and therefore recipients of red blood cells should be monitored for thrombosis.

### [Platelet transfusion practice pattern before and after implementation of a local restrictive transfusion protocol in a neonatal intensive care unit](#)

This study aimed to determine the impact of a local restrictive transfusion protocol on the number of platelet transfusions given to newborns at the Sainte-Justine Hospital, Canada. The study compared the decision-making strategies for platelet transfusion before and after implementation of the protocol, by comparing operation in 2013 with 2019. In the two years used for comparison, platelet transfusions decreased from 9.2% to 5% of cases and adherence to protocol thresholds was 70%. Platelet transfusion justifications and determinants remained similar; however, the new protocols reduced the proportion of platelet transfused newborns by almost half.

### [Evaluation of the association of platelet count, mean platelet volume, and platelet transfusion with intraventricular haemorrhage and death among preterm infants](#)

Researchers investigated the association between platelet transfusion count (PC) and volume (MPV) and the chance of intraventricular haemorrhage (IVH) and mortality in preterm infants. They found that platelet transfusion was associated with an increased risk of mortality, while decreased PC was associated with increased risks of IVH and mortality.

### [International Society for Blood Transfusion guidelines for validation of automated systems in blood establishments](#)

The International Society for Blood Transfusion guidelines for validation of automated systems in blood establishments have been updated to expand on qualifications, data recovery and review processes. The aim of these guidelines is to provide guidance on the validation of automated systems in blood establishments which may affect the safety and quality of blood components and services.

### [Aged versus fresh autologous platelet transfusion in a two-hit healthy volunteer model of transfusion-related acute lung injury](#)

This study investigated whether longer platelet concentrate (PC) storage time increases the risk of transfusion related acute lung injury (TRALI). Eighteen volunteers received experimental endotoxemia (2 ng/kg lipopolysaccharide), followed by fresh (2-day old) or aged (7-day old) autologous PC, or physiological saline. After 6 hours, changes in TRALI pathways were determined using spirometry, chest X-ray, and bronchoalveolar lavage (BAL). Researchers found that with an adequate hit of experimental endotoxemia and platelet storage lesion, transfusion of 7-day-old PC did not increase pulmonary inflammation compared with 2-day-old PC.

### [Association between in-ICU red blood cells transfusion and 1-year mortality in ICU survivors](#)

This study assessed the association between in-ICU red blood cells transfusion and 1-year mortality in a multicentre European cohort. Researchers found that among 1551 ICU-survivors, 42% received at least one unit of red blood cells while in intensive care unit, and that transfusion during the ICU stay was associated with a higher risk of death during the year following discharge.



#### [Laser incubation for the rapid detection of red cell alloantibodies in human blood samples](#)

Pre-transfusion antibody screening requires the detection and identification of immunoglobulin G (IgG) antibodies against red blood cells (RBCs). Researchers compared a laser incubation method to the more typical heating block technology when conducting an indirect antiglobulin test. Presence of an alloantibodies were detected after 1-min incubation for 96% of samples with no samples requiring longer than 3 min of laser incubation to detect the antibodies. No samples required longer than 5 min to achieve an equivalent result to that of the 5-min heating block incubation and the laser did not damage cells or antibodies.

#### [Modelling the outcomes of different red blood cell transfusion strategies for the treatment of traumatic haemorrhage in the prehospital setting in the United Kingdom](#)

Researchers analysed the potential benefits of prehospital transfusion (PHT) of trauma haemorrhage patients with O RhD-positive red blood cells (RBCs) compared to no PHT to determine if these units could be a suitable replacement for the high demand group O RhD-negative. They found that while the use of RhD-positive RBCs carries risks, the benefits are higher than if no PHT is administered, even for women of childbearing age. Researchers concluded that the use of group O RhD-positive RBCs could be considered in the case of a national shortage of RhD-negative RBCs.

#### [Whole blood transfusion and paroxysmal nocturnal haemoglobinuria meet again: Minor incompatibility, major trouble](#)

This report presents a case study of a patient who received a standard low-titre group O whole blood transfusion during pre-hospital transportation. Following the transfusion, the patient suffered a haemolytic transfusion reaction with researchers suggesting that the haemolysis was likely due to minor incompatibility between the plasma from the transfused whole blood and the patient's Paroxysmal nocturnal hemoglobinuria (PNH) red cells. Recovery was uneventful but highlights the issue of minor incompatibility in the case of emergency transfusion.

## 4 Product management

This section includes published research on product management to improve patient outcomes and reduce wastage of blood products.

### 4.1 Storage

#### [Frozen and freeze-dried solvent/detergent treated plasma: Two different pharmaceutical formulations with comparable quality](#)

Octapharma have released a new freeze-dried form of its plasma product OctaplasLG. OctaplasLG and the new product OctaplasLG Lyo are used for treating complex coagulation factor deficiencies. Octapharma have stated that the new product offers quicker reconstitution, enabling more flexible storage conditions and utilisation.

#### [A data-driven approach to determine daily platelet order quantities at hospitals](#)

Researchers developed a prediction model to guide the daily ordering quantity of platelet units at a hospital that ordered units from a central supplier. The model places orders at the end of each day to bring the platelet inventory to the predicted demand for the next day while also factoring in inventory costs of wastage and shortage.

## 4.2 Treatment

### [Prothrombin complex concentrate in cardiac surgery for the treatment of coagulopathic bleeding](#)

This review assessed whether use of prothrombin complex concentrates (PCCs) could be an alternative treatment option to the use of fresh frozen plasma in reducing the risk of bleeding following cardiac surgery. Researchers found that PCC treatment reduced red blood cell (RBC) transfusion overall and there was no reported difference to blood clots, death, intensive care stay or the requirement of dialysis. However, researchers did acknowledge that the small number of participants was likely insufficient to detect an outcome difference.

### [Effects of recombinant erythropoietin on haemoglobin levels and blood transfusion needs in patients with preoperative anaemia undergoing cardiac surgery](#)

In this study, the effects of recombinant erythropoietin on haemoglobin (Hb) levels and blood transfusion needs in patients with preoperative anaemia undergoing cardiac surgery were evaluated. Patients were randomly divided into two groups with only the intervention group receiving recombinant erythropoietin one to three days before surgery. Intra and postoperative Hb levels and the need for blood transfusion were recorded for 3 days after surgery. Researchers found that the use of recombinant erythropoietin before cardiac surgery limited the reduction of Hb and decreased blood transfusion needs.

### [Red cells manufactured from lipaemic whole blood donations: Do they have higher haemolysis?](#)

This study aimed to investigate associations between lipoproteins in plasma and haemolysis of red cells stored in saline–adenine–glucose–mannitol (SAGM). Lipaemia in blood donations is thought to influence haemolysis in stored red blood cell (RBC) components. They found no significant difference in haemolysis in RBC manufactured from lipaemic and non-lipaemic whole blood donations when stored in SAGM; however, the proportion of RBC from lipaemic donations with higher haemolysis was greater than the controls.

## 5 Immunoglobulin

This section includes published research and industry publications on the use of immunoglobulin therapies to improve patient outcomes.

### [Outcomes of ICU patients treated with intravenous immunoglobulin for sepsis or autoimmune diseases](#)

Researchers conducted a retrospective study of adult patients with sepsis or autoimmune diseases who received intravenous immunoglobulin (IVIg). They found that septic patients had a shorter ICU stay, received IVIg early, and had reduced mortality if treated with high dose IVIg. Patients with autoimmune diseases did not have a favourable outcome despite IVIg treatment, however, IVIg was administered later than in the sepsis group.

### [Medical Research Future Fund \(MRFF\) grant recipients](#)

Successful applicants under the Medical Research Future Fund (MRFF) [2021 Research and Data Infrastructure Grant Opportunity](#) and [2021 Optimising the Clinical Use of Immunoglobulins Grant Opportunity](#) were confirmed. This included \$2.9 million in funding to the Monash University National Transfusion Dataset Team to expand the national transfusion dataset (NTD) from five to 20 hospitals nationally, and to provide a more comprehensive view of transfusion practice and outcomes. It also includes just over \$800,000 for a national registration process to track, collect and evaluate chronic inflammatory demyelinating polyneuropathy (CIDP) patient outcomes with real world data– optimising data collection and reporting through BloodSTAR to enable research and examination of Ig dosing in CIDP. The NBA is a supporting partner of both projects.



## 6 Gene therapies

This section includes industry updates and research on the progress of gene therapies through regulatory bodies as well as gene therapy safety.

### 6.1 Gene therapies: blood and bleeding disorders

#### [FDA approves first gene therapy for haemophilia B](#)

The US FDA has approved CSL's gene therapy etranacogene dezaparvovec (Hemgenix) for the treatment of haemophilia B. Hemgenix is an adeno-associated virus vector-based gene therapy which consists of a viral vector carrying a gene for clotting factor IX. CSL, which licensed Hemgenix from Dutch biotechnology company UniQure, will market the one-time gene therapy at an expected \$3.5 million USD which will make it the most expensive medicine for a single-use treatment in the US.

#### [AHCDO Gene Therapy Roadmap - AHCDO - Australian Haemophilia Centre Directors' Organisation](#)

The Australian Haemophilia Centre Directors' Organisation (AHCDO) has developed the Gene Therapy Roadmap to provide a Clinical Implementation Plan that sets out AHCDO's position on the preferred approach to implementation of gene therapy for haemophilia in Australia, with a focus on patient needs that is informed by clinical experience.

#### [Mainstreaming cell and gene therapy – Realizing its potential](#)

This article looks at the cell and gene therapy landscape and comments on the challenges in this space such as the complexities around running clinical trials for these types of therapies.

#### [Gene therapy approvals bring validation as field closes year on high](#)

Since August 2022, the Food and Drug Administration (FDA) has approved more gene therapies for inherited diseases than it had in the five years previous. The regulator has cleared treatments for a severe form of the beta thalassemia, haemophilia B and a childhood brain disease. Each of these gene therapies costs several million dollars, posing barriers to patient access while testing an insurance system not set up to cover one-time curative medicines.

#### [Current strategies employed in the manipulation of gene expression for clinical purposes](#)

This review describes the different molecular tools that can be used to regulate gene expression and discuss their potential for clinical applications. These molecular tools are delivered into the host's cells in the form of DNA, RNA or protein using vectors that can be grouped into physical or biochemical categories. The review also discusses the recent developments in viral and non-viral vector technology.

#### [Gene therapy for sickle cell disease, beta thalassemia enters regulatory reviews](#)

Vertex Pharmaceuticals and CRISPR Therapeutics' gene therapy for sickle cell disease and beta thalassemia, exagamglogene autotemcel treatment (exa-cel), has been accepted for review by the US FDA, the European Medicines Agency, and the UK Medicines and Healthcare products Regulatory Agency.

#### [BioMarin gets FDA decision date for haemophilia gene therapy, but questions on review remain](#)

The US FDA has accepted BioMarin Pharmaceutical's approval application for the haemophilia A gene therapy, valoctocogene roxaparvovec (Roctavian) and has set a target decision date of 31 March 2023. This is the company's second attempt to win FDA clearance for its therapy, after the company was asked for longer-term data on treated patients. The company has provided updated data and has also offered to follow patients who participated in its research for 15 years.

#### [FDA creates "Super Office" to manage growing cell and gene therapy workload](#)

The US FDA has reorganised the Office of Tissues and Advanced Therapies (OTAT) into a "Super Office" within the Center of Biologics Research and Evaluation (CBER) to meet a growing cell and gene therapy workload.



### [Pfizer, Sangamo set to resume gene therapy study after safety delay](#)

Pfizer and Sangamo will restart the phase 3 trial of their haemophilia A gene therapy giroctocogene fitelparvovec, after the Food and Drug Administration (FDA) lifted a clinical hold on the study. The trial was paused voluntarily after patients treated with the therapy produced higher than expected levels of Factor VIII.

## 7 COVID-19

This section contains news articles, peer reviewed papers and industry publications on the coronavirus disease (COVID-19) pandemic and its effect on blood and blood related treatments and services.

### 7.1 COVID-19 effect on blood, blood diseases and related services

- [COVID-19 disruptions led to lowest number of public elective surgeries performed in over a decade](#)
- [Court intervenes after baby's parents refuse 'vaccinated blood' transfusion](#)

### 7.2 COVID-19 research and treatment

#### [A systematic review of the safety and efficacy of convalescent plasma or immunoglobulin treatment for people with severe respiratory viral infections due to coronaviruses or influenza](#)

Meta-analysis of 32 studies found little evidence to support the general effectiveness of convalescent plasma (CP) or hyperimmune immunoglobulin (hIVIg) in treating patients with severe respiratory disease requiring hospitalisation. The review notes that the lack of controlled studies and the different amount of neutralizing antibodies contained in the CP used between studies affected the outcome of their analysis. The authors suggest that patients who are immunocompromised or have not produced antibodies prior to hospitalization would benefit the most from future studies and that a minimum titre for neutralizing antibodies should be established for studying the effectiveness of CP.

#### [COVID-19 associated coagulopathy in children: A multicentre observational cohort study](#)

This study looked at thrombosis and bleeding in children infected with COVID-19 to assess thromboprophylaxis use. The five-month study included 79 patients aged up to 18 years who had been admitted to paediatric hospitals in Canada with COVID-19 infection. Eleven patients received anticoagulant thromboprophylaxis with one thrombotic event recorded and one major bleed event observed.

#### [Convalescent plasma treatment for COVID-19 infected high-risk patients](#)

Researchers performed a retrospective analysis of 55 hospitalised COVID-19 patients at the University Hospital Duesseldorf who were treated with convalescent plasma due to high risk for disease progression. Researchers found that in COVID-19 patients with severe comorbidities, convalescent plasma did not significantly reduce mortality at the critical phase. However, they found that reduction in mortality is achievable with early convalescent plasma administration.

#### [Heterologous SARS-CoV-2 IgA neutralising antibody responses in convalescent plasma](#)

Researchers investigated and compared the impact of convalescent plasma IgA with IgG on virus neutralisation and antibody effector functions. They found that plasma IgA response to COVID-19 is relatively transient, peaking during acute infection and dominating the acute plasma neutralising response. While convalescent plasma IgA contributed to the neutralising antibody response, this response was variable and overall less potent than convalescent plasma IgG.

#### [Selective IgA deficiency may be an under-recognized risk factor for severe COVID-19](#)

Researchers investigated if patients with selective Immunoglobulin A (IgA) deficiency may be at higher risk of severe COVID-19 as the virus gains entry primarily through the upper respiratory tract mucosa, where IgA plays a critical protective role.

### [Efficacy of therapeutic plasma exchange in severe COVID-19 disease: A meta-analysis](#)

This study assesses the effectiveness of therapeutic plasma exchange (TPE) in reducing mortality in severe COVID-19 disease compared to standard treatment. Researchers identified 382 participants from six studies, including one randomised control trial and found overall, the length of ICU stay did not differ between patients who received TPE versus standard care. However, researchers did find TPE significantly reduced mortality in severe COVID-19 disease compared to standard treatment.

### [Prior vaccination has changed the composition of the COVID-19 convalescent plasma inventory](#)

In this paper researchers discuss convalescent plasma as an antibody therapy for COVID-19. They suggest there are significant differences in antibodies collected from non-vaccinated individuals at the beginning of the COVID epidemic compared to convalescent plasma currently being collected.

### [Acute-type acquired haemophilia A after COVID-19 mRNA vaccine administration: A new disease entity?](#)

Researchers report a case in which a young patient developed acute acquired haemophilia A (AHA) after receiving an mRNA COVID-19 vaccine but improved rapidly. Researchers compared this case with other reports of AHA after COVID-19 vaccination and suggest that the levels of FVIII inhibitors associated with acute AHA decrease more rapidly in such cases than in idiopathic AHA.

## 8 Other items of interest

This section contains general industry and regulator updates as well as developments in non-blood and non-COVID related diseases that may have flow on affects to the blood industry.

### [Abstracts for the Australian and New Zealand Society of Blood Transfusion \(ANZSBT\) stream of the BLOOD 2022 Meeting 11th – 14th September 2022](#)

Abstracts for the Australian and New Zealand Society of Blood Transfusion (ANZBT) stream from the Blood 2022 Meeting held in Sydney earlier this year was made available 29 November 2022.

### 8.1 NBA - National Blood Sector Research and Development Program

#### [Completed Grants from the National Blood Sector Research and Development Program | National Blood Authority](#)

This page has been updated to include all publications and outcomes from projects completed through the National Blood Sector Research and Development Program.

#### [The effect of intravenous iron and blood transfusion on patients outcomes in women with low haemoglobin after birth](#)

This Patient Blood Management (PBM) Project grant from [Round 2](#) of the NBA's grant program has recently completed. The project was led by A/Prof Seng Chai Chua at the Western Sydney Health District. This study evaluated levels of haemoglobin postpartum after intravenous (IV) iron versus red blood cell (RBC) transfusion. The study of 120 women showed that IV iron infusion was as effective as RBC transfusion, and that IV iron was tolerated well, with no increase in adverse events including infection. The study has possible impacts on known evidence gaps in the NBA Patient Blood Management Guidelines, Module 5. The project team noted that using IV iron over RBC transfusions is projected to generate \$348.63 worth of savings per patient. Once published, the outcomes from this project will be made available on the [NBA website](#).

### 8.2 Lifeblood

#### [Lifeblood: Things that make you go "hmm"](#)

Lifeblood have compiled some fun facts about blood and blood donation in Australia.



### 8.3 Research and development news

#### [A new Vega enters the galaxy with bleeding disorder antibody set for 2023 trial](#)

Biotech incubator Star Therapeutics has launched another galaxy-themed drug developer, Vega, which next year will test a new antibody for von Willebrand disease (VWD), currently treated by Takeda's Vonvendi.

#### [International Society of Blood Transfusion Working Party on Red Cell Immunogenetics and Blood Group Terminology Report of Basel and three virtual business meetings: Update on blood group systems](#)

The International Society of Blood Transfusion has released an update on blood group systems, with 378 antigens now recognised, of which 345 are clustered within 43 blood group systems while 33 still have an unknown genetic basis.

#### [Mini 'bone marrow in a dish' could boost anti-cancer treatments](#)

Scientists in the UK have made the first bone marrow 'organoids', recreating the key features of human bone marrow. It will allow for the screening of multiple anti-cancer drugs at the same time, as well as testing personalised treatments for individual cancer patients. The senior study author hopes that this new technique will speed up the development and trials of new blood cancer treatments, getting novel products to patients faster.

#### [Lab grown blood given to people in world first clinical trial](#)

Scientists have transfused ex-vivo grown blood cells for the first time. A clinical trial in the United Kingdom is studying the lifespan of the lab grown cells compared with infusions of standard red blood cells from the same donor. Two people have been transfused with the lab grown red cells and are being closely monitored with no untoward side effects reported. Grown blood cells could improve treatment for sufferers of rare blood diseases while reducing demand on blood supplies

#### [A data-informed system to manage scarce blood product allocation in a randomized controlled trial of convalescent plasma](#)

Researchers designed a custom-made, computerised system to manage the inventory and allocation of COVID-19 convalescent plasma (CCP). A model with supply and demand forecasting was developed to guide the equitable allocation of CCP at hubs across Canada (excluding Québec).

#### ['Smart' red blood cells could address the antibiotic resistance crisis, scientists say](#)

Researchers have modified red blood cells and tested their potential as drug carriers. They found that the modified red blood cells safely carried potent antibiotics to selectively target and kill bacteria, without harming healthy cells.

#### [Citruillinated fibrinogen forms densely packed clots with decreased permeability](#)

This study investigated the effect of fibrinogen citruillination on the structure of fibrin clots. Citruillinated fibrinogen has been detected in human plasma and it decreases the decomposition and mechanical resistance of fibrin clots.

#### [Genetically modified herpes combats advanced cancers](#)

Researchers have modified a version of the herpes simplex virus to treat a range of advanced cancers, with a quarter of treatment recipients experiencing tumour size reduction in early testing.

### 8.4 Industry news

#### [Bluebird sells regulatory fast pass to Argenx for \\$102M](#)

Gene therapy developer Bluebird bio has sold a voucher that speeds up US drug reviews to Dutch biotechnology company Argenx. The sale comes after the FDA approved two of the company's rare disease gene therapies, Zynteglo and Skysona, both of which came with so-called priority review vouchers that can be resold to other companies for use on their new drug applications.



### [Grifols says U.S. blood donors' lawsuit won't have material impact, shares down](#)

Grifols has confirmed that around 54,000 donors in Illinois have filed a lawsuit claiming the company breached data protection regulations.

### [Blood BioTech Aegros to build \\$352m manufacturing hub in Qld](#)

Local biopharmaceuticals company Aegros will establish a \$352 million manufacturing facility in Queensland for therapeutic plasma products. The facility will be built at BioPark Australia in Greater Springfield, with the expectation to have a peak output capacity of one million litres of blood plasma products when operational.

### [Private investment firm snaps up Pfizer facility in Western Australia](#)

Bridgewest Group, a private investment firm, has signed an agreement to purchase Pfizer's sterile injectable facility in Perth. Pfizer was planning to stop manufacturing in 2023 and close the site officially in 2024. The Bridgewest facility has approval to supply around 90 countries with drug products and will be acquiring several other drug products from Pfizer to make and sell.

### [Australia's CSL in mRNA vaccine licensing deal with U.S.-based Arcturus](#)

CSL Ltd has signed a licensing deal with Arcturus Therapeutic that will provide access to the US drug developer's messenger RNA (mRNA) vaccine technology. CSL have stated they will seek to develop vaccines for influenza, COVID-19, and other respiratory viral diseases with the mRNA technology.

### [Novo Nordisk announces the completion of the Forma](#)

Novo Nordisk has completed its acquisition of Forma Therapeutics, a clinical-stage biopharmaceutical company focused on treatments for people with sickle cell disease (SCD) and other rare blood disorders.

### [BioNTech to build an mRNA hub in Australia](#)

BioNTech has announced a partnership with the state of Victoria to establish a messenger RNA research and manufacturing hub in Melbourne. BioNTech will build a facility with the ability to produce mRNA vaccines locally but will focus primarily on research and development.

### [Australia's CSL raises annual profit forecast on Swiss acquisition](#)

Australian biopharmaceutical company CSL Ltd has raised its annual profit guidance by \$2.4- 2.5 billion, as a result of its purchase of Swiss drugmaker Vifor Pharma.

## 8.5 Government & policy

### [The accelerated approval pathway is evolving in plain sight, with or without congressional help](#)

The FDA is prioritising the reform of its accelerated approval pathway, with the agency signalling it's willing to act on the reforms without immediate movement from Congress.

### [White paper on pandemic preparedness in the blood supply](#)

The WHO has released a recommendations paper covering seven key issues requiring action to improve planning for future pandemics. The main themes included the value of preparedness, current risks to the blood supply, supply chain vulnerabilities, and the role of innovation in increasing resiliency and safety.

## 8.6 Other diseases and developments

### 8.6.1 Malaria

- [Smartphone-connected device uses light to detect malaria – in 10 seconds](#)
- [World malaria report 2022](#)
- [Invasive Asian mosquito 'can survive anywhere,' could alter malaria landscape in Africa](#)
- [Placental malaria may slow glucose flow to the fetus, NIH-funded study suggests](#)
- [Monoclonal antibodies against malaria](#)



### 8.6.2 Dengue

- [Climate change 'brings diseases such as dengue fever to Europe'](#)
- [Takeda's dengue vaccine wins EU approval](#)
- [Why is dengue becoming such a serious public health threat?](#)
- [Mosquito study finds genetics at play when it comes to who gets bitten more frequently](#)
- [Soaring platelet demand after spike in dengue cases](#)

### 8.6.3 Japanese Encephalitis

- [Ozzie vs Mozzie](#)
- [Estimating the Distribution of Japanese Encephalitis Vectors in Australia Using Ecological Niche Modelling](#)
- [Japanese encephalitis virus warning ahead of wet summer](#)
- [Aust scientists fear encephalitis outbreak](#)
- [Australian Government Department of Health and Aged Care: Japanese encephalitis virus](#)

### 8.6.4 Monkeypox

- [U.S. FDA authorizes Roche's monkeypox test](#)
- [Scientists warn dangerous monkeypox variant circulating in central Africa could fuel new outbreaks](#)
- [Worldwide Monkeypox Cases Surpass 70,000, WHO Says](#)
- [Research collaboration to provide data needed to stop monkeypox in its TraX](#)
- [Interim guidance for monkeypox among patients with HIV](#)

### 8.6.5 Ebola

- [Ebola Screening Activated in the UK](#)
- [Can mRNA vaccines transform the fight against Ebola?](#)
- [What is Ebola and why is Uganda's outbreak so serious?](#)
- [Ebola has moderate risk of spreading outside Uganda, WHO says](#)
- [Ebola: Uganda introduces its first lockdown to tackle the virus while it waits for vaccines](#)

### 8.6.6 Ross River Virus

- [Ross River virus - Urgent Warning](#)

### 8.6.7 Polio

- [NSW Health on high alert for polio cases in Australia](#)
- [Is polio back? Cases emerge overseas and Australia starts testing sewage](#)