**Table of contents**

<table>
<thead>
<tr>
<th>Executive summary</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overview of the Centre for Innovation</td>
<td>5</td>
</tr>
<tr>
<td>Research and development progress</td>
<td>6</td>
</tr>
<tr>
<td>Safety and sufficiency of the blood supply</td>
<td>6</td>
</tr>
<tr>
<td>Blood products</td>
<td>11</td>
</tr>
<tr>
<td>Hematopoietic stem cells</td>
<td>19</td>
</tr>
<tr>
<td>Organ and tissue donation and transplantation</td>
<td>21</td>
</tr>
<tr>
<td>Building capacity in transfusion and transplantation science and medicine</td>
<td>22</td>
</tr>
<tr>
<td>Formal training</td>
<td>22</td>
</tr>
<tr>
<td>Education opportunities</td>
<td>24</td>
</tr>
<tr>
<td>Knowledge dissemination</td>
<td>28</td>
</tr>
<tr>
<td>Increasing impact through collaborations</td>
<td>32</td>
</tr>
<tr>
<td>An international collaboration to develop clinical guidelines for transfusion medicine</td>
<td>32</td>
</tr>
<tr>
<td>The Alliance of Blood Operators</td>
<td>33</td>
</tr>
<tr>
<td>Risk-based decision-making framework for blood safety</td>
<td>34</td>
</tr>
<tr>
<td>Provision of research samples and data</td>
<td>35</td>
</tr>
<tr>
<td>Governance</td>
<td>35</td>
</tr>
<tr>
<td>References cited</td>
<td>38</td>
</tr>
<tr>
<td>Appendix I: Funded projects</td>
<td>44</td>
</tr>
<tr>
<td>Appendix II: Publications</td>
<td>51</td>
</tr>
<tr>
<td>Appendix III: Health Canada financial contribution</td>
<td>73</td>
</tr>
</tbody>
</table>
Dear readers,

Canadian Blood Services, through its Centre for Innovation, improves today’s transfusion and transplantation products, services, and clinical care for Canadians, and enriches tomorrow’s possibilities for innovative approaches in our field. The Centre for Innovation pursues these goals by fostering relevant discovery and development research, facilitating dissemination and application of knowledge, educating the next generation of scientific and health-care experts, and engaging with an interdisciplinary network of partners in Canada and beyond.

We are pleased to submit a Progress Report for 2016–2017, which describes the output of our program and the impact achieved, as measured by our performance measurement framework and as illustrated by highlights of our cumulative and collaborative work.

A selection of achievements from the past year:

- Clarified how pathogen inactivation technology affects the quality parameters of blood products and validated the production process for platelets treated with pathogen inactivation technology.
- Showed that apheresis fresh frozen plasma remains biologically active after 120 hours of refrigerated storage, providing evidence for an upcoming change in regulations to reduce waste while maintaining the high quality of Canadian Blood Services’ plasma products.
- Developed two new potential anticoagulant drugs that rapidly and safely dissolve clots in mouse models.
- Advanced the development research required to deliver Canada’s first plasma-reduced blood forming stem cell unit, enabling a reduction of the freezing solution needed and a shorter transfusion time.
- Provided the scientific knowledge and evidence needed to support important improvements in Canadian Blood Services’ supply chain operations, such as the transition from 5 to 7-day platelets and the shift to new manufacturing equipment.
- Designed and facilitated a new research funding program, in close collaboration with Héma-Québec, to generate scientific evidence to evaluate alternative screening approaches for blood or plasma donors, specifically with respect to deferral policies for men who have sex with men. This program was developed with the generous incremental support of Health Canada, an important partner in this work.
- Supported investigation into mitigating iron deficiency in blood donors, leading to changes in the inter-donation interval and hemoglobin requirements that further enhance donor safety.
- Further developed the Alliance of Blood Operators (ABO) Risk-Based Decision-Making Framework for Blood Safety, facilitated its international uptake, and obtained benefit from applying the framework to a number of issues affecting the Canadian blood supply.
- Launched a new Professional Education website, focusing on relevant and high-quality transfusion and transplantation content. The site has attracted more than 62,000 visitors, viewing 167,000 pages since launch in August 2016.
- Mobilized International Collaboration for Transfusion Medicine Guidelines (ICTMG) through systematic reviews to develop clinical guidelines, a new website, and, together with the AABB, a platelet guidelines podcast.
Achieved national expansion of Transfusion Camp, in partnership with Drs. Callum and Lin from Sunnybrook Health Sciences Centre, engaging over 170 postgraduate medical residents from seven Canadian universities and one university in the United Kingdom.

Developed and delivered a Products and Patients training module, in collaboration with Canadian Blood Services Quality and Regulatory Affairs, reaching more than 3,300 Canadian Blood Services employees.

Program outputs by the numbers:

- Our research network published 312 peer-reviewed publications and delivered over 300 oral and poster presentations at national and international conferences.
- The Centre for Innovation shared 29 technical reports within Canadian Blood Services and with partners to inform product and process improvements.
- 25 professionals were formally trained through our national training programs.
- Over 70 major education events were organized or supported, attracting an estimated 6,500 professionals.
- Our research informed four Health Canada license amendments and three changes in national and international standards.

This report details the progress that has been made over the last year by our research and education community, including scientific and medical staff, adjunct investigators, grantees and collaborators. We remain deeply grateful for the ongoing support we receive from Health Canada, the provincial and territorial ministries of health, and our partners and colleagues across the transfusion and transplantation medicine communities. And we remain inspired to engage in future research, development, and education to support a safe and effective system of blood and related biologics for Canadian patients — a system that is well-positioned to address emerging scientific and clinical knowledge, risks, opportunities and technologies.

Sincerely,

Dr. Dana Devine  
Chief Medical and Scientific Officer  
Canadian Blood Services

Judie Leach Bennett  
Director, Centre for Innovation  
Canadian Blood Services
Overview of the Centre for Innovation

The Canadian Blood Services Centre for Innovation drives improvements in blood transfusion, cellular therapy and transplantation — bringing clarity and insight to an increasingly complex health care future. In collaboration with an extended network of partners, the Centre fosters discovery and clinical research, conducts product and process development research, translates knowledge through leading practices, and builds capacity through training and education.

The Centre for Innovation focuses on making a measurable impact across five program areas: Research, Product and Process Development, Knowledge Mobilization and Education, Policy Research and Leading Practices, and International Collaboration. Over the last year, our programs have delivered value to the system as exemplified by the key metrics highlighted below and by our key achievements and their impact highlighted throughout this report.
Research and development progress

Through its competitive research funding programs, its dedicated Product and Process Development group and facility, and its support to 11 principal investigators and 29 medical experts and epidemiologists, Canadian Blood Services continues to facilitate research for the creation of new knowledge that informs decision-making and ensures that Canada’s health-care system is well-positioned to address emerging medical and scientific trends in transfusion and transplantation.

Safety and sufficiency of the blood supply

Donors and donations

To protect donor health, Canadian Blood Services tests donors for hemoglobin prior to every whole blood donation. However, iron stores (ferritin levels) are not routinely assessed. Drs. Mindy Goldman and Sheila O’Brien* recently performed a large study in over 12,000 donors.¹ They found that 2.9 per cent of first-time male donors, 41.6 per cent of repeat male donors, 32.2 per cent of first-time female donors, and 65.1 per cent of female repeat donors had low ferritin levels (<25 µg/l). Risk factors for iron deficiency were female sex, frequency of donation, and for male donors, having a hemoglobin level close to the cut-off. Based on these findings and international precedent, Canadian Blood Services changed the interdonation interval to 84 days (from 56 days) for female whole blood donors in December 2016 and increased the minimum hemoglobin level for male donors to 130 g/l in March 2017.

These policies are considered first steps towards addressing iron deficiency in blood donors, and the impact on donor return and hemoglobin deferral is being closely monitored. Drs. Goldman and O’Brien, along with international colleagues, are exploring additional measures that may be needed to ensure donor health², including improved education of all donors about iron needs³, and selective ferritin testing of donors. Further research will focus on reducing the cost and enhancing the benefit of selective ferritin testing. We will also continue to increase donor and physician knowledge about iron through a variety of channels, including our RED blog.

In August 2016, Canadian Blood Services and Héma-Québec reduced the blood donation ineligibility period for men who have sex with men (MSM) from five years to one year. In June 2016, the Minister of Health announced that Health Canada would provide $3M to Canadian Blood Services and Héma-Québec to implement an MSM Research Program. The overall rationale for this program is to ensure the generation of adequate evidence-based research for alternative screening approaches for blood donors, which could evolve the current one year deferral policy for MSM while maintaining the safety of the blood supply.

* The names of Canadian Blood Services staff, including Centre for Innovation investigators, medical experts and epidemiologists, are bolded throughout the report.
Under the leadership of the Centre for Innovation and in collaboration with Héma-Québec and Health Canada, a two-day international workshop was held in January 2017 to identify knowledge gaps and develop research priorities to address those gaps. Representatives from Canadian Blood Services and Héma-Québec met with Canadian researchers from a variety of disciplines and experts from around the world to discuss the research required to evaluate approaches to donor screening and their impact on the supply and safety of blood products. Representatives from Health Canada, patient groups, and members of the LGBTQ community also participated. Based on the workshop discussions and the research priorities identified, a new competitive MSM Research Grant Program was launched in February 2017 with research projects expected to be identified and funded in Summer 2017.

Blood-borne pathogens

The Zika virus outbreak has been a major concern for blood operators around the world in 2016 and 2017. To guide donor deferral policies in Canada, Drs. Goldman and O’Brien collaborated with the Ottawa Hospital Research Institute to examine the risk of exposure to blood products during pregnancy in 45,179 women. They found that very few pregnant women received blood products — only 0.124 per cent received a transfusion during pregnancy, with approximately one-third occurring during the first trimester. This suggests that risk of maternal and fetal exposure to Zika and other emerging pathogens through blood products is very low. An abstract by Héma-Québec investigators and co-authored by Drs. O’Brien, Goldman, Margaret Fearon and Dana Devine describing the risk-based approach used by Canadian blood operators to make decisions on Zika virus risk mitigation was presented at the 2016 AABB annual meeting and the full manuscript has been accepted for publication by Transfusion. Based on their risk evaluation, a Health Canada license amendment for Zika-related travel deferral was approved.

For nearly two decades, Canadian Blood Services has deferred donors who have spent a cumulative time of three months in the U.K. or France, or five years or more in Western Europe, since 1980. In 2005, stop dates were implemented based on the estimated decreased risk of transfusion-transmitted variant Creutzfeldt-Jakob disease (vCJD). Drs. Goldman and O’Brien reported on the impact of stop dates on donor deferral rates and donor response in an abstract presented at the AABB. They found that stop date implementation for U.K./France travel decreased the donor deferral rate from 2.1 per cent to 1.1 per cent for first-time donors and from 0.2 per cent to 0.03 per cent for repeat donors. However, stop dates had little to no effect on deferrals for Western Europe travel (no change in first-time donors, and a decrease from 0.03 per cent to 0.02 per cent for repeat donors). Donor surveys showed that 94 per cent of deferred donors confirmed deferrable travel history, and only 0.3 per cent of donors were non-compliant with the U.K./France deferral, indicating that most deferrals are correctly applied and non-compliance is rare. Their findings confirm the benefit to Canadian Blood Services from implementing stop dates as a way to attract more new donors that would otherwise be deferred.

“All in all, [the meeting] was an extremely productive experience. One that led to a better understanding of the issues around deferral policies for blood donors who are men who have sex with men and to the establishment of new collaborations among researchers, regulators, blood operators and stakeholders.”

Dr. Graham Sher, CEO of Canadian Blood Services, in RED blog (Read more)
Drs. O’Brien, Goldman and Fearon released a short report describing the residual risk of HIV, HCV and HBV in Canada. They found that all three viruses continue to have a very low risk of transmission through Canadian blood products. The incidence rate per 100,000 person years for HIV was 0.28, HCV 1.0 and HBV 0.26. The residual risk of HIV was 1 per 21.4 million donations; HCV was 1 per 12.6 million donations and HBV was 1 per 7.5 million donations.

Hepatitis E is a virus of emerging importance to blood suppliers, as it is a cause of transfusion-transmitted infection. This virus was commonly thought to be a cause of hepatitis primarily in developing countries, transmitted through contaminated water or food. It is now recognized as a cause of infection in endemic countries as well, where it is likely to be a zoonotic infection associated with swine and wild game. The prevalence of this virus in Canada was previously unknown, but a Canadian Blood Services group headed by Drs. Fearon, O’Brien and Mark Bigham and Vito Scalia, in collaboration with Héma-Québec and the National Microbiology Laboratory in Winnipeg, conducted a donor prevalence and risk survey. Donor prevalence based on antibody testing was 5.8 per cent. The results of this analysis will soon be published in the journal Transfusion. A larger survey, using nucleic acid testing (50,000 Canadian blood donors) is now taking place, under the same team, in collaboration with Héma-Québec and the American Red Cross. This study will produce the largest amount of data on hepatitis E (including antibody, genotyping, and viral load testing) available to date in Canada.

The Ebola virus outbreak in 2014–2016 was a concern for blood operators around the world. Although the threat of Ebola to the Canadian blood system was always very low and is even lower now that the outbreak has passed, development of effective treatment options will be important for future outbreaks. In collaboration with national and international experts, Dr. Donald Branch has been studying how Ebola virus infects its hosts. They discovered that Ebola virus inhibits stress granule formation, which may be involved in antiviral innate immunity. Improving our understanding of viral mechanisms may help in the development of new therapeutic options.

Pathogen inactivation (PI) technology is a potential solution to the problem of blood-borne pathogens, particularly emerging pathogens or those insufficiently detected in tests. Mirasol, a PI treatment provided by Terumo BCT, is currently licensed in Canada for platelets and plasma products. Development of this technology for red blood cells has been more challenging due to its harmful effects on red blood cell quality. Drs. Devine and William Sheffield found that Mirasol treatment of whole blood altered red blood cell quality parameters and increased the proportion of cells undergoing eryptosis during storage in blood bank conditions. Dr. Devine did a proteomics analysis of red blood cells derived from Mirasol-treated whole blood and identified changes in seven membrane proteins. Research to clarify how Mirasol impacts red blood cell quality will be important for optimizing PI methods for all blood products.

Influence on clinical practice and system safety

Our research and our experts have informed the development of new clinical guidelines related to cytomegalovirus (CMV).

“The National Advisory Committee recommends that CMV safe (leukoreduced) and CMV IgG seronegative products be considered equivalent except for intrauterine transfusion.”
In similar efforts, Dr. Devine has completed several studies examining how platelets respond to Mirasol. Her research group found that Mirasol significantly reduced mRNA levels in platelets; shorter mRNA strands were more sensitive to this effect.\textsuperscript{11} Qualitative proteomic analysis showed that 26 unique proteins were changed by PI treatment.\textsuperscript{12} This was the first study to show that platelets can synthesize proteins despite the riboflavin and UV treatment. Dr. Devine found that PI increased reactive oxygen species generation, cytochrome c release and mitochondrial translocation of the BAX and BID proteins in platelets during storage.\textsuperscript{13} These changes are associated with decreased platelet quality and were prevented by a mitogen-activated protein kinase inhibitor. By furthering our understanding of platelet response to PI, this research could lead to improved PI processes that enhance platelet quality. Dr. Devine recently worked with collaborators in Canada, the Netherlands and Norway to validate the production processes for PI-treated platelets.\textsuperscript{14} They showed that transport conditions and four hours of ambient light exposure had no negative effect on the in vitro quality of Mirasol-treated platelets.\textsuperscript{14} This research will be helpful if routine Mirasol treatment of platelets is implemented by Canadian Blood Services.

Trauma transfusion packages consist of red blood cells, plasma, and platelets at a set ratio.\textsuperscript{15} Dr. Devine validated a new assay for platelet function, rotational thromboelastometry\textsuperscript{16}, and used it to examine the effects of PI on trauma transfusion packages.\textsuperscript{15} Although PI-treated platelets and plasma had decreased hemostatic ability, simulations of transfusion scenarios based on 30 per cent blood replacement with a transfusion trauma package showed no difference in hemostatic ability among packages containing treated and non-treated blood components.\textsuperscript{15} This suggests that the decreased quality observed after PI treatment has little effect on recipient outcome unless a large (>50 per cent) volume of blood is replaced.

### Adverse transfusion reactions

Adverse transfusion reactions can occur in a patient following transfusion of blood products. Understanding how and why those reactions occur can help prevent them.

Transfusion-related acute lung injury (TRALI) presents as acute respiratory distress after a transfusion and is a leading cause of transfusion-related mortality. Researchers believe TRALI is caused by antibodies or other bioactive molecules from the donor, but there is limited understanding of the basic mechanisms involved. Dr. John Semple and Dr. Wolfgang Kuebler received funding from the Canadian Blood Services/Canadian Institutes of Health Research (CIHR) operating grant program to study the mechanisms of TRALI. Dr. Semple discovered last year that C-reactive protein (CRP) worsened TRALI in a mouse model; this year his group followed up by examining CRP levels in human TRALI patients. They found that CRP levels were significantly elevated in TRALI patients compared to transfused control patients, suggesting that CRP might be a risk factor for TRALI and that targeting CRP could be an effective therapeutic strategy.\textsuperscript{17} Drs. Semple and Kuebler collaborated on a project investigating the role of T-regulatory cells and dendritic cells in TRALI. They found that both T-regulatory cells and dendritic cells provided protection from TRALI in a mouse model.\textsuperscript{18} Furthermore, injection of interleukin 10 completely prevented the development of TRALI in mice, suggesting another promising therapeutic approach. Drs. Semple and Kuebler also developed a new mouse model of TRALI based on intraperitoneal injection of lipopolysaccharide followed by transfusion of aged platelets.\textsuperscript{19} This model will allow further study of TRALI mechanisms and testing of new potential drugs.

Red blood cell alloimmunization can cause severe hemolytic transfusion reactions that may lead to death. Dr. Mark Scott is studying the ability of membrane-grafted methoxypoly(ethylene glycol) (mPEG) to prevent this alloimmunization through immunocamouflage. His group recently investigated concerns raised over the immunogenic risk of PEG by treating mice with soluble PEG or mPEG-red blood cells and found that mice did not develop anti-PEG antibodies.\textsuperscript{20}
The monocyte monolayer assay is a test that predicts the clinical significance of a transfusion recipient’s antibodies. Although it has been used clinically for over 35 years, the conditions were never fully optimized. Dr. Branch recently determined the ideal anticoagulants, blood storage conditions and pH for the assay. The assays using autologous patient monocytes gave consistent results that corresponded to clinical outcomes, but allogeneic monocytes did not, indicating that only autologous monocytes should be used. Dr. Branch found that the assay is very versatile and can be used to examine Fcγ receptor-mediated phagocytosis. This work continues to refine a time-tested technique that predicts whether or not a patient’s antibodies will result in red blood cell destruction if blood from specific donors is transfused. Improvements to this assay could reduce ineffective transfusions and adverse events.

Serious adverse transfusion reactions may be caused by hemolysis of transfused red blood cells. Dr. Jason Acker and collaborators found that excessive hemolysis of transfused red blood cells led to toxicity from acute iron overload in cardiac surgical patients. This research suggests that mitigating the iron overload could reduce the severity of red blood cell transfusion reactions.

Blood conservation and utilization
To maintain a sufficient blood supply, reduce health-care costs and protect the health of potential transfusion recipients, it is important to ensure that blood products are transfused only when the benefits outweigh the risks.

Dr. Devine collaborated with Dr. Marc Germain from Héma-Québec and other members of the BEST collaborative to investigate changing trends in red blood cell use (Trends for Collection study). They examined red blood cell use in blood centres across the U.S. and in national or provincial blood services around the world and found that, overall, red blood cell distribution has declined from fiscal years 2010 to 2014. However, the proportion of O-negative units distributed increased over the same time period, leading to recurring shortages. Prof. Nancy Heddle and two of Canadian Blood Services’ medical officers, Drs. Donald Arnold and Michelle Zeller, worked with other colleagues from the McMaster Centre for Transfusion Research (supported by a Centre for Innovation Program Support Award) to complete a two-year retrospective study examining the use of group O red blood cell units at three academic hospitals. They found that many patients with non-O blood were being transfused with group O units. The percentage of group O red blood cells transfused to ABO non-identical recipients has been increasing, going from 7.8 per cent in 2011 to 11.1 per cent in 2013. This suggests that hospital policies should be targeted to ensure that red blood cell units are being transfused appropriately to maintain a sustainable blood supply. This goal is furthered by the work of Dr. Kathryn Webert and her collaborators, who have been studying ways to evaluate the appropriateness of red blood cell transfusions. In 2016, they published a BloodBrief – An update on ONeg – and issued a hospital customer letter to promote optimal utilization of O-negative units. Dr. Webert and her collaborators used retrospective chart review to audit 10 Ontario hospitals and determined that the optimal evaluation method was a chart audit of 50 red blood cell transfusions with adjudication using robust criteria. This optimized method will be used in future studies to evaluate the utilization of blood products in Canada in order to inform clinical practice.
Dr. Shane English, a neuro-intensivist and adult intensivist at the Ottawa Hospital and associate professor at the University of Ottawa, received a Canadian Blood Services/CIHR operating grant to study red blood cell transfusion in acute aneurysmal subarachnoid hemorrhage patients. His team has published a protocol for the SAHaRA pilot clinical trial, which compares a liberal transfusion strategy (hemoglobin ≤100 g/l) with a restrictive strategy (hemoglobin ≤80 g/l). This trial will help determine the optimal red blood cell transfusion strategy for this unique patient group.

Blood conservation strategies are important to minimize the number of transfusions needed. Dr. Donald Brooks, a professor at the University of British Columbia’s Centre for Blood Research, received a Canadian Blood Services/CIHR operating grant to develop new methods for sealing blood vessels to improve blood conservation. His research team has developed a biocompatible cellulose membrane that can adhere to cut tissue margins and efficiently arrest human red blood cells, stopping bleeding. This new material could improve wound dressings and potentially decrease the amount of blood products that are needed in a trauma setting.

Dr. Melissa Parker, an associate professor and staff physician at McMaster Children’s Hospital, received a Canadian Blood Services/CIHR New Investigator Salary Award to improve the outcomes for children with sepsis. This project included evaluating the use of blood products to treat septic shock. She completed the SQUEEZE pilot study, which examined the efficacy of a fluid-sparing strategy versus usual care. The SQUEEZE trial also provided the opportunity to examine the experiences of substitute decision-makers by interviewing parents and guardians of critically ill children enrolled into a resuscitation trial without their knowledge or prior consent. This research could change the way that blood products are used to treat septic shock in pediatric patients. Dr. Parker also collaborated with the Canadian Critical Care Trials Group to identify barriers and facilitators for conducting high-quality randomized controlled trials in pediatric critical care. They found that lack of funding and time were the main barriers, and that research networks and increased funding were the major facilitators, suggesting that funding support (such as that provided by Canadian Blood Services) and further development of research networks could improve the quality of future clinical trials.

### Blood products

**Red blood cells**

Red blood cells are the most common blood product Canadian Blood Services distributes. During refrigerated storage, which may be up to 42 days, red blood cell units undergo changes which are collectively termed the storage lesion. It remains unclear to what extent, if any, these changes affect recipient outcomes. Supported by a Program Support Award for the McMaster Transfusion Research Program, Canadian Blood Services adjunct scientist Prof. Heddle collaborated with researchers from Canada (including Drs. Webert and Arnold), Australia, the U.S. and Israel to study the effects of red blood cell storage time on recipient outcome in the INFORM trial. The INFORM study examined the outcomes of 20,858 patients with type A or O blood and found that mortality rates were no different between patients given the freshest-available vs. the oldest-available red blood cell units. These findings confirm the results of several smaller studies published recently and will reassure transfusion medicine practitioners that older blood may be transfused.
without an increased risk of death. However, morbidity was not addressed in this study. New technology that allows detailed non-invasive analysis of each red blood cell unit could help connect the effects of the storage lesion on patient morbidity.

Liposome treatment has been suggested as a way to improve red blood cell quality by reducing damage during storage. Dr. Jelena Holovati, a Canadian Blood Services adjunct scientist, and Dr. Acker showed that treatment with unilamellar liposomes decreased the hemolysis of rat red blood cells. The treatment did not impair the ability of red blood cells to compensate for anemia in a rat model. Immune stimulation is a potential safety concern with liposome treatment. In a collaboration with Dr. Branch, the groups found that liposome treatment did not change the immune profile of stored red blood cells, supporting the development of this new technology for red blood cell processing. With Prof. Heddle and Dr. Andrew Shih from McMaster University, Dr. Acker compared two processing methods for red blood cells (red blood cell filtration vs. whole blood filtration) by quantifying cell-free DNA, which is an emerging biomarker associated with adverse patient outcomes. Units processed using whole blood filtration had higher levels of cell-free DNA, suggesting that such information may be considered when evaluating processing methods. In collaboration with Dr. Michael Kolios from Ryerson University, Dr. Acker developed two new technologies for monitoring the quality of red blood cells. Dr. Acker’s laboratory also evaluated how hemolysis is affected by the different equipment and procedures used by sixteen members of the BEST Collaborative. They found that hemolysis varied significantly from 0.16 to 0.32 per cent depending on the combination of methods.

The use of di-ethylhexyl-phthalate (DEHP) in blood bags has been questioned recently due to concerns about potential toxicity. Dr. Devine, in collaboration with Dr. Acker and others from the BEST Collaborative, polled 15 blood centres in nine countries and found that none have fully switched to non-DEHP blood bags. About half of the centres said they would move to an alternative red blood cell storage solution to improve red blood cell quality. These international studies that compare various blood operators’ practices in red blood cell manufacturing and storage provide evidence-based data for investigating ways to maximize the safety and efficacy of the blood products we produce.

To prevent bacterial contamination, the “30-minute rule” requires the discard of red blood cell units that are exposed to uncontrolled temperatures for more than 30 minutes. Dr. Sandra Ramírez-Arcos collaborated with Héma-Québec researchers to provide final evidence supporting the recent decision to move to a “60-minute rule” in Canada. They spiked red blood cells with two types of bacteria (mesophilic and psychrophilic) and left the units out at room temperature for 30 or 60 minutes, six times during storage. Mesophilic bacteria did not proliferate in the red blood cell units; the growth rate of psychrophilic bacteria was not different between the 30-minute and 60-minute units. This research, and several earlier studies, contributed to the Canadian Standards Association’s decision to extend the 30-minute rule to 60 minutes. Effective in 2016, this new standard will reduce the number of units of red blood cells discarded and is expected to save the blood system significant funds without affecting blood product efficacy or patient safety. More recently,
the Canadian Society for Transfusion Medicine (CSTM) published a new version of its Standards for Hospital Transfusions Services in which the 30-minute rule was revised to 60 minutes.

A retrospective study by Dr. Dean Fergusson (funded by a Canadian Blood Services/CIHR operating grant) with Dr. Acker and collaborators from Université Laval and the Ottawa Hospital Research Institute suggested that donor characteristics may affect transfusion outcomes. In their study, based on information from The Ottawa Hospital Data Warehouse, Canadian Blood Services and the Institute for Clinical Evaluative Sciences, red blood cell transfusions from younger donors and from female donors were linked with a slightly higher risk of death (adjusted hazard ratios of 1.06–1.08 and 1.08, respectively). This was the first study to suggest a link between the age or sex of the blood donor and the outcome of the recipient; however, retrospective studies must be interpreted with great caution, as they can easily be confounded by unknown factors. Before using these findings to guide any decisions, the results must be rigorously confirmed in additional studies, especially in light of a recent publication showing no link between donor characteristics and recipient outcomes in a Scandinavian population.

Dr. Acker also collaborated with researchers in Pittsburgh and Seattle to examine donor sex differences in red blood cell hemolysis. Red blood cells from male donors were more susceptible to hemolysis than those from female donors. In mice, orchiectomy improved red blood cell storage stability and testosterone treatment reversed this effect, suggesting that the effect is caused by testosterone levels in the donor. This research lays the foundation for learning more about how donor characteristics relate to recipient outcomes.

Although red blood cell units are normally refrigerated until being transfused, units of rare blood types may be frozen. Cryopreservation is not done routinely due to the high cost and potential toxicity associated with the current cryopreservation protocols. Dr. Robert Ben and Dr. Acker received Canadian Blood Services/CIHR funding to improve the cryostorage process for red blood cells. Dr. Ben developed a high-throughput screening method for identifying novel ice recrystallization inhibitors. This screen could generate new cryoprotectants to reduce the cell damage caused by ice crystal formation during the freezing process. Dr. Ben and Dr. Acker have identified key structural features of O-aryl-glycoside ice recrystallization inhibitors that predict cryopreservation efficacy. They showed that a new cryoprotectant formula containing hydroxyethyl starch and two small-molecule ice recrystallization inhibitors improved the quality of thawed red blood cells relative to the standard glycerol-based cryoprotectant.

The development of synthetic alternatives to red blood cells has been an active area of research for many years. Canadian Blood Services has awarded operating grants in this area. At the University of Toronto, Dr. Ronald Kluger has been developing chemical processes to produce chemical replacements for hemoglobin, including a hemoglobin-avidin-hemoglobin triple protein and a bis-hemoglobin tetramer. These large molecules are designed to avoid the vasoconstrictive side effects seen previously with hemoglobin replacements in animal models. Synthetic red blood cells could reduce the need for regular blood donors and would help address problems with inconsistent supply of blood products. If more shelf-
stable replacements can be developed, they would be extremely valuable in emergency settings where access to blood products is limited (for example, in search and rescue or military operations).

**Platelets**

Platelets are critical for the formation of blood clots. Many conditions can lead to low platelet numbers (thrombocytopenia) and require transfusion to manage the increased risk of bleeding. Canadian Blood Services supplied approximately 120,000 platelet doses in 2016–2017.

For platelets to maintain their function, platelet units must be stored at room temperature with constant gentle agitation. These storage conditions increase the risk of bacterial growth if the unit is contaminated. While transfusion reactions due to bacterial contamination are rare, they are an important concern as they can be fatal. **Dr. Ramirez-Arcos** is an expert in bacterial growth. She leads the development research group that supports Canadian Blood Services in implementing appropriate processes to minimize bacterial contamination. Platelet units are screened for possible bacterial contamination using samples drawn on day one and monitored throughout the platelets’ storage period. However, low levels of bacteria may not be detected in the screen. **Dr. Ramirez-Arcos** reported a case study of a woman who went into septic shock after transfusion of a platelet unit containing a visible clot. The transfused platelet unit tested positive for *Staphylococcus aureus*, which matched the strain in the patient’s blood; however, this contamination was not detected during routine screening. This case report highlights the need for routine visual inspection of platelet units before transfusion.

**Dr. Ramirez-Arcos’** research group showed recently that eight bacterial strains showed different growth patterns throughout the buffy coat platelet production process. For example, two strains that were isolated from expired platelet units (not detected during routine screening) did not grow during the initial holding step, whereas two strains involved in fatal transfusion events proliferated rapidly. The texture of the platelet bag may also affect the detection of bacteria through routine screening. A researcher funded by a Graduate Fellowship Program award, Narges Hadjesfandiari, worked with **Drs. Ramirez-Arcos and Devine** to show that bacterial adhesion and biofilm formation were significantly higher on rough bag surfaces. These findings could help in the development of improved platelet manufacturing processes or screening methods used to identify contaminated units.

Although **Dr. Ramirez-Arcos** mainly studies ways to improve the blood system in Canada, her research may also help people in other countries. She recently collaborated with researchers at Johns Hopkins University, Makerere University and the University of Montreal to study platelet transfusions in Uganda. Bacterial contamination was less frequent than previously reported, but was still a safety risk (0.3 per cent to 2.1 per cent of platelet units were contaminated). The researchers determined that Gram staining was an inadequate screening tool due to its low sensitivity, and recommended developing alternative methods. This could help reduce transfusion reactions in Uganda.

**Dr. Ramirez-Arcos’** international reputation contributed to her being asked to edit a special issue of the *Journal of Blood Transfusion* in 2016 – an issue devoted to the safety and quality of blood products. She was assisted by Dr. Denese Marks of the Australian Red Cross and **Drs. Acker and Sheffield** as associate editors. Included in the issue was a comprehensive review of established and emerging quality assessment methods for blood products contributed by **Drs. Acker, Marks, and Sheffield**. The authors concluded that, despite the development of novel quality assays, the current tests (including coagulation factor VIII activity for plasma, pH and yield for platelets, and hemolysis for red blood cells) are user-friendly and remain valuable tools to determine blood product quality, although evidence linking in vitro quality tests to clinical effectiveness remains sparse.
To optimize safety and improve cost-effectiveness, the Centre for Innovation examined bacterial detection in pooled platelets over a seven-day storage period. The team led by Dr. Ramirez-Arcos found that delaying sampling for bacterial detection in platelets from 24 hours to 36 hours or later, coupled with increased sampling volume to test growth in both aerobic and anaerobic conditions, improves the safety of platelet concentrates. The technical report has been accepted by our Supply Chain group, and will be used to support a Health Canada submission for moving to a seven-day shelf life for platelets. Based on analysis by Dr. John Blake, the change is expected to relieve inventory pressure and reduce platelet wastage.

Blood operators routinely monitor the pH of apheresis platelets as a marker for quality. To determine whether donor characteristics may affect platelet quality, Héma-Québec, in collaboration with Canadian Blood Services (Dr. Acker) and five other blood operators worldwide (BEST collaborative), compared the pH test results of 21,671 apheresis platelets with several donor characteristics. Donors with multiple pH test results had a strong correlation between each test, and a pH measurement below the 10th percentile was associated with female and younger donors. This suggests that platelet quality is influenced by donor-specific factors which remain constant over time.

Platelet apoptosis is a frequently studied factor in research examining platelet disorders. Dr. Heyu Ni and colleagues recently showed that mitochondrial inner transmembrane potential depolarization is not a good universal marker of platelet apoptosis, despite its common use for this purpose, as it may have false-positive results. This finding could improve the accuracy of future studies of apoptosis in platelets, which may be linked to platelet quality.

Dr. Patrick Provost, at Université Laval, received a Canadian Blood Services/CIHR operating grant to study platelet microparticles and microRNAs, which may be additional markers of platelet quality. With collaborators at Université Laval and Harvard Medical School, Dr. Provost recently used high-dimensional flow cytometry analyses to examine extracellular vesicles released by platelets and red blood cells. They found that computational algorithms revealed subtypes of arthritic patients based on extracellular vesicle heterogeneity, suggesting that similar algorithms could be used to investigate the function of these microparticles and their potential use as biomarkers. Dr. Provost also showed that microparticle release from platelets was affected by processing methods; platelet-rich plasma platelet concentrates had higher levels of extracellular vesicles than platelets processed by the buffy coat method or apheresis. Microparticles released by platelets can be particularly procoagulant, and it is not yet clear whether or not they improve the ability of platelet products to stem bleeding in patients, or if they are risk factors for harmful intravascular clot formation. Research such as that conducted by the Provost laboratory should shed light on this important question.

The Centre for Innovation netCAD Blood for Research Facility in Vancouver, managed by Janet McManus, uses a controlled test environment to support Canadian Blood Services’ internal process development. Working closely with staff from Canadian Blood Services Supply Chain, our Product and Process Development team identifies opportunities for process improvement. With Canadian Blood Services looking at changing their equipment across their manufacturing sites, netCAD provided extensive support to test and recommend equipment. Specifically, netCAD supported the implementation of new centrifuges and blood extractors for platelet and whole blood processing. At the same time, the processes were optimized. For example, the buffy coat platelet production process was streamlined, eliminating several unnecessary rinsing and mixing steps. These evidence-based changes are designed to improve productivity and staff ergonomics while ensuring our continued commitment to product quality.
for optimum patient outcomes. Our development work allows us to identify and solve issues with the process or equipment before Supply Chain starts the formal validation and production processes.

Current regulations require a small subset of blood products to be retained for quality control testing at product expiry, precluding their entry into the inventory and transfusion to patients. Dr. Acker and Ken McTaggart, from the Product and Process Development team, have been working with Janet McManus at netCAD to develop and validate non-destructive testing protocols for red blood cell units. Their research, showing equivalent quality parameters between the parent unit and small volume samples, was presented at the 2016 AABB meeting. At the same meeting, Ken McTaggart and researchers in Dr. Devine’s laboratory presented their progress optimizing the size and shape of the mini-bags used for non-destructive sampling of platelet units. If the quality of red blood cell and platelet products could be accurately evaluated by non-destructive sampling, it would prevent the destruction of precious products.

**Plasma and plasma protein products**

Plasma is the protein-rich liquid component of blood that supports the immune system and controls excessive bleeding. It is transfused to prevent or treat bleeding. Canadian Blood Services distributed approximately 130,000 plasma units in 2016–2017. Additionally, much of the plasma collected by Canadian Blood Services is sent to international companies for fractionation to make plasma-derived protein products such as intravenous immune globulins (IVIg).

A study led by Dr. Sheffield, with Craig Jenkins from the Product and Process Development group, provided evidence to change Canadian regulations for thawed plasma products. Currently, frozen plasma (FP; obtained from whole blood donations and frozen within 24 hours) may be transfused within 120 hours of thawing, whereas apheresis fresh frozen plasma (FFPA; obtained from apheresis donations and frozen within 8 hours) may only be transfused within 24 hours of thawing. The researchers showed that the activity of coagulation factor (F)VIII, an important quality control parameter, was non-inferior in FFPA compared with FP. In fact, the activity levels of several coagulation factors including FVIII were significantly higher in FFPA than in FP after 120 hours of refrigerated storage. This research supports an upcoming change in regulations to reduce waste while maintaining the high quality of Canadian Blood Services’ plasma products.

---

“…at netCAD, scientists, medical professionals, blood manufacturing technology vendors and collection and production experts can innovate, evaluate improvements, develop new processes, and try out new equipment. It’s also where experts can access blood products for discovery research and the applied development of current and next-generation blood products and manufacturing technologies.”

*Janet McManus, netCAD Blood for Research Facility Manager, in RED blog (Read more)*

---

“We’ve engineered proteins to last longer in the circulation by combining them with albumin, and we’ve done molecular studies trying to understand how natural inhibitors of coagulation work.”

*Dr. Sheffield, Centre for Innovation Associate Director, Research and Senior Scientist, in RED blog (Read more)*

---
IVIg is a plasma-derived product that includes the pooled antibodies of thousands of donors. In the past five years, researchers funded by Canadian Blood Services have made significant progress in understanding how IVIg works, optimizing its use in the clinic, and developing alternative therapeutics that may have fewer drawbacks.63-71

IVIg is a standard treatment for immune thrombocytopenia (ITP), an autoimmune platelet disorder for which the disease mechanisms remain unclear. ITP cases account for 10 to 20 per cent of IVIg utilization in Canada. However, many ITP patients do not respond to standard treatments such as IVIg and corticosteroids. Dr. Arnold received funding from the Canadian Blood Services/CIHR operating program to study the mechanisms underlying ITP and their association with clinical outcomes. As Dr. Arnold noted in a correspondence to the American Journal of Hematology, accurate diagnosis of ITP can be difficult.72 Dr. Arnold recently helped validate a rapid automated assay for the diagnosis of immune heparin-induced thrombocytopenia.73 This could improve patient outcomes by identifying treatment options earlier. To explore patient satisfaction with IVIg treatment, Dr. Arnold and Prof. Heddle led a pilot study using a treatment satisfaction questionnaire administered seven days after IVIg treatment in adult ITP patients.74 Overall, patients were satisfied with IVIg despite finding it inconvenient; 6 of the 12 patients enrolled reported side effects, but most found them tolerable. Dr. Arnold performed a meta-analysis examining the safety and efficacy of high-dose dexamethasone for ITP patients, and found that it did not improve durable platelet count responses compared with standard-dose prednisone.75 However, the response time was quicker with dexamethasone, indicating that it might be preferred over prednisone for patients with severe ITP who require a rapid rise in platelet count.

There is limited evidence supporting treatment options for ITP in pregnant women. To address this gap, Drs. Arnold and Nadine Shehata, with collaborators, performed a retrospective study of 195 women (235 pregnancies). They found that treatment was not required in the majority of pregnancies (58 per cent); for those who did need treatment, neonatal outcomes were similar for IVIg and corticosteroids.76 This research has provided key information that could lead to better treatments for patients with ITP, while potentially reducing the need for IVIg and other blood products.
**Dr. Ni** and Dr. John Semple, an adjunct scientist with Canadian Blood Services, also received funding to study ITP mechanisms. **Drs. Ni** and Semple examined how IVIg acts in a mouse model of ITP. They showed that ITP was associated with a deficiency in splenic dendritic cells, and that IVIg rescued the deficiency. Dr. Semple also found that in vitro IVIg treatment of spleen cells from ITP patients increased the percentage of myeloid-derived suppressor cells. They showed that the spleen is the primary site responsible for platelet destruction and also plays a large role in the antibody response. Splenectomy diminished anti-platelet antibody production and raised platelet counts in this mouse model of ITP. CD8+ cytotoxic T lymphocytes also play an important role in the platelet destruction associated with ITP. **Dr. Ni** collaborated with researchers in China to investigate how these cells contribute to ITP. They found that ITP patients with cytotoxic CD8+ T cells had higher levels of platelet desialylation than other ITP patients or controls. In vitro, cytotoxic CD8+ T cells induced platelet desialylation and phagocytosis by hepatocytes. These findings build on earlier work by **Dr. Ni** which suggested that platelet desialylation is important in the pathogenesis of ITP. The sialic acid in platelets is important for their function, and cleavage of platelet sialic acid residues (desialylation) is associated with platelet loss from the circulation. **Dr. Ni** and his collaborators in China, Canada and the Netherlands showed recently that platelet desialylation may be an important biomarker for determining an ITP patient’s response to treatment; non-responders had significantly higher levels of platelet desialylation. Supporting further study of the mechanisms of ITP, **Dr. Branch** published detailed protocols for the use of mouse models of ITP based on a CD41 platelet antibody. An improved knowledge of IVIg mechanisms of action will support the development of better treatment strategies for optimum patient outcomes.

Rh immune globulin (RhIg) is a specific type of IVIg used to prevent red blood cell alloimmunization during pregnancy. Pregnant women whose blood type is Rh negative (D-) typically receive RhIg prophylaxis to prevent hemolytic disease of the fetus and newborn (HDFN). Sometimes D serology is unclear, leading to variable follow-up procedures. A team of Canadian Blood Services medical experts led by **Drs. Goldman** and **Gwen Clarke** recently examined the efficacy of using an algorithm to identify appropriate patients for D genotyping. They found that genotyping of patients with weak D serology led to an identified genotype in most patients and that the use of a serologic algorithm to select patients for RhD genotyping identifies a majority of patients with weak D types not at risk for alloimmunization.

Like other forms of IVIg, the mechanism of action for RhIg is poorly understood. **Dr. Branch** collaborated with researchers in the U.S. to study immunoprophylaxis in a mouse model of red blood cell alloimmunization. They found that the recipient mice needed to have either functional Fcγ receptors or complement (C3) for the immunoprophylaxis effect. This suggests that RhIg immunoprophylaxis may also rely on these redundant recipient pathways. **Dr. Alan Lazarus** has been developing potential alternatives to RhIg. His research group used a mouse model of alloimmunization to explore why monoclonal antibodies to replace RhIg have shown disappointing results in the past. They found that polyclonal antibodies were more effective than monoclonal antibodies at suppressing the immune response, but that blends of monoclonal antibodies targeting different epitopes were just as effective as...
the polyclonal antibodies. This research has exciting implications for the development of new replacements for RhIg based on monoclonal antibodies. Commercialization efforts in the category of Antibodies, IVIg, and Immune Regulators have been facilitated by the Centre for Innovation through intellectual property protection and collaboration agreements with interested industry partners.

Anticoagulant drugs are critical for preventing harmful blood clots that may provoke strokes or heart attacks, but these widely used treatments may produce dangerous bleeding side effects that must then be countered using blood products. Dr. Ed Pryzdial is investigating new therapeutic strategies to treat harmful clots without the side effects of current treatments. In collaboration with researchers at the University of British Columbia and the University of Illinois, Dr. Pryzdial’s laboratory recently developed a synthetic, nontoxic polycation that is a universal heparin reversal agent (UHRA). In mice, UHRA neutralized the anticoagulant activity of heparins without the lung injury seen with protamine, a medication currently used to reverse the effects of heparin.

With Dr. Sheffield, Dr. Pryzdial also developed a chemically modified coagulation factor (Xai-K) which rapidly dissolved blood clots in a mouse model and did not cause systemic fibrinolysis activation, unlike the conventional treatment. Dr. Ni’s laboratory has also been developing a novel anticoagulant treatment strategy. Monoclonal antibodies targeting a particular domain of β3 integrin, a platelet surface protein, inhibited platelet aggregation in vitro and prevented blood clot formation in animal models. Similar to Dr. Pryzdial’s novel therapeutic, the monoclonal antibodies did not cause significant bleeding side effects. As part of its commercialization efforts, Canadian Blood Services has licenced Dr. Ni’s patents to CCOA Therapeutics Inc., a start-up company scientifically led by Dr. Ni. These projects show how Centre for Innovation research could be mobilized into new drugs for the benefit of Canadian patients.

Hematopoietic stem cells
Transplantation of hematopoietic stem cells (HSCs) has been used for many years to treat both malignant and non-malignant blood disorders. Canadian Blood Services manages a registry of adult HSC donors, the OneMatch Stem Cell and Marrow Network, and operates the national Cord Blood Bank. Canadian Blood Services also provides autologous HSC collection, manufacturing and storage services to some hospitals. In collaboration with The Ottawa Hospital and the Cord Blood Bank, the Centre developed the Cord Blood for Research Program, which distributes fresh and frozen cord blood units to researchers across Canada. In addition, through the expertise of our investigators and our Funding Programs, the Centre for Innovation fosters innovative research in HSC transplantation.

While cord blood transplantation has many advantages over adult HSC transplantations, it is associated with slow cell engraftment, leading to delayed recovery. Recent clinical trials have shown that expanding the numbers of stem cells in the laboratory improves engraftment time, but platelet recovery remains delayed. Dr. Nicolas Pineault, from the Product and Process Development group, focuses his research on

“We are trying to create larger numbers of cells through a cellular engineering approach where we place the cord blood cells in a culture to expand them before we transplant them in the patient,” explains Dr. Pineault, Centre for Innovation Development Scientist. “The hope is that this approach could help patients recover faster and reduce the need for further interventions.”

Pulse (Read more)
the development of strategies to expand cord blood cells while improving their ability to produce platelets. He recently showed that growing cord blood cells in osteoblast-conditioned culture medium (OCM) increased the number of CD34+ cells by 1.5-fold relative to normal culture medium and that OCM produced by immature osteoblasts was more effective at improving the production of committed and multipotent progenitor cells.

Another focus of Dr. Pineault’s research is on optimizing the freezing and thawing processes for cord blood units to increase product quality and enhance engraftment. This work is performed in collaboration with Dr. Ben from the University of Ottawa. With funding from our training programs, postdoctoral fellow Dr. Javed Manesia and graduate student Jennie Briard are investigating a new class of cryoprotectant (N-aryl-D-aldonamides) to prevent cellular damage during the freezing process. They have identified several molecules that are highly effective inhibitors of ice recrystallization. Functional assays showed that addition of these molecules to the normal cryoprotectant solution improved the recovery of committed and multipotent hematopoietic progenitors. The impact of these inhibitors on the engraftment activities of cord blood stem cells is now under investigation in a mouse model.

Dr. Ramirez-Arcos, from the Product and Process Development group, completed an evaluation study to determine the suitability of a new BacT/ALERT culture bottle for the sterility testing of cord blood units. Her technical report provided the evidence for our Cord Blood Bank to endorse the new bottle with confidence that safety of our products would not be impacted.

Dr. Acker, from the Product and Process Development group, together with adjunct scientist and Cord Blood Bank consultant Dr. Holovati, worked closely with Canadian Blood Services’ stem cell manufacturing lab in Edmonton to develop a process to manufacture plasma reduced human progenitor cells (HPCs). This process was necessary due to an update in HPC apheresis system technology at the Edmonton hospital which led to higher HPC collection volumes as additional plasma was being collected with the stem cells. The volume reduction process, developed in collaboration with our researchers, was implemented by Canadian Blood Services in March 2017. This is the first Canadian lab to implement the Sepax 2 process for autologous HPC products. This leadership ensures the provision of high quality autologous stem cell products to Canadian patients.

A Small Project Grant was recently awarded to Dr. David Allan, adjunct scientist and Cord Blood Bank medical consultant, to demonstrate the feasibility of sharing data between the OneMatch registry and the Canadian Blood and Marrow Transplant Group (CBMTG) registry. This study will focus on projects that have been identified as priority projects by the Canadian transplant registry. In the short time since this project was awarded, a working group has been established, projects have been identified and data sharing agreements are in the process of being finalized. Data sharing is an important component of the Centre for Innovation research strategy. This study will provide a foundation for future collaborative opportunities that will be critical for improving clinical outcomes for Canadian transplant patients.

Dr. Blake develops computer models to help guide changes in Canadian Blood Services’ policies. His group recently modelled the ideal composition for the OneMatch adult stem cell registry to optimize
Canadian HSC self-sufficiency and ethnic diversity.\textsuperscript{90} OneMatch is focusing on increasing the numbers of younger and male donors while also increasing the ethnic diversity of the registry. \textbf{Dr. Blake} used two linear programming models to show that improving the ethnic composition would be difficult without targeted recruiting strategies and that more than 25,000 individuals would need to be recruited each year to have a meaningful effect on registry composition.\textsuperscript{91} This research will help Canadian Blood Services identify recruiting strategies for optimizing the composition of registered donors in OneMatch.

\section*{Organ and tissue donation and transplantation}

The Centre for Innovation, in consultation with Canadian Blood Services’ Organ and Tissue Donation and Transplantation group, supports research in the area of organ and tissue donation and transplantation. Both the James Kreppner Fellowship Program and the Kenneth J. Fyke Award identify research priorities related to the issues of organ and tissue donation and are open to all Canadian researchers, while our Small Project Funding Program is open to internal staff, including those affiliated with the Organ and Tissue group. In addition, the Centre partners with CIHR to support the Canadian National Transplant Research Program (CNTRP).

The James Kreppner Fellowship Program funded Maeghan Toews, a research associate at the University of Alberta, who is developing legal and policy strategies to optimize organ donation. In the second and final year of her fellowship, she published a “Fast Facts” document on the topic through the CNTRP, which is intended to inform policymakers about topics related to organ donation and transplantation.\textsuperscript{92} Toews also published an article showcasing her legal and policy analyses of the issue in each jurisdiction across Canada.\textsuperscript{93} She also continued her work examining legal and ethical considerations arising from various financial and non-financial incentive mechanisms for donation. With the support from the fellowship, she widely disseminated her research through speaking engagements\textsuperscript{94} as well as in the media. She also led a research ethics workshop session discussing barriers and ways to improve organ donation intervention research in Canada. Toews, who has now completed her James Kreppner fellowship, is an integral part of the transplantation community and will continue to contribute to this field of research to benefit organ donors and their families as well as organ recipients.

In the second year of their Kenneth J. Fyke Award, Drs. Maureen Meade and Frederick D’Aragon further developed Canada-DONATE to support national clinical trials and improve the care of organ donors. The four-centre DONATE pilot examining the feasibility of an observational study of clinical practices in organ donations will be complete in 2017.\textsuperscript{95} Based on the results of the study, the group has developed two knowledge translation products. The first is a Practice Report which details current clinical practices at a given site and contrasts these practices with the Canadian Blood Services guidelines for donor management and with the practices at all participating centres. Practice Reports show where current practices at different sites may be deviating from the recommended guidelines. This can improve patient care by identifying areas where either practice or policy should be changed. They have also created Evidence Bulletins, which are evidence-based tools for health-care professionals to use at the bedside to

\textit{“This fellowship has been an incredibly rewarding experience that has allowed me to integrate into a fantastic community of clinicians, researchers, and professionals from a wide range of disciplines and backgrounds.”}

\textbf{Maeghan Toews, James Kreppner Fellowship recipient, in RED blog (Read more)}
help guide clinical practice. Each Evidence Bulletin is for a single medical intervention used in the care of organ donors, and summarizes current recommendations, the evidence underlying these recommendations, current practices, and tips for clinical application. In addition to its immediate clinical relevance, this research has paved the way for a larger study now underway across Canada, engaging all provincial organ donation organizations and over 32 intensive care units.

Building capacity in transfusion and transplantation science and medicine

The Centre for Innovation facilitates the development of professionals in the transfusion and transplantation sciences and medicine by providing formal training and education opportunities and by promoting knowledge dissemination.

Formal training

Training the next generation of transfusion and transplantation scientists

The Centre for Innovation administers competitive award programs designed to support professionals at various stages of their research training (Table 1). In 2016–2017, the Summer Research Scholarship Program supported nine undergraduate students to complete a short research project within a Canadian Blood Services research laboratory. One of them remained in Dr. Ni’s laboratory and is now completing a Master’s thesis with the University of Toronto. The Graduate and Postdoctoral Fellowship Programs provided stipend or salary support to 24 junior researchers, including four new fellows in the last year. Most fellowship recipients (19/24) complete their two- to four-year training under the mentorship of a Canadian Blood Services principal investigator or adjunct scientist, and a small number (5/24) within a Canadian academic group external to Canadian Blood Services. With the Canadian Blood Services/CIHR New Investigator Award Program, the Centre also supports principal investigators early in their academic careers. While this partnered program was discontinued in 2015, two ongoing awardees, Drs. Shehata and Melissa Parker, continued to receive support in 2016–2017.

In 2016, the Centre established a new partnership with Mitacs to strengthen its Graduate Fellowship Program. Through the Mitacs Accelerate Program, graduate fellows in laboratories external to Canadian Blood Services conduct research projects that are highly relevant to our blood operations and have access to critical materials, equipment and knowledge that are unique to our organization. Through this new partnership, a graduate student in Dr. Ben’s laboratory at the University of Ottawa is receiving a Graduate Fellowship for her research on small molecule ice recrystallization inhibitors for red blood cell cryopreservation.

The Centre for Innovation facilitates additional training opportunities for scientists through a unique partnership with the Centre for Blood Research in Vancouver. In the last year, with

Deb Chen is a graduate student at the University of British Columbia who has used the fellowship stipend to work on two major projects focusing on red blood cells. Chen’s research is helping us understand how treatments, like gamma irradiation, and various new technologies, may affect blood quality.

RED blog (Read more)
financial support from the Centre for Innovation and other partners, the Centre for Blood Research supported eight postdoctoral fellows and undergraduate and graduate students from the University of British Columbia to conduct research at Centre for Blood Research laboratories (Table 1).

In addition, the Centre for Innovation’s 11 principal investigators, who have cross-appointments with academic institutions, supervise graduate trainees and postdoctoral fellows with funding from research grants or external sources.

**Training the next generation of transfusion medicine specialists**

The Centre for Innovation facilitates the training of transfusion medicine specialists by providing salary support to medical residents enrolled in the Transfusion Medicine Areas of Focused Competency (AFC) diploma program. This Royal College of Physicians and Surgeons of Canada (RC) program is offered at four accredited Canadian universities and the curriculum is delivered in partnership with Canadian Blood Services and other stakeholders in the transfusion community, including Héma-Québec. Canadian Blood Services’ medical directors, under the leadership of Dr. Robert Skeate, continue to play significant roles in the curriculum development and delivery of this program.

In 2016–2017, two new transfusion medicine residency fellowships were awarded to fellows completing the diploma at McMaster University and University Toronto, and two fellowships for a fellow at McMaster University and a fellow at University of British Columbia were renewed. The impact of this program in ensuring the next generation of transfusion medicine specialists in Canada is well recognized. For example, Dr. Shih, a 2016 graduate of the Transfusion Medicine diploma program and a recipient of the Canadian Blood Services fellowship, is now a transfusion specialist at Vancouver Coastal Health Authority.

### Table 1: Number of new, ongoing, and completed training awards in 2016–2017

<table>
<thead>
<tr>
<th>Program</th>
<th>New</th>
<th>Ongoing (including renewals)</th>
<th>Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Centre for Innovation training programs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summer research scholarship program</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Graduate fellowship program</td>
<td>3</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Postdoctoral fellowship program</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>New investigator program</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Area of Focused Competence (AFC)-diploma program in transfusion medicine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion medicine residency fellowship</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Centre for Blood Research training programs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summer studentship</td>
<td>19</td>
<td>N/A</td>
<td>Not recorded by the Centre</td>
</tr>
<tr>
<td>Graduate award program</td>
<td>7</td>
<td>7</td>
<td>Not recorded by the Centre</td>
</tr>
<tr>
<td>Postdoctoral transition grant</td>
<td>1</td>
<td>1</td>
<td>Not recorded by the Centre</td>
</tr>
</tbody>
</table>
Training Canadian Blood Services staff about the products we manufacture and the patients we serve

The Centre for Innovation, through a close collaboration with Canadian Blood Services Quality and Regulatory Affairs, led the development and delivery of a new training module mandatory for all Canadian Blood Services staff. Launched in August 2016, the one-and-a-half-hour module entitled “Products and Patients” is part of our organization’s quality learning courses and provides employees with a basic understanding of blood and blood components, the biologics manufactured from blood, and the patients who benefit from those biologics. The objective of this course is to increase the quality mindset within the organization. More than 110 in-person or webinar presentations were delivered by Centre for Innovation staff and medical experts between August 2016 and April 2017, training more than 3,300 employees from across the country. A survey of attendees suggested that 86 per cent agreed with the statement “this training session enhanced my knowledge about the Products we manufacture or distribute” and 78 per cent agreed with the statement “this training session enhanced my knowledge about the Patients we serve” (percentages are based on 160 responses). The impact of this training module goes beyond Canadian Blood Services staff; the module is being delivered to other groups, such as Canadian Blood Services’ Board of Directors, the National Liaison Committee and the Regional Liaison Committee, who may benefit from a deeper understanding of the biologics we produce and the patients we serve. To facilitate delivery of this training module to Canadian Blood Services staff, the Centre for Innovation developed an e-learning version now available through our organization’s Learning Management System.

Education opportunities

Partnering with the University of Toronto to deliver an innovative education opportunity for medical residents across Canada

Transfusion medicine is an area of clinical expertise and practice that impacts most medical and surgical specialties. However, there is considerable evidence that postgraduate medical trainees lack transfusion medicine knowledge. “Transfusion Camp”, a unique longitudinal program consisting of five one-day sessions over the academic year, was established in 2012 for University of Toronto postgraduate medical trainees to acquire up-to-date knowledge in transfusion medicine. Transfusion Camp provides a total of 14.5 hours of didactic lectures and 15 hours of problem-based learning tutorials. The program receives unrestricted educational grants from CSL Behring and Grifols. In 2015, the Centre for Innovation partnered with Drs. Jeannie Callum and Yulia Lin from Sunnybrook Health Sciences Centre to expand the Camp to other university sites. Starting in July 2016, didactic lectures given in Toronto are webcast for remote live-attendance and recorded for later viewing by other sites. The problem-based learning tutorials are shared and delivered by local transfusion medicine specialists in Toronto and at satellite sites. Ontario Regional Blood Coordinating Network (ORBCoN) provides support for lunches and refreshments at Ontario sites. The Centre for Innovation provides support for the webcasting and recording of the lectures, as well as a digital platform to share course materials across all sites and administrative support for evaluation of the program performance. Canadian Blood Services medical experts participate in the curriculum development and delivery.

“Great presentation. Very valuable information. Would love to see this type of information continuously promoted and available!”

Feedback from staff on Module 2: Products and Patients
During Transfusion Camp 2016–2017, more than 170 postgraduate medical trainees from seven Canadian universities (University of British Columbia, University of Toronto, McMaster University, University of Saskatchewan, Dalhousie University, University of Ottawa, and Queen’s University) and one English university (Oxford University), representing 13 specialties (e.g., anesthesia, pathology, critical care medicine, obstetrics), participated. Transfusion medicine knowledge pre- and post-camp is being assessed using a validated knowledge assessment tool and feedback is being obtained from program directors and residents using survey tools. So far, informal feedback from participants is extremely positive, supporting the need for this type of educational initiative to enhance transfusion practice in Canada for the benefit of patients.

Delivering transfusion education webinars across Canada

Under the leadership of its medical experts, Canadian Blood Services offers the LearnTransfusion series. This series offers weekly seminars via webcast to trainees and practitioners in the field of transfusion medicine. In 2016–2017, a total of 30 seminars were held. A recent analysis of the program demonstrated an average of 44 participants per seminar with 96 per cent of participants being from Canada; most were affiliated with hospitals (48 per cent) or Canadian Blood Services (37 per cent). Seminars had high “overall presentation effectiveness” (excellent or good 99 per cent of the time) and “relevance to practice” was rated excellent or good 95 per cent of the time. The data suggests that the LearnTransfusion series continues to be an effective tool for dissemination of current transfusion medicine knowledge and best practices, not only for transfusion medicine specialty trainees, but also for the broader transfusion medicine audience that is geographically diverse.

Partnering with Grifols to deliver an education course to transfusion professionals in Canada

In June 2016, the Centre for Innovation and Grifols partnered to offer a Transfusion Science Education Course to blood transfusion professionals. This one-and-a-half-day course built on the scientific and technical abilities of blood transfusion professionals, and discussed laboratory techniques and methods for resolving complex serological cases. More than 100 physicians and medical laboratory technologists attended the free event held in Winnipeg, and group viewing sessions were organized at five Canadian Blood Services locations across the country. Attendees represented Canadian Blood Services, hospitals and private diagnostics laboratories. The course was well designed with a variety of learning experiences such as lectures, focused discussions, and interactive participation. For this Winnipeg event, a Canadian Blood Services associate medical director, Dr. Clarke, and medical officer, Dr. Debra Lane, contributed

“The best transfusion is the most appropriate transfusion, and that’s what we’re trying to teach residents. In these specialties, specifically, they’ll have to order transfusions during their residency and obtain consent from a patient for that transfusion. We want to make sure they have the knowledge to make those decisions.”

Dr. Yulia Lin, Sunnybrook Health Sciences Centre Transfusion Medicine Specialist, in Pulse (Read more)
to the course content by leading the panel discussion and delivering a lecture on warm auto-antibodies. The feedback from the attendees was positive with an average overall satisfaction rating of 3.3 out of 4.

Partnering with provincial blood coordinating offices to deliver education events for transfusion professionals in Canada

The Centre for Innovation, with the leadership of Canadian Blood Services’ medical groups and principal investigators, works in partnership with provincial blood coordinating offices across the country to deliver educational events. These events are targeted primarily to health-care professionals working in Canadian hospitals who are involved in the transfusion of blood products. They highlight new advances in the field and offer educational opportunities for professionals working in large, as well as rural hospitals.

Dr. Peter Lesley, with ORBCoN, co-organized the 11th Annual Northern and Eastern Ontario Annual Transfusion Medicine Education Videoconference in April 2016. The theme was the Choosing Wisely Recommendations for Transfusion Medicine. To increase the reach of this videoconference, the Centre for Innovation facilitated group webinars across the country. Ten Canadian Blood Services sites and 81 hospital sites registered for the videoconference event, with a total of 702 reported attendees including 77 from Canadian Blood Services. The majority (58 per cent) of the attendees were medical laboratory technicians (MLTs); 14 per cent were nurses and 9 per cent were physicians. Overall satisfaction was excellent or good for 95 per cent of attendees, and 76 per cent indicated that based on their new knowledge, they would modify the way they practice in relation to the use of blood products. Presentations are available online at the ORBCoN website.

Canadian Blood Services experts work with the Alberta Vein-to-Vein Society to deliver annual education events. In March 2017, Drs. Clarke, Dale Young and Acker presented at the Alberta Vein-to-Vein Conference providing up to date information on the prevention of hemolytic disease of the fetus and newborn, the HLA-matched platelet program, and the storage and stability of blood products. Presentations are available online on the society’s website.

In British Columbia, principal investigator Dr. Scott and transfusion medicine residency fellowship recipient, Dr. Jacqueline Trudeau, presented in September 2016 at the BC Provincial Blood Coordinating Office Education Session. Presentations are available online on the BCPBCO website.

BloodTechNet

Through the BloodTechNet competition and with unrestricted education funding from Grifols, the Centre for Innovation funds innovative projects aimed at delivering educational tools and resources that support the development of skills, knowledge and expertise of health professionals in the transfusion, cellular therapy and transplantation communities in Canada. Three BloodTechNet projects were funded in 2016. Dr. Warren Fingrut received funding for “The Stem Cell Club: Educating Medical Students about Stem Cell Transplantation.” The Stem Cell Club, which equips medical students with skills to become health advocates for patients in need of stem cell transplants, is developing an evidence-based volunteer training program that can be expanded nationally. In the “Social media for knowledge
translation and education 3 (SoMe-KTE3)” project, Dr. Shih is leading a multidisciplinary collaboration to use social media and technology to promote awareness of best practices in transfusion medicine. The goal is to develop an up-to-date, learner-centred, and free online curriculum about the management of bleeding and thrombosis, including relevant aspects of transfusion medicine that will connect a previously untapped audience to transfusion safety and hemovigilance. Dr. Shehata received a BloodTechNet award to develop two podcasts about the guidelines determined by the International Collaboration for Transfusion Medicine Guidelines (ICTMG) on fetal and neonatal alloimmune thrombocytopenia (FNAIT) and red blood cell specifications for hemoglobinopathies. These three projects will help improve the decision-making process for health-care professionals.

Launch of an education portal
Canadian Blood Services previously managed two independent professional education websites that provided information and tools for transfusion medicine and organs and tissues, respectively. In August 2016, under the leadership of the Centre for Innovation, the new Canadian Blood Services Professional Education website (professionaleducation.blood.ca) was launched. The new website integrates content for both communities in one dynamic digital platform. It is mobile-friendly and will be regularly updated to provide relevant, real-time educational resources for health-care professionals. An initial analysis of the website analytics suggests that it has been well received by the community with 76,815 total sessions (August 25, 2016 through March 31, 2017) and the engagement of 62,694 unique visitors. A total of 161,147 pages were viewed, suggesting that users visit more than one page during each session. The largest number of users – 48 per cent – were from Canada while 24 per cent came from the U.S. Compared with industry average, the bounce rate is fairly low at less than 50 per cent.

With the migration of the content to the new platform, the Centre for innovation focused its efforts on updating the transfusion content. With the editorial leadership of Dr. Clarke, extensive work on the Clinical Guide to Transfusion was performed to update its content and facilitate its dissemination. Revisions to eight out of the 18 chapters were published during the year and five additional chapters are under revision. This invaluable online resource for health-care professionals is now available as searchable html content and is also downloadable as PDF. Since the launch of the new website in August 2016, there have been 18,082 English and 2,336 French page views for all chapters combined, with an average of 2.6 and 2.3 minutes spent on each page, English and French respectively. In addition, there have been 2,069 PDF Clinical Guide chapter downloads from the site.

Canadian Blood Services’ associate medical director West, Dr. Tanya Petraszko, updated the original article entitled “Transfusion-related acute lung injury (TRALI).” This article continues to be the most visited page on the website with more than 30,000 page views (equivalent to 19 per cent of website traffic) and an average of six minutes spent on the page.

Dr. Goldman and a Canadian Blood Services medical consultant, Dr. Chantale Pambrun, updated in March 2017 the original article entitled “The importance of iron for whole blood donors: a Canadian perspective.” This article provides valuable information for blood donors and their physicians about maintaining healthy levels of iron.
Knowledge dissemination

**Canadian Society for Transfusion Medicine, Canadian Blood Services and Héma-Québec Annual Meeting**

The Centre for Innovation contributes financially to the Canadian Society for Transfusion Medicine (CSTM) Annual Meeting and, in collaboration with Héma-Québec and other key members of the transfusion community, develops its scientific and workshop programs. This national event is the premier meeting for the Canadian transfusion medicine community and engages more than 300 professionals from hospitals, academia, blood operators, and the private sector. In 2016, the event was held in Vancouver and many Centre for Innovation researchers presented, including Drs. Branch, Lazarus and Sheffield. Canadian Blood Services medical consultant and graduate of the Transfusion Medicine Fellowship Program, Dr. Zeller, won Top Clinical Abstract Award for her research on intravenous iron ordering practices for inpatients and outpatients at a large academic institution. Dr. David Donkor, a Canadian Blood Services-funded postdoctoral fellow in Dr. Sheffield’s laboratory, won the Top Scientific Abstract Award for his work on the selection and characterization of a DNA aptamer that inhibits a coagulation factor and may have a role as an anti-thrombotic drug.

**Canadian Blood Services annual international symposium**

This year’s symposium, co-chaired by Drs. Sheffield and Webert, focused on the intersections of hematopoietic stem cell transplantations and transfusion medicine. Key topics included ex vivo production of platelets, HLA typing, transfusion strategies for HSC transplant recipients, cord blood banking and transplantation practice. The presentations from national and international experts educated physicians, medical laboratory technologists and researchers on current knowledge and challenges in the field. The Continuing Medical Education-accredited event was received well by attendees, with the majority (88 per cent) agreeing that the event enhanced their knowledge. To further disseminate the knowledge shared at the symposium, a report was published in *Transfusion Medicine Reviews.*

**Centre for Blood Research symposiums and seminars**

Through the Program Support Award to the Centre for Blood Research and the activities of Canadian Blood Services scientists located at the Centre for Blood Research, the Centre for Innovation contributed to the Annual Norman Bethune Symposium, the Centre for Blood Research’s Research Day, and the Earl W. Davie Symposium. Attendance at these events reached almost 600 attendees. The events were also broadcasted live and archived on the Centre for Blood Research website. The Program Support Award also allows the Centre for Innovation to contribute to the Centre for Blood Research weekly and summer seminar series, which have average attendance of 80–140 attendees and are also broadcasted live to increase the reach of the events.
Participation at international meetings

More than 40 Canadian Blood Services staff members attended the 2016 AABB meeting to discuss the latest trends in the field of transfusion medicine and cellular therapy. At this meeting, Prof. Heddle, a Canadian Blood Services adjunct scientist, was awarded the Emily Cooley Memorial Award and Lectureship, which “recognizes an individual who has demonstrated teaching ability and has made a major contribution to the field of transfusion medicine or cellular therapies.” Canadian Blood Services researchers moderated four sessions and presented eight invited talks, 11 additional oral presentations and 33 posters, including two Top Posters generated by the research groups of Drs. Goldman and O’Brien. Centre for Innovation researchers also facilitated key invited education sessions on topics including platelet manufacturing and the impact of extending shelf life; recent advances in IVIg and IVIg substitutes in response to a growing concern related to global sufficiency of supply; and case studies demonstrating the value of using the Risk-Based Decision-Making Framework for Blood Safety: babesia (Canadian Blood Services), HTLV (Australia), pathogen inactivation (United Kingdom), and HTLV (Republic of Ireland). The knowledge from the meeting was shared with all Canadian Blood Services staff through an AABB Conference Report and a KnowledgeInfusion webinar organized in February 2017.

In addition to the AABB meeting, many of our staff presented at the Platelets 2016 International Symposium and at the 2016 meetings for the International Society of Blood Transfusion (ISBT), Society for Cryobiology and American Society of Hematology.

Knowledge dissemination within Canadian Blood Services

Internally, the Centre for Innovation organizes “lunch and learn” webinars for Canadian Blood Services staff. These events showcase presentations by Canadian Blood Services’ research groups as well as from the Alliance of Blood Operators and highlight the impact of ongoing research projects on the blood system and operators. To further extend the reach of these events, recordings are available on the Canadian Blood Services intranet for Canadian Blood Services staff. Over the last year, eight events were organized, attracting a total of 769 participants (live audience and webinar viewers).

Science communication

The Centre for Innovation, in collaboration with Canadian Blood Services’ Public Affairs division, fosters a robust science communications strategy to showcase our research output and education activities. By sharing compelling research stories, we build credibility and increase the impact of our initiatives.

The monthly Research and Education Round Up newsletter, compiled by science communications specialist Jenny Ryan, curates and celebrates the work of Canadian Blood Services’ Medical Services and Innovation research and education network. Content includes new scientific publications, events, educational materials and plain language summaries of high-impact research. The newsletter is currently delivered to more than 520 subscribers. Newsletter readership has increased by more than 300 since April 2016, when the newsletter was opened to external subscribers and a subscribe link was added to the Professional Education website. The open rate is 47 per cent, which is much higher than industry average of 20 per cent. It also seems to get shared to a much wider audience as the number of opens is always many hundreds more than number
Table 2: Key education and knowledge dissemination events organized by the Centre or delivered in partnership in 2016–2017

<table>
<thead>
<tr>
<th>Event (Location)</th>
<th>Primary Partner</th>
<th># of Attendees</th>
<th>Audience</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Events led by the Centre for Innovation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian Blood Services Annual International Symposium (Toronto)</td>
<td>N/A</td>
<td>100</td>
<td>Health-care professionals, researchers, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>Canadian Blood Services Centre for Innovation Annual Research Day (Vancouver)</td>
<td>N/A</td>
<td>54</td>
<td>Centre for Innovation staff, Canadian Blood Services medical directors, researchers</td>
</tr>
<tr>
<td>KnowledgeInfusion Webinar series – 8 events (Webinar)</td>
<td>N/A</td>
<td>~ 100 per event</td>
<td>Canadian Blood Services staff and volunteers, Health Canada staff</td>
</tr>
<tr>
<td>LearnTransfusion Seminar Series – 30 events (Webinar)</td>
<td>N/A</td>
<td>~50 per event</td>
<td>Health-care professionals</td>
</tr>
<tr>
<td>Canadian Blood Services Module 2 – &gt;110 events (Classroom sessions, webinar sessions)</td>
<td>Canadian Blood Services Quality and Regulatory Affairs;</td>
<td>&gt;3,300</td>
<td>Canadian Blood Services staff</td>
</tr>
<tr>
<td><strong>Events delivered in partnership</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norman Bethune symposium (Vancouver, broadcast)</td>
<td>Centre for Blood Research</td>
<td>200</td>
<td>Researchers, health-care professionals, basic science and clinical trainees, members of the public, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>Earl W. Davie symposium (Vancouver, broadcast)</td>
<td>Centre for Blood Research</td>
<td>190</td>
<td>Researchers, health-care professionals, basic science and clinical trainees, members of the public, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>CBR Research Day (Vancouver)</td>
<td>Centre for Blood Research</td>
<td>180</td>
<td>Researchers, health-care professionals, basic science and clinical trainees, members of the public, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>Centre for Blood Research weekly seminar series – 24 events (Vancouver, broadcast)</td>
<td>Centre for Blood Research</td>
<td>80 – 140 per event</td>
<td>Researchers, health-care professionals, basic science and clinical trainees, members of the public, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>Centre for Blood Research summer seminar series – 11 events (Vancouver)</td>
<td>Centre for Blood Research</td>
<td>80 – 140 per event</td>
<td>Researchers, health-care professionals, basic science and clinical trainees, members of the public, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>11th Annual Transfusion Medicine Symposium (Ottawa, broadcast)</td>
<td>Ontario Regional Blood Coordinating Network</td>
<td>702</td>
<td>Health-care professionals primarily in northern and eastern Ontario, Canadian Blood Services staff</td>
</tr>
<tr>
<td>Transfusion Science Educational Course (Winnipeg, broadcast)</td>
<td>Grifols</td>
<td>116</td>
<td>Health-care professionals, Canadian Blood Services staff</td>
</tr>
</tbody>
</table>
of subscribers. Popular content (common click throughs) includes transfusion and transplantation education events and professional education resources, as well as RED blog posts and recent peer-reviewed publications.

Our RED (research, education, and discovery) blog can be found on the publicly accessible blood.ca website. Publishing content every week since its launch in February 2016, the blog tells our research, education and discovery stories and celebrates the people responsible. More than 52 blog posts were published in 2016–2017, showcasing the Centre for Innovation’s research in blood science and transfusion medicine and cellular therapies (in particular blood stem cells), as well as organ donation and transplantation. The RED blog also provides a new approach to educate the general public and increase their awareness, trust and understanding of transfusion and transplantation science and medicine.

Our blog posts had more than 48,000 page views, with time spent on pages averaging around 3-5 minutes indicating that most visitors are reading the entire post. The posts that received the most attention this year include “Ferritin findings: Investigating iron and impacts on donors” (7,306 views); “Research uses big data to understand donor characteristics on transfusion outcomes” (2,323 views); “Research aims to close knowledge gaps on donor screening for MSM” (1,220 views); and “The wonder drug you’ve probably never heard of – yet” (1,257 views).

To extend the reach of the blog posts, Canadian Blood Services promotes the blog on three key channels: Twitter, Facebook and LinkedIn. Science and research-based posts have been positively received and while showcasing our work, also helped to support our donor relations colleagues in explaining difficult deferral policies and managing change.

- In April 2016, ten science-based social media posts reached 22,000 people and engaged 349. Six posts related to published research reached 19,000 people and engaged 277. The most successful post was “Stealth blood cells: Fooling the immune system to make transfusion safer for hard-to-match patients.” It reached 5,300 people, earned 55 reactions, and prompted well-informed questions on Facebook.
- In July 2016, a Facebook post about a JAMA Internal Medicine publication on the associations between donor characteristics and patient outcomes earned many comments from our followers and prompted over 1,600 visits to a blog post describing the research findings. The impact of this Facebook post suggests that Canadian Blood Services’ social media audiences are interested in research stories.
- In October 2016, science content on Canadian Blood Services’ social media channels outperformed the average of all content posted for the month. A RED blog post helped to manage negative feedback following the announcement of iron eligibility changes by summarizing the research that led to the change and how it will protect donor health.
In 2016–2017, Canadian Blood Services issued two research-specific news releases. “Researchers find unexpected association between younger donor age, female sex and transfusion outcomes” was prepared in collaboration with research partners at the University of Ottawa and The Ottawa Hospital and was issued in July 2016. This publication received significant mainstream media attention (Altmetric score 777). “Blood processing methods affect microparticles and mtDNA linked to blood transfusion reactions” was issued in April 2016 and highlighted the publication of important work by Dr. Acker’s laboratory and collaborators at Blood Systems Research Institute in the U.S. This release received 2,467 views via AAAS Eurekalert science release distribution service.

A new section of blood.ca (Our Research Impact) was developed and launched in the past fiscal year to showcase the impact of Canadian Blood Services’ research and education activities and provide transparency for our funders. Here, RED blog posts, research highlights and vignettes, ResearchUnits, our publications and funded projects databases, and research-based news releases are collected in one convenient spot. The landing page has received almost 5,000 views since its launch.

Increasing impact through collaborations

The Centre for Innovation seeks formal and informal arrangements with external stakeholders to combine expertise and resources, and maximize the impact of its activities. This collaborative approach allows the Centre to extend its reach and align its impact with the needs of stakeholders while remaining within its financial and expertise constraints. In this section, key collaborative activities are highlighted.

An international collaboration to develop clinical guidelines for transfusion medicine

Health-care systems around the world are experiencing rising costs, fueled by more expensive technologies and an increased demand from an aging population. Clinical guidelines and leading practices, while improving patient outcomes, can also increase efficiency by reducing inappropriate or unnecessary treatments. The International Collaboration for Transfusion Medicine Guidelines (ICTMG) group was established in 2011 and includes international transfusion experts from nine countries. The Centre for Innovation continues to support the work of the ICTMG group by providing coordinating services and expert support with the medical leadership of Dr. Shehata. ICTMG uses a consensus-based process to choose topics for guideline development. Fetal and neonatal alloimmune thrombocytopenia (FNAIT) poses an opportunity to improve patient outcomes because patients with FNAIT have a high risk of mortality and morbidity and there is a discrepancy between evidence-based knowledge and day-to-day clinical practice. In the last year, ICTMG conducted three systematic reviews to provide evidence for the development of guidelines for the management of FNAIT. While two reviews are nearing completion, one was published in the journal Blood and highlighted in Transfusion News. The preliminary guideline was presented at the 2016 AABB annual meeting. The ICTMG group is also completing a systematic review and developing guidelines for red blood cell specifications for patients with hemoglobinopathies. As with
FNAIT, there is currently a discrepancy between evidence-based knowledge and current day-to-day clinical practice which could be improved by the development of clear clinical guidelines.

In 2016, recognizing that effective knowledge dissemination is essential to increase adoption of clinical guidelines by health-care professionals, the ICTMG launched a website (ictmg.org), with the Centre’s support, to complement the publications and conference presentations. In addition, in collaboration with the AABB, the group created a three-part podcast to educate clinicians about platelet transfusion based on two platelet transfusion guidelines published independently by the two groups. The podcast, which offers CME credits from AABB, has been heard more than 200 times through SoundCloud since its launch in October 2016.

The Alliance of Blood Operators
As a member of the Alliance of Blood Operators (ABO), Canadian Blood Services collaborates with blood operators around the world to improve operational activities and strengthen the blood systems. Each year, the Centre for Innovation’s medical and scientific experts contribute to the annual ABO horizon scan. This scan identifies global trends in the blood sector and provides an opportunity for members to develop a shared approach. Another key activity of the ABO, which is coordinated by the Centre for Innovation, is to facilitate knowledge exchange to identify good practice and encourage performance improvement. For example, in the last year, the ABO Donor Engagement Group launched an initiative to explore how to identify and recruit the blood donor of the future. The result of this effort is a set of predictions based on evidence and expert opinions. The paper identifies five areas of change that ABO predicts will have serious impacts on the donor pool: changing population demographics; evolving belief systems, attitudes, and behaviors; innovations in the healthcare system; technological breakthroughs; and political and economic developments and environmental challenges. Canadian Blood Services is actively using this information as it plans for the future with its donor-focused Deeper Connections program.

In a very different area that is nonetheless essential for Canadian Blood Services operations, the ABO knowledge exchange program informed the development of cybersecurity policy and processes that form the basis for protecting our IT system and data. In total, the Centre for Innovation coordinated about 79 ABO knowledge exchanges in the last year to inform current operational activity and future planning.

“The ABO benchmarking program and best practice sharing have provided sustained insight and high value to members since the early days of ABO. Being able to understand similarities and differences in practice, to question why one operator does something differently, to talk about it with your team: this kind of information highlights opportunities for improvement and enables blood operators to reinvest resources in growth areas.”

Dr. Sally Thomas, Australian Red Cross Blood Services Director of International Services, in RED blog (Read more)
Risk-based decision-making framework for blood safety

The Alliance of Blood Operators’ Risk-Based Decision-Making Framework for Blood Safety (RBDM) was developed with leadership from the Centre for Innovation (Judie Leach Bennett and Sheila Ward), and an online set of tools has been created: https://riskframework.allianceofbloodoperators.org/log-in/. However, the framework remains a mere theoretical concept unless it can be viably applied to real-time decision-making challenges and unless there is broad uptake in the blood sector, credibility with decision-makers, and demonstrable progress in shifting the decision-making paradigm. In the last year, early adopters in Canada, Australia, U.K., Republic of Ireland, and U.S. have completed or started RBDM analyses on a varied set of risk issues.

With the support of the Centre for Innovation, Canadian Blood Services has applied the framework in the development of a proactive approach to emerging babesia risk in Canada, as well as to the questions of proportionality of current CMV risk-reduction measures and the risk tolerability of a narrower testing strategy. The RBDM framework also served to characterize anticipated security of supply risks to IVIg for Canadian patients and to evaluate available risk management options according to many factors including cost and health outcomes; this novel application of the framework informed the development of Canadian Blood Services’ plasma strategy.

Other blood operators are using the RBDM framework to make decisions regarding HTLV testing (Australian Red Cross Blood Service and Irish Blood Transfusion Service), pathogen inactivation (Australian Red Cross Blood Service), donor deferral requirements (National Health Service Blood & Transplant), donor iron (Blood Systems Inc., American Red Cross, ABC), Zika testing (European Blood Alliance). While blood operators have been the most frequent users of the framework, policy-making and regulatory bodies have also shown interest and support for the RBDM approach. The U.S. Food and Drug Administration invited a presentation on the ABO RBDM approach at a workshop on emerging tick-borne diseases. Additionally, the World Health Organization invited ABO to present RBDM at a consultation to develop a “tool for developing countries that estimates the impact of emerging infections onto the blood supply, in order to predict and estimate risks, and to provide a common basis for potential risk management options.”

Dr. Fearon, Centre for Innovation Medical Director, in RED blog (Read more)

“While we still consider the risk of babesiosis to Canada’s blood supply to be very low at the moment, it is important to remain vigilant and plan for changing levels of risk, should they occur. The risk analysis process has given us the opportunity to review possible options in advance of having to make decisions around an increasing threat. Although circumstances may change, this provides valuable information on which to base rational and cost effective mitigation strategies.”

Judie Leach Bennett, Centre for Innovation Director, in RED blog (Read more)

“It’s not just the structured approach. There’s a strong element of stakeholder participation in the framework to inform decision-making, to conduct risk communication and to build trust. There’s also a piece of the framework that focuses on health economics and analysis. So, taking a system view, we can determine where the risk resides and how to best allocate resources to it looking at that entire system, and looking at opportunity cost.”

Judie Leach Bennett, Centre for Innovation Director, in RED blog (Read more)
regulatory decisions.”

The full impact of the introduction of RBDM in the blood sector will not be known until we have a critical mass of cases with which to explore any overall shifts in decision-making trends. However, we do know that the framework is having an impact today on a case-by-case basis, by enabling blood operators and others to develop proportional risk responses with a transparent, consistent approach.

**Provision of research samples and data**

The Centre for Innovation continues to facilitate research by providing unique products to Canadian researchers at very low costs. Through the Centre’s netCAD facility in Vancouver, researchers have access to a range of blood products that are collected from deferred donors. In 2016–2017, a total of 3,930 research products including apheresis plasma and platelets, whole blood units, buffy coats, plasma, red blood cell units, pooled platelets, specimen tubes and apheresis chambers were distributed to 62 research projects (39 internal and 23 external to the Centre) across Canada. For example, one major project supported was the non-destructive testing project led by the Centre’s Product and Process Development group in support of Canadian Blood Services Quality and Regulatory Affairs.

Continuing to enhance and extend impact by working with industry and other partners, the Centre for Innovation entered into new netCAD collaborations in 2016–2017 with LightIntegra Technology regarding the development of the dynamic light scattering technology used to test platelet quality pre-transfusion and with Centre of Excellence for the Prevention of Organ Failure (PROOF) to support organ transplantation research.

In addition, through a partnership with Canadian Blood Services Cord Blood Bank and The Ottawa Hospital, the Centre facilitates the distribution of cord blood that is not suitable for transplantation. In 2016–2017, 241 cord blood samples were distributed to seven projects across Canada and the Program increased its product offerings to include processed frozen cord blood units. These formal programs support discovery research and applied development projects on current and next generation blood products and manufacturing technologies.

---

**Governance**

Canadian Blood Services continues to provide a sound governance structure for the Centre for Innovation activities. Oversight continues to be provided by the external Scientific and Research Advisory Committee and by the Safety, Research and Ethics Committee of Canadian Blood Services’ Board of Directors.

Specific research ethics oversight is provided by Canadian Blood Services’ Research Ethics Board (REB), in accordance with the provisions of the Tri-Council Policy Statement: Ethical Conduct for Research
Involving Humans -- TCPS 2 (2014). In 2016–2017, the REB reviewed 30 new research applications and renewed 72 applications, to ensure adherence to national ethics standards by all research projects supported by Canadian Blood Services. Complementing the efforts of the REB, the newly established external Bioethics Advisory Committee began its work in reviewing the increasingly complex ethical challenges in the domain of biological products and services offered by Canadian Blood Services.

Attention to good governance practices in the administration of the Research and Training Programs remains a priority. In the last year, guidelines for seven programs were updated and 10 competitions were held with strictly observed peer-review processes and appropriate financial controls. Information about funded projects is now shared on blood.ca.

This governance framework and expertise were leveraged to develop the MSM Research Grant Program, which was launched on February 1, 2017. This new research funding program followed a stakeholder workshop organized by Canadian Blood Services, Héma-Québec and Health Canada and will fund projects to generate scientific evidence to evaluate alternative screening approaches for blood or plasma donors, specifically with respect to deferral policies for men who have sex with men. This program is funded via additional funding received from Health Canada for this priority.

Program administration is strongly supported by Canadian Blood Services’ enabling functions: Talent Management, Finance, Legal, Information Technology, and others. Significant value and rigour are achieved by the contributions of these support services and the infrastructure surrounding the research, development, and education programs operated by the Centre for Innovation.

Through its partnership with the ABO members, Canadian Blood Services participates in an international Research and Development working group. The purpose of the group, chaired by Dr. Devine, is to improve the impact and effectiveness of ABO members’ R&D programs by examining the managerial, administrative and leadership issues affecting R&D. In the last year, with support from the Centre for Innovation, the group published a second R&D performance report. This international benchmarking exercise will help determine key performance indicators as well as identify areas of potential collaborations and optimization for the R&D programs.

Under the leadership of Ken McTaggart, the Centre for Innovation Product and Process Development group strengthened its governance structure to increase participation of knowledge users throughout the life of a project and to ultimately facilitate knowledge uptake. An internal Product Development working group was established three years ago with participation from the Centre for Innovation, Supply Chain, and Quality and Regulatory Affairs. In addition, the knowledge users are engaged early in the development research process, with the Supply Chain involvement increasing and the Development team involvement decreasing as the project progresses. Furthermore, in the last year, exchanges were facilitated to provide opportunities for Centre for Innovation staff to visit the production environment and observe processes in action, learn about problems, test potential solutions and identify the most relevant research questions. Similarly, staff from the manufacturing environment were able to visit our netCAD facility to participate in the research projects. The Product and Process Development group has also been working more closely with the industry vendors to provide input to the development of their equipment and supplies to more precisely meet the needs of Canadian Blood Services manufacturing process. This
improved knowledge mobilization process recently supported the implementation of equipment changes needed in our manufacturing environment.

The Centre for Innovation continues to report on performance and progress with regard to stated objectives to Canadian Blood Services’ Executive Management Team and Board of Directors, Health Canada, and to the Provincial/Territorial Blood Liaison Committee. This annual progress report highlights many of the important accomplishments of the Centre for Innovation and, together with the outputs and outcomes reported as part of its performance measurement framework (Table 3, Appendices I, II and III), it demonstrates the value of the Centre’s activities in improving patient outcomes and system performance while ensuring maximal cost-efficiency. In the last year, a stakeholder survey was developed to evaluate stakeholder awareness and use of the research knowledge created by the Centre for Innovation. Results from the survey, which are expected in June 2017, will further clarify the value of our research activities and inform our future research strategy.

Table 3: Centre for Innovation performance measurement framework results, April 2013–March 2017

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge Products</td>
<td>Number and type of knowledge products developed</td>
<td>284</td>
<td>296</td>
<td>355</td>
<td>362 (Appendix II)</td>
</tr>
<tr>
<td>Knowledge Exchange Mechanisms</td>
<td>Number and type of knowledge exchange mechanisms developed/used</td>
<td>221</td>
<td>404</td>
<td>436</td>
<td>419</td>
</tr>
<tr>
<td>Awards and grants</td>
<td>Number of awards and grants by program</td>
<td>92</td>
<td>145</td>
<td>160</td>
<td>151 (Appendix I)</td>
</tr>
<tr>
<td>Partnerships/collaborative working arrangements</td>
<td>Number of partnerships/collaborative working arrangements</td>
<td>25</td>
<td>31</td>
<td>38</td>
<td>46</td>
</tr>
<tr>
<td>Key stakeholders in the transfusion and transplantation community are knowledgeable about the evidence/knowledge generated by R&amp;D projects</td>
<td>Level of reported knowledge</td>
<td>&gt;85%</td>
<td>&gt;85%</td>
<td>&gt;85%</td>
<td>&gt;85%</td>
</tr>
<tr>
<td>Percent of Canadian Blood Services staff researchers with an H-index that meets the Canadian Science Standard of 10.6</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>N/A</td>
</tr>
<tr>
<td>Number of highly qualified people completing training by training level</td>
<td>21</td>
<td>14</td>
<td>22</td>
<td>25</td>
<td>82</td>
</tr>
<tr>
<td>Key stakeholders in the transfusion and transplantation community apply knowledge created by R&amp;D projects</td>
<td>Number and type of new or updated policies, procedures, practices, products, and standards</td>
<td>5</td>
<td>29</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Perceptions of key stakeholders of the usefulness and quality of the knowledge created</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Pending</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Note: Targets for all measures were met in all fiscal years.
References cited
(see Appendix II for a full list of the Centre for Innovation’s publications for fiscal year 2016–2017)


39. van der Meer PF, Devine DV, on behalf of the BEST Collaborative. Alternatives in blood operations when choosing non-DEHP bags. *Vox Sang* 2017; 112: 183-4.


## Appendix I: Funded projects

### Summary of funded research project by program

<table>
<thead>
<tr>
<th>Projects receiving funding in fiscal year 2016-2017</th>
<th>Total: 151</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research program</strong></td>
<td>52</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR partnership operating grants</td>
<td>25</td>
</tr>
<tr>
<td>Blood utilization and conservation (18)</td>
<td></td>
</tr>
<tr>
<td>Transfusion-related acute lung injury (3)</td>
<td></td>
</tr>
<tr>
<td>Blood supply risk (4)</td>
<td></td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR partnership new investigator awards</td>
<td>2</td>
</tr>
<tr>
<td>Intramural operating grants</td>
<td>9</td>
</tr>
<tr>
<td>Small projects funding</td>
<td>9</td>
</tr>
<tr>
<td>James Kreppner fellowships</td>
<td>2</td>
</tr>
<tr>
<td>Kenneth J. Fyke award</td>
<td>1</td>
</tr>
<tr>
<td>CIHR partnership: Transplantation research</td>
<td>1</td>
</tr>
<tr>
<td>Supplementary funding</td>
<td>3</td>
</tr>
<tr>
<td><strong>Product and Process Development program</strong></td>
<td>56</td>
</tr>
<tr>
<td>Deepening the understanding of our products and the processes used to manufacture them</td>
<td>20</td>
</tr>
<tr>
<td>Developing new or next generation products and the processes used to develop them</td>
<td>5</td>
</tr>
<tr>
<td>Improving current generation products and the processes used to manufacture them</td>
<td>15</td>
</tr>
<tr>
<td>Improving and/or enabling the product and process development group</td>
<td>6</td>
</tr>
<tr>
<td>Improving and/or enabling Canadian Blood Services</td>
<td>9</td>
</tr>
<tr>
<td><strong>National training program</strong></td>
<td>40</td>
</tr>
<tr>
<td>Transfusion medicine fellowships</td>
<td>4</td>
</tr>
<tr>
<td>Postdoctoral fellowships</td>
<td>7</td>
</tr>
<tr>
<td>Graduate fellowships</td>
<td>17</td>
</tr>
<tr>
<td>Summer research scholarships</td>
<td>9</td>
</tr>
<tr>
<td>BloodTechNet awards</td>
<td>3</td>
</tr>
<tr>
<td><strong>Program Support Award for Canadian Transfusion Medicine and Science Research</strong></td>
<td>3</td>
</tr>
</tbody>
</table>
### Canadian Blood Services/CIHR Partnership National Operating Grant Program

**Purpose:** Blood utilization and conservation

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of antibody-mediated immune suppression as a model in the development of a replacement for RhD prophylaxis in haemolytic disease of the fetus and newborn</td>
<td></td>
</tr>
<tr>
<td>Improving the cryostorage of blood products using novel small molecule cryoprotectants</td>
<td></td>
</tr>
<tr>
<td>Development of novel blood vessel and organ sealants for blood conservation in surgical practice</td>
<td></td>
</tr>
<tr>
<td>Platelet microRNAs during storage under blood bank conditions</td>
<td></td>
</tr>
<tr>
<td>Transfusion of red cells in hematopoietic stem cell transplantation: The TRIST Study</td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid versus placebo to reduce perioperative blood transfusion in patients undergoing major liver resection: a pilot randomized controlled trial</td>
<td></td>
</tr>
<tr>
<td>Understanding host mechanisms responsible for immune platelet destruction and thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Polyhemoglobin catalase superoxide dismutase carbonic anhydrase: a novel soluble biotherapeutic with no cardiac toxicity for hemorrhagic shock and other uses</td>
<td></td>
</tr>
<tr>
<td>Characterization of the hematopoietic reconstitution enhancing activity of osteoblasts derived from human mesenchymal stromal cells</td>
<td></td>
</tr>
<tr>
<td>Design and implementation of circulatory oxygen therapeutics derived from human hemoglobin by improved systematic chemical coupling and cross-linking</td>
<td></td>
</tr>
<tr>
<td>Release, delivery and cell programming effects of platelet microparticles and microRNAs</td>
<td></td>
</tr>
<tr>
<td>Microfluidic devices to measure the deformability of stored red blood cells</td>
<td></td>
</tr>
<tr>
<td>Understanding transcriptional and epigenetic control by Gfi1b towards the development of a therapy for sickle cell disease</td>
<td></td>
</tr>
<tr>
<td>Pathogenesis and treatment of immune thrombocytopenia: Are there fundamental differences between anti-GP1ba- and anti-GPllbllla-mediated thrombocytopenia?</td>
<td></td>
</tr>
<tr>
<td>Defining disease mechanisms in Immune Thrombocytopenia (ITP) and their association with clinical outcomes</td>
<td></td>
</tr>
<tr>
<td>Polymer-based manufacturing tolerogenic miRNA-based therapeutics</td>
<td></td>
</tr>
<tr>
<td>Aneurysmal SubArachnoid HemorrhAge - Red blood cell transfusion And outcome (SAHaRA): a pilot randomized controlled trial</td>
<td></td>
</tr>
</tbody>
</table>

### Myocardial Ischemia and Transfusion. The MINT rollover trial

**Purpose:** Transfusion-related acute lung injury

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanisms of antibody-independent transfusion-related acute lung injury (TRALI)</td>
<td></td>
</tr>
<tr>
<td>Identification of host cellular immune mechanisms responsible for the initiation and/or modulation of Transfusion Related Acute Lung Injury (TRALI)</td>
<td></td>
</tr>
<tr>
<td>Transfusion-Related Acute Lung Injury and delayed TRALI: a prospective study in critically ill children</td>
<td></td>
</tr>
</tbody>
</table>

### Transfusion-related Epstein-Barr Virus (EBV) infection among allogeneic stem cell transplant pediatric recipients: A multicenter prospective cohort study (TREASuRE Study)

**Purpose:** Blood supply risk

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short and long-term clinical effects of blood donor characteristics in transfusion recipients</td>
<td></td>
</tr>
<tr>
<td>Exploratory analyses to determine if method of donor blood processing affects outcome in transfused recipients</td>
<td></td>
</tr>
<tr>
<td>Examining the relationship between repeated blood donations in female donors on maternal/neonatal outcomes: a cohort study</td>
<td></td>
</tr>
</tbody>
</table>
## Canadian Blood Services/CIHR Partnership New Investigator Program
- Transfusion requirements in cardiac surgery II (TRICS II)
- Code sepsis: defining and translating optimal resuscitation and care for children with septic shock

## Intramural Operating Grant Program
- **Human monoclonal CD44 antibodies as potential IVIg replacements**
- **Plasma versus plasma protein concentrate transfusion for coagulopathic control**
- **A multifaceted intervention to optimize red blood cell transfusion practice in two provinces**
- Antibodies to CD44 as a potential replacement for IVIg in ITP
- Residual risk of transfusion-transmitted cytomegalovirus infection: incidence and pathogenesis
- Defining the components of transfusable plasma that reduce bleeding
- Elucidation of the mechanism of IVIg-associated hemolysis
- Role of blood component manufacturing on microvesicle-induced transfusion-related immune modulation
- Monoclonal antibodies with anti-D-like activity in the amelioration of murine immune thrombocytopenia

## Small Projects Funding Program
- **National evaluation of platelet transport bags to reduce wastage**
- **Use of red blood cell antigen genotyping to assess RhD diversity in sickle cell disease patients**
- **Neonatal outcomes after transfusion of ABO non-identical blood (Neo-ABO)**
- Understanding brain death: a multipurpose educational video aimed to a diverse public and professional audience
- **Data sharing with CBMTG registry**
- **Incidence of intracranial hemorrhage in pediatric oncology patients**
- **Red cell genotyping using buccal swab DNA**
- **Pre-transfusion furosemide for TACO**
- **ROTEM-guided transfusion protocols – impact on the manufacturer**

## James Kreppner Fellowship in Blood System Studies
- Legal and policy strategies to optimize organ donation in Alberta
- Organ donation in Canada: engaging with stakeholders and proposing solutions to current legal and ethical challenges

## Kenneth J. Fyke Award Program
- Prospective observational study of organ deceased donor management in three ICUs – a pilot study (the DONATE pilot study)

## Supplementary Funding Program
- **Purpose: External grant top-up**
- **CIHR: Polymer-grafted allogenic leukocytes and systemic immune modulation**
- **Heart & Stroke Foundation: Auxiliary cofactors in fibrinolysis**
- **Burroughs Wellcome Fund: Innovation in regulatory science**
- **CIHR: Pathogenesis of fetal and neonatal alloimmune thrombocytopenia and IVIg anti-FcRn therapies**
### Titles of projects conducted by Product and Process Development program

#### Deepening the understanding of our products and the processes used to manufacture them

- Bacterial growth in red blood cells prepared in different additive solutions (derived from the 30-minute rule)
- Plasma protein evaluation at different freezing temperatures
- The interaction between red cell transfusion and lung injury: the influence of manufacturing conditions
- Quality assurance in red cell components – does it matter where the red cells are stored
- Understanding blocked filters
- Characterization of white blood cell concentration and viability in stored red cell concentrates
- Cord blood transient warming events
- Impact of donor variation on platelet quality
- Genomic studies to understand *Staphylococcus epidermidis* predominance as a platelet contaminant
- Evaluation of synthetic antimicrobial peptides for their ability to inhibit biofilm formation
- Investigation of the structure of the cell wall bacterial biofilms
- Supernatant reduction of gamma-irradiated red cell concentrate for pediatric transfusion
- Feasibility assessment of using stem cell patient blood product support to examine changes in blood component manufacturing
- Impact of donor sex, age and hemoglobin status on hemolysis
- Quality assessment of cryopreserved/irradiated CPD/SAGM red blood cell units
- Investigation of an adverse transfusion reaction
- Product characterization - quality monitoring program for cord blood derived hematopoietic stem cells
- Product characterization - quality monitoring program for 2015-2016
- Correlation of expiry hemolysis in red cell concentrates with number of transportation events

#### Developing new or next generation products and the processes used to manufacture them

- ACP-215 closed system cryopreservation
- Feasibility study: non-invasive prenatal testing using single exon fetal RhD determination
- Bacteria detection in buffy coat pooled platelets sampled at 36 hours and stored for seven days
- BacT proficiency testing seven day platelets
- Haemonetics Solx/Fenwal Esol ACP-215 study

#### Improving current generation products and the processes used to manufacture them

- Supply chain equipment request for proposal
- Non-destructive quality control testing for platelet products
- Modeling unit volumes after non-destructive testing
- Non-destructive quality control testing for red blood cell products
- Product volume reduction – adult hematopoietic cell stem cell manufacturing
- Modeling support for rare red blood cell inventory
- Confirmatory testing – positive BacT/ALERT cultures
- B2 study – evaluation of 16 hour hold at 24°C
- Validation of sterility testing of stem cells with the BACTEC system
- Production of Macopharma B1s cold
- Exploration of options to test cord blood units that contain antibiotics for bacterial contamination
- Bacterial growth during storage of thawed cryoprecipitate at 20-24°C for 24 hours
- Evaluation of the ADAM instrument for residual white blood cell testing
- Data review for future use of one pack type with no cooling trays
- Development of cord blood unit thawing protocol
<table>
<thead>
<tr>
<th>Improving and/or enabling the product and process development group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streamlining project and portfolio management in the product and process development group</td>
</tr>
<tr>
<td>Build the netCAD (Network Centre for Applied Development) donor base</td>
</tr>
<tr>
<td>Product and process development test method validation: standardization and qualification of test assays in Centre for Innovation labs supporting product and process group projects</td>
</tr>
<tr>
<td>Increasing netCAD testing capabilities</td>
</tr>
<tr>
<td>NetCAD4cord</td>
</tr>
<tr>
<td>Improve netCAD operational efficiency project</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Improving and/or enabling Canadian Blood Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developing a model to optimize apheresis HLA/HPA matched platelet program</td>
</tr>
<tr>
<td>Holiday platelet planner</td>
</tr>
<tr>
<td>Modeling and simulation education and training</td>
</tr>
<tr>
<td>Canadian Blood Services clinic simulator</td>
</tr>
<tr>
<td>Alberta inventory and logistics</td>
</tr>
<tr>
<td>Five day versus seven day platelets</td>
</tr>
<tr>
<td>84-day deferral</td>
</tr>
<tr>
<td>Hospital ordering behaviour and management of O- inventory</td>
</tr>
<tr>
<td>Saskatchewan stock holding unit</td>
</tr>
</tbody>
</table>
### Titles of projects funded by National Training Program

Note: Projects that are italicized are those for which funding was initiated in fiscal year 2016–2017.

Visit our online [Funded Research Projects database](#) for project details.

#### Postdoctoral Fellowship Program

<table>
<thead>
<tr>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenesis of fetal and neonatal alloimmune thrombocytopenia and mechanisms of IVIg therapy</td>
</tr>
<tr>
<td>Transfusion options in coagulopathy: efficacy in controlling bleeding</td>
</tr>
<tr>
<td>Understanding IVIg mechanism(s) of action in alleviating immune platelet destruction and thrombocytopenia</td>
</tr>
<tr>
<td>Understanding the factors that influence bacterial proliferation and biofilm formation in platelet concentrates</td>
</tr>
<tr>
<td>Mechanism of anti-D-like antibody-mediated amelioration of immune thrombocytopenia (ITP)</td>
</tr>
<tr>
<td>DNA aptamers for detection of red blood cells destined for rapid post-transfusion clearance</td>
</tr>
<tr>
<td>Development of a small molecule-based stem and progenitor expansion protocol to accelerate engraftment after cord blood transplantation</td>
</tr>
</tbody>
</table>

#### Graduate Fellowship Program

<table>
<thead>
<tr>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>The in vivo effects of liposome treatment on minimizing membrane injury in rat red blood cells during hypothermic storage</td>
</tr>
<tr>
<td>Identification of protein biomarkers for red cell quality</td>
</tr>
<tr>
<td>MRI-guided focused ultrasound facilitated IVIg immunotherapy as a therapeutic approach for Alzheimer's disease</td>
</tr>
<tr>
<td>Assessment of fluorinated ice crystallization inhibitors; cryopreservation of hematopoietic stem cells and red blood cells</td>
</tr>
<tr>
<td>Characterization of the role of MSI2 in human hematopoietic stem cell self-renewal</td>
</tr>
<tr>
<td>Role of skin disinfection and buffy coat platelet production on residual bacterial contamination in platelet concentrates and cord blood stem cells</td>
</tr>
<tr>
<td>Towards the impact of protein synthesis in human platelets to transfusion medicine</td>
</tr>
<tr>
<td>Investigation of pathophysiology, prevention and treatment of murine transfusion related acute lung injury (TRALI)</td>
</tr>
<tr>
<td>Cellular therapy to improve CD4+ T-cell responses in humanized mice infected with HIV-1: adoptive transfer of CD4+ T-cells lacking s-Src activity</td>
</tr>
<tr>
<td>Impact of storage on the function of cord blood hematopoietic stem and progenitor cells</td>
</tr>
<tr>
<td>Small molecule inhibitors of phagocytosis to replace intravenous immunoglobulin (IVIg)</td>
</tr>
<tr>
<td>Dengue virus replication by anucleate cells: impact on pathogen reduction efficacy</td>
</tr>
<tr>
<td>Recombinant Fc multimers to replace IVIg</td>
</tr>
<tr>
<td>Study of the mechanisms implicated in platelet microparticle internalization by blood cells</td>
</tr>
<tr>
<td>Platelet desialylation: novel mechanism of platelet clearance and immune tolerance</td>
</tr>
<tr>
<td>Improving pathogen inactivation: the dengue virus-induced platelet proteome</td>
</tr>
<tr>
<td>Small molecule ice recrystallization inhibitors as cryo-additives for red blood cell cryopreservation</td>
</tr>
</tbody>
</table>
### Summer Research Scholarships

<table>
<thead>
<tr>
<th>Topic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Towards artificial plasma produced by cultured cells</td>
<td>Reducing the concentration of dimethyl sulfoxide in platelet cryopreservation and improving recovery using small-molecule ice recrystallization inhibitors</td>
</tr>
<tr>
<td>Small molecule and recombinant protein inhibitors of phagocytosis to replace IVIg therapy</td>
<td>Identification of biofilm-related virulence factors in the predominant platelet contaminant Staphylococcus epidermidis</td>
</tr>
<tr>
<td>Roles of IVIg and anti-FcRn in amelioration of pathogenesis in fetal and neonatal alloimmune thrombocytopenia</td>
<td>A pilot study of IVIg or rituximab for immune-mediated disorders</td>
</tr>
<tr>
<td>Role of insulin-growth factor (IGF) proteins in mediating the growth promoting activity of osteoblast conditioned medium</td>
<td>Use of umbilical cord blood for regenerative therapy and immune modulation: an updated systematic review of clinical studies</td>
</tr>
</tbody>
</table>

### BloodTechNet Award Program

<table>
<thead>
<tr>
<th>Topic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Stem Cell Club: educating medical and nursing students to develop professional skills</td>
<td>Social media for knowledge translation and education 3 (SoMe-KTE3): Transfusion, thrombosis, and hemostasis</td>
</tr>
<tr>
<td>Podcast for FNAIT and ICTMG red cell specifications for hemoglobinopathies guidelines</td>
<td></td>
</tr>
</tbody>
</table>

### Titles of projects funded by Program Support Award for Canadian Transfusion Medicine and Science Research

<table>
<thead>
<tr>
<th>Organization</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>McMaster Transfusion Research Program</td>
<td>University of Ottawa Centre for Transfusion Research</td>
</tr>
<tr>
<td>The Centre for Blood Research</td>
<td></td>
</tr>
</tbody>
</table>
# Appendix II: Publications

Summary of peer-reviewed and non-peer-reviewed publications from fiscal year 2016-2017

<table>
<thead>
<tr>
<th>Publication Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td># of peer-reviewed and non-peer-reviewed publications in fiscal year 2016-17</td>
<td>362</td>
</tr>
<tr>
<td><strong>Peer-Reviewed Publications</strong></td>
<td></td>
</tr>
<tr>
<td>Journal Articles</td>
<td>122</td>
</tr>
<tr>
<td>Review Articles</td>
<td>23</td>
</tr>
<tr>
<td>Clinical Guidelines</td>
<td>1</td>
</tr>
<tr>
<td>Comments/Letters/Editorials</td>
<td>15</td>
</tr>
<tr>
<td>Books/Book Sections</td>
<td>6</td>
</tr>
<tr>
<td>Published Abstracts</td>
<td>145</td>
</tr>
<tr>
<td><strong>Non-Peer-Reviewed Publications</strong></td>
<td>50</td>
</tr>
<tr>
<td>CBS Website Publications</td>
<td>20</td>
</tr>
<tr>
<td>Fast policy facts</td>
<td>1</td>
</tr>
<tr>
<td>Technical Reports</td>
<td>29</td>
</tr>
</tbody>
</table>

Summary of h-index factor analysis

![h-index chart]

Notes: i) H-Index factors measured using GoogleScholar on March 27 2017. ii) Mean H-index calculated using H-Index factors from the 15 core investigators. Core investigators include (Jason Acker, John Blake, Donald Branch, Dana Devine, Margaret Fearon, Mindy Goldman, Alan Lazarus, Heyu Ni, Sheila O’Brien, Nicolas Pineault, Ed Pryzdial, Sandra Ramirez-Arcos, Mark Scott, William Sheffield, and Kathryn Webert). iii) H-Index is a single bibliometric indicator that is a measure of both the productivity and impact of published work. H-Index is an indicator of research users being aware of and valuing published research evidence. Average H-index for Canadian university professors in the biological sciences is 10.6.
Publications’ Details

Author Legend:
Bold – Centre for Innovation investigators and senior staff; Canadian Blood Services medical directors; Directors of transfusion medicine research programs receiving funding via the Program Support Award for Transfusion Medicine and Science Research.
Underlined – Non-Canadian Blood Services investigators funded in part by Canadian Blood Services.

Visit our online Publications database for publication details.

Journal Articles


113. van der Meer PF, Devine DV, on behalf of the BEST Collaborative. Alternatives in blood operations when choosing non-DEHP bags. Vox Sang 2017; 112: 183-4.


**Review Articles**


**Clinical Guidelines**


**Comments/Letters/Editorials**


Books/Book Sections


Published Abstracts


38. Fallis R. Impact of phenotype reagent antiserum utilization following the discontinuation of retyping red cell components labeled as antigen negative by CBS. *Canadian Society For Transfusion Medicine Website* 2016.
57. Jahan S, Pineault N. Prolonged processing delays of cord blood units is associated with reduced engraftment activities. *Transfusion* 2016; 56: 43A.


83. Nielsen R. The management of a quarantine or recall when a significant number of blood products are involved. Transfusion 2016; Suppl: 249A.
86. O'Brien S, Fearon M, Devine D, Goldman M, Germain M, Delage G. Estimated risk to the Canadian blood supply from sexually transmitted Zika virus. Transfusion 2016; 56: 12A.
94. Parvizian S, Heddle N, Athale U, Goldman M, Verhove B. Red cell antigen genotyping compared to serological phenotyping in sickle cell disease patients in Canada: potential for reducing alloimmunization. Transfusion 2016; 56: 153A.


104. Ramirez-Arcos S, Perkins H, Yi Q, Jenkins C, Sheffield W. Extending storage of thawed cryoprecipitate from 4 hours to 24 hours at 20C to 24C poses a safety risk to transfusion patients. Transfusion 2016; 56: 76A.

105. Resz I, Gill B, Angus N. Implementation of automated phenotype testing on the neo. Transfusion 2016; 56: 146A.


appropriate use of red blood cell transfusion: a quality audit at 10 hospitals. Canadian Society For Transfusion Medicine Website 2016.


Canadian Blood Services Website Publications


2. **Branch D**. ResearchUnit: Mastering the monocyte monolayer assay. blood.ca website 2016.


8. **Heddle N**. ResearchUnit: Older blood as good as new: no harmful effects of storage time before transfusion. blood.ca website 2016.

9. **Lazarus A**. ResearchUnit: United we stand, divided we fall: using monoclonal antibody combinations to improve drug effectiveness. blood.ca website 2016.


17. **Pryzdial E**. ResearchUnit: Designing a new and improved drug to dissolve blood clots. blood.ca website 2017.


Fast Policy Facts

Technical Reports


Appendix III: Health Canada financial contribution

Summary of Expenditures – April 1 2016 to March 31 2017

**Schedule 1: Overview**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating funds (Schedule 2)</td>
<td>1,186,440</td>
</tr>
<tr>
<td>Funding programs (Schedule 3)</td>
<td>4,459,244</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5,645,684</strong></td>
</tr>
</tbody>
</table>

**Schedule 2: Operating funds**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centre for Innovation program administration</td>
<td>556,834</td>
</tr>
<tr>
<td>MSM program administration</td>
<td>175,000</td>
</tr>
<tr>
<td>NetCAD operations</td>
<td>217,867</td>
</tr>
<tr>
<td>Intellectual property protection and other legal activities</td>
<td>236,739</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,186,440</strong></td>
</tr>
</tbody>
</table>

**Schedule 3: Funding programs**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Blood Services/CIHR partnership operating grant program</td>
<td>1,908,142</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR new investigator program</td>
<td>120,000</td>
</tr>
<tr>
<td>Canadian Blood Services intramural research grant program</td>
<td>798,016</td>
</tr>
<tr>
<td>Small projects funding program</td>
<td>92,184</td>
</tr>
<tr>
<td>James Kreppner fellowship in blood system studies program</td>
<td>75,000</td>
</tr>
<tr>
<td>Postdoctoral fellowship program</td>
<td>223,944</td>
</tr>
<tr>
<td>Graduate fellowship program</td>
<td>342,167</td>
</tr>
<tr>
<td>Summer research scholarship program</td>
<td>70,703</td>
</tr>
<tr>
<td>Program Support Award for Canadian transfusion medicine and science research</td>
<td>728,464</td>
</tr>
<tr>
<td>CIHR partnership: Transplantation research</td>
<td>50,000</td>
</tr>
<tr>
<td>Additional funding for research projects</td>
<td>50,624</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4,459,244</strong></td>
</tr>
</tbody>
</table>

Notes:
- Funding programs include capital expenditures under $10,000