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Executive summary

The Centre for Innovation at Canadian Blood Services (the Centre) supports a safe, effective, and responsive system of blood and related biologics for Canada. Through its multi-faceted activities, the Centre fosters and supports relevant discovery and applied research, and facilitates the dissemination and application of created knowledge. These activities promote the creation and translation of new knowledge into new and enhanced practices, services, and technologies for the benefit of Canadian patients and the health-care system, now and in the future.

The Centre for Innovation employs 11 principal investigators, cross-appointed to Canadian academic institutions, and actively engages with Canadian Blood Services’ medical, epidemiology and supply chain staff. In 2014–2015, this internal network was complemented by 27 external Canadian investigators who received funding from the Centre to complete research studies or mentor trainees at their academic institutions. Through targeted partnerships, the Centre’s network expands nationally and internationally. Over the last year, it formalized or renewed 31 partnerships with industry, academia and not-for-profit organizations and associations.

The Centre for Innovation achievement highlights for 2014–2015 include:

- 254 peer-reviewed publications, including articles in high-impact journals such as Blood, the Journal of Clinical Investigation, the Journal of Immunology, and Thrombosis and Haemostasis. The average H-index of 24 of the Centre’s core investigators reflects their productivity and citation impact.
- 24 technical reports shared within Canadian Blood Services and with partners. Subject-matter expertise and data included in these reports informed product and process improvements.
- 14 professionals formally trained within Canadian Blood Services and with partners. Subject-matter expertise and data included in these reports informed product and process improvements.
- Over 200 oral and poster presentations at national and international conferences.
- Over 80 major education events organized or supported, attracting an estimated 7,000 professionals. These included the LearnTransfusion webinar series, the Canadian Blood Services Annual International Symposium, and the Red Cell Club Meeting.
- Three Health Canada licence amendments supported to achieve process improvements while also maintaining safety and quality:
  - Removing the requirement to balance centrifuges prior to whole blood centrifugation.
  - Removing the confidential unit exclusion step from the blood collection procedure.
  - Changing the Macopharma whole blood collection set and introducing the Macopharma platelet pooling set.
- Provision of evidence-based data to the Canadian Standards Association that informed changes in red blood cell storage standards.
- Contributions to the execution of several clinical trials, including the PREPARES trial which will provide the necessary information for the licensing of the pathogen inactivation technology Mirasol in Canada.
- Publication of systematic reviews and clinical guidelines to influence clinical practice. These include guidelines for platelet utilization by the International Collaboration for Transfusion Medicine Guidelines and by the AABB.
- Establishment of the Canadian Blood Utilization Collaborative to optimize blood utilization to improve patient outcomes in a cost-effective manner.
Overview of the Centre for Innovation

Objective
Through its Centre for Innovation, Canadian Blood Services conducts and facilitates research and education activities in transfusion and transplantation science and medicine. This report describes the progress the Centre has made during fiscal year 2014–2015 and highlights its key achievements as they relate to the Centre’s goal of contributing to the safety, quality and supply of blood and related biologics.

Expertise
Eleven principal investigators (bolded names throughout report) are core to the Centre for Innovation scientific and process engineering expertise. Employees of Canadian Blood Services, they are tightly linked to our organization and aware of the system’s research needs, overall goals and strategy. In particular, the investigations led by the Centre’s product and process development investigators address key issues raised by our supply chain. Furthermore, the cross-appointments of our core investigators at Canadian academic institutions create a bridge and leverage resources available through academic institutions.

Supplementing the group of core investigators, the Centre engages with 29 Canadian Blood Services medical experts and epidemiologists (bolded names throughout report). This group provides the medical expertise to the network.

This internal network is strengthened by contributions from external investigators. In 2014–2015, there were 27 Canadian Blood Services adjunct scientists and Canadian academic researchers who led a research project funded by the Centre’s research and training programs. The Centre's network also expands nationally and internationally through partnerships with industry, academia, and not-for-profit organizations and associations.

Programs and projects
The Centre for Innovation develops a series of research and education programs to achieve its goal of creating new knowledge in areas of significance and to disseminate this knowledge. Centre employees administer these programs while leveraging Canadian Blood Services’ financial, legal, IT, communication and human resources services.

In 2014–2015, through the Centre’s competitive research and training programs, the research group funded 51 research projects, 29 trainee awards and three Program Support Awards for Canadian transfusion medicine and science research (Appendix 1). The product and process development group worked on 54 research and investigational studies supporting our supply chain or with industry partners (Appendix 1). The knowledge mobilization group organized or supported 81 education events, maintained its transfusion education website and enhanced some of its primary educational tools.

The Centre for Innovation plays a leadership role in the establishment of significant collaborative projects. The Risk-Based Decision Making Framework initiative was completed during the year, while the International Collaboration for Transfusion Medicine Guidelines successfully published its first set of guidelines. Finally, a new initiative, the Canadian Blood Utilization Collaborative, was established to optimize blood utilization to improve patient outcomes in a cost-effective manner.

The successes of these projects and programs are highlighted throughout this report. These successes were made possible by the continued funding received by the Centre for Innovation from Health Canada, the provincial and territorial ministries of health, and our partners. The blood donors who contribute to our research are also gratefully acknowledged.
Research and development progress

Canadian Blood Services must maintain the safety, quality and sufficiency of the blood and blood products supply for Canadian patients. The blood and blood product supply chain is a complex process involving many steps (Fig. 1). The knowledge created through the Centre for Innovation’s research and development programs contributes to this process at multiple levels. This section of the report presents the Centre’s research and development achievements for 2014–2015, including highlights of the impact of these achievements on the safety, quality and sufficiency of the blood, blood products, and hematopoietic stem cells supply.

Figure 1: The vein-to-vein path of blood and blood products for transfusion and transplantation

Safety and sufficiency of the blood supply
Under the leadership of Drs. Margaret Fearon, Mindy Goldman, and Sheila O’Brien, Canadian Blood Services carries out comprehensive surveillance of bloodborne pathogens to monitor for changing trends in known pathogens and to identify the risks associated with new or emerging pathogens. Within Canadian Blood Services, the team works closely with the regulatory and quality groups, and leverages the expertise, testing and research capacity available in our National Testing Laboratory. The team also collaborates extensively with national and international partners. Surveillance information allows Canadian Blood Services to put additional safeguards in place to reduce any risk to recipients of blood products.

In Canadian Blood Services’ 2014 Surveillance Report, the epidemiology and surveillance group reported that the rates of tested transmissible disease per 100,000 donations continues to be very low.¹ Through rigorous methodology, the group estimated that the residual risk of a transfusion-transmitted infection also remains very low. This data confirms the safety of the blood supply for the viruses we screen. Through this report, residual risk information is also made available to physicians and their patients to inform their transfusion decisions. The 2014 report also highlighted potential risks to the blood supply associated with emerging parasites and viruses, including Babesia microti, Hepatitis E, Chikungunya, and Ebola.

In collaboration with Dr. Gilles Delage from Héma-Québec, Dr. Fearon evaluated the seroprevalence of Babesia microti and Hepatitis E virus in Canadian blood donors. Antibody testing for Babesia microti showed no evidence of babesiosis in the almost 15,000 blood donors tested. Hepatitis E DNA testing using polymerase chain reaction was performed on all donors and antibody testing was performed on a subset. A Hepatitis E seroprevalence rate of 5.9 per cent was found, although no evidence of active infection has been observed (0 DNA-positive donors). The results of these studies indicate there is no evidence to support implementation of new donor testing policies or procedures for these bloodborne pathogens at this time, although ongoing surveillance and additional research is needed.²-⁴

Starting in late 2013 and continuing through 2014, a large outbreak of a mosquito-borne infection, Chikungunya virus, occurred in the Caribbean, extending into South and Central America. This was the first outbreak of Chikungunya documented in the Americas. Although no cases of transfusion-related transmission have been reported to date, Canadian Blood Services conducted research to evaluate the risk associated with this virus. Dr. Fearon interacted with the Public Health Agency of Canada National Microbiology Laboratory, blood providers and other international groups to monitor the infection rates in different countries. In collaboration with Dr. O’Brien’s group, they also completed a travel survey of 8,908 blood donors. Data from the travel survey, as well as the natural history of Chikungunya virus, was used to estimate the risk of collecting a donation from an infected donor. Given that the risk was extremely low (less than one in six million donations), and that there are no reports of Chikungunya virus ever being transmitted by transfusion, there is currently no evidence that any intervention to address risk from Chikungunya virus is warranted.
A large outbreak of Ebola virus in West Africa prompted Canadian Blood Services to put together contingency plans to address risk from potentially infected donors who may have come in contact with cases in Canada. Donors returning from West Africa are already deferred for 12 months for malaria risk and so do not pose a risk to blood safety. Under the leadership of Dr. Fearon, Canadian Blood Services developed information for donors and staff to address risk in the unlikely event of an infection acquired in Canada.

Working with an international group, Dr. O’Brien led a study to examine the relationship between epidemiologic data, public environment and operational feasibility in the “evolution” of malaria-risk-reduction policies in different countries. The focus was on selective testing policies and deferral-only policies, as used in Canada. The greatest risk of malaria is from former residents of endemic countries, whereas the greatest operational impact is from short-term travellers who have a very low risk of malaria. The malaria-risk appears to be well-managed by either selective testing or deferral-only policies. However, selective testing has the advantage of impacting fewer donors for a shorter period. Importantly, the group observed that additions and revisions had been made to all policies in response to concerns. The group was concerned that this sporadic “evolution” resulted in different policies in each of the participating countries, and that if policies were to be developed afresh they would not necessarily be those currently in place. The participation of Canadian Blood Services in international studies such as this one prepares our organization for potential future changes in this area.

In 2013, Canadian Blood Services implemented a new eligibility policy to allow blood donation from “men who have had sex with men” (MSM) more than five years ago. Drs. O’Brien and Goldman continue to monitor the impact of the policy on the safety and sufficiency of the blood supply. To date the rate of detection of HIV-positive donors after implementation of the new policy has not increased. A large anonymous survey of male donors was completed in April 2015 to assess donor compliance to the new policy before and after implementation. Many male donors in the pre-implementation survey did not support the previous policy, under which men who had had sex with a man even one time since 1977 were ineligible to donate blood. In particular, young donors felt that a man who has had sex with a man should be allowed to donate as long as he meets all other criteria. The group will continue to monitor the impact of the new policy and the compliance of blood donors with this policy. The group provided a study report to Health Canada to inform regulators. Canadian Blood Services also continues to discuss this contentious issue in the literature. Finally, in early 2015, netCAD, Canadian Blood Services’ research development facility, held a “rainbow clinic” to engage with donors who may be affected by the policy and to encourage individuals who are ineligible to donate blood to the main blood supply due to the MSM policy to donate blood for research purposes. During the course of the day, participants had the opportunity to learn about the research projects supported by or conducted at netCAD and to donate their blood to research. Highlighted in many media outlets, the rainbow clinic succeeded in engaging ineligible donors with Canadian Blood Services.

Cytomegalovirus (CMV) is a common virus infecting most people during their lifetime, but rarely causing illness in the healthy population. However, in some patients (e.g., organ transplant recipients), CMV can cause serious illness or even death. The use of leukofiltration to reduce the number of white blood cells eliminates almost all the risk of acquiring CMV from blood transfusion. However, a very low risk of infection remains.

In 2001, recommendations for the use of CMV-negative blood products (e.g., products that test negative for CMV) for high-risk populations were developed. However, variability in their interpretation and application has led to disparate local policies among both hospitals and blood operators, and wide variability across provinces. To gather information that could inform development of a national policy, Drs. Dana Devine and Lani Lieberman (of the University Health Network and a recent graduate of our transfusion medicine residency program) convened an international forum to gather information around the wide range of practices related to donor testing of CMV, the use of CMV-negative products in specialized populations, and the impact of this product line on inventory management. This information provides a snapshot of the variation in the standard of care in various jurisdictions. Finally, Drs. Fearon and O’Brien are collaborating in a large CMV study with Dr. Jutta Preiksaitis (University of Alberta) to evaluate various testing modalities and to compare CMV positivity in transfused organ recipients and blood donors. Preliminary results will be presented in the coming year.
While ensuring a sufficient blood supply is important to blood operators, this cannot be achieved at the detriment of donor health. Drs. Goldman and O’Brien previously reported that a significant proportion of donors have low or absent iron stores, which may lead to significant health risks.9,10 In the last year, Canadian Blood Services has worked to educate donors on iron deficiency and to better screen donors at risk. All donors who are ineligible to donate blood as a result of low hemoglobin levels now receive a letter advising them to visit their physicians to identify and correct the cause of low hemoglobin levels. Drs. Goldman and O’Brien have assessed donor understanding of this letter and the actions donors take as a result of it. Unfortunately, while donors understand the letter and the reason they are ineligible to donate, few donors take action to increase their iron stores.11 Canadian Blood Services is currently conducting a study to assess the operational feasibility of measuring ferritin levels in donors. The data will be used to assess the effectiveness and operational feasibility of various potential interventions to inform policy decision-making to protect our donors.

Prior to blood donation, Canadian Blood Services donors must complete a health history questionnaire and confidentially indicate whether they think their donation should not be used. The confidential unit exclusion (CUE) process was introduced into the blood collection procedure in Canada in the 1980s as a mechanism for donors to confidentially indicate that they believed their blood may not be safe. However, it has been shown that CUE does not contribute to blood safety in Canada, as a result of improvements in the donor screening process, improvements in public health, and advances in donor testing for human immunodeficiency virus (HIV) and other infectious diseases. It has also been shown that those individuals who should be selecting the “do not use my blood” option are not, while hundreds of donors who have no risk are selecting the discard option in the CUE in error. Based on evidence collected by Drs. Goldman and O’Brien, Canadian Blood Services submitted and received a licence amendment change from Health Canada to remove the CUE step from the blood collection procedure, streamlining the blood collection process without affecting blood safety.12

The Centre for Innovation product and process development group undertakes investigations that generate the evidence needed to improve Canadian Blood Services’ operations. In 2014, the group was instrumental in the selection of the new collection bags required by Canadian Blood Services. By performing comprehensive quality measurements, the group made recommendations for the selection of bags that would meet our quality control standards.13,14 This evidence was used to obtain a Health Canada licence amendment for the introduction of new whole blood and platelet collection bags.15 The successful implementation of the new bags was completed in early 2015. The product and process development group informed another licence amendment to Health Canada that led to a manufacturing process improvement. Canadian Blood Services no longer requires the routine balancing of centrifuges prior to whole blood centrifugation.16 The elimination of this step improves efficiencies without impacting the quality of blood products.

Adequate donor skin disinfection is important to ensure the safety of blood components. Currently, Canadian Blood Services uses the Chloraprep swabstick produced by CareFusion as the primary method to disinfect donor skin. For donors with hypersensitivity to chlorhexidine, a two-step method, also produced by CareFusion, is used. CareFusion has informed our organization that the production of the alternative two-step method will be suspended later in 2015. Therefore, to ensure the continuity of the blood supply, Canadian Blood Services needs to identify another alternative skin disinfection method for the approximately three per cent of donations where the two-step method is used. Drs. Goldman and Sandra Ramirez-Arcos conducted a study to evaluate two alternative methods. The results led to the selection of one method which will be implemented by Canadian Blood Services in 2015.17

**Red blood cells**

Red blood cell units are the most common blood product Canadian Blood Services distributes to hospitals. One of the major challenges in the production of red blood cell units is red blood cell storage lesions, or changes in red blood cells observed over time. Red blood cell lesions are thought to affect oxygen delivery and thus may have clinical implications.

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**Red blood cells** are manufactured from whole blood and stored for up to 42 days at 1-6°C prior to transfusion. Canadian Blood Services distributes ~800,000 units annually.
Current regulations permit red blood cells to be stored for up to 42 days. This regulation is thought to minimize red blood cell storage lesions. However, whether these lesions matter clinically is heavily debated. Retrospective studies have produced conflicting results and questioned the quality of “older blood” — blood that is closer to the end of its 42-day shelf life. In 2015, the University of Ottawa Centre for Transfusion Research, supported by the Centre for Innovation, completed the Age of Blood Evaluation (ABLE) trial. This landmark study prospectively compared the clinical outcomes of critically ill adult patients transfused with “fresh blood” (blood stored for less than seven days) to those transfused with “standard blood.” The study showed that transfusion with “fresh blood” was not associated with a reduction in in-hospital mortality. Similarly, the McMaster Transfusion Research Program, also with support from the Centre, retrospectively evaluated the effect of age of blood on in-hospital mortality in patients with cardiovascular diagnoses. This study also found no association between the age of blood and in-hospital mortality. These results support the Age of Red Blood Cells in Premature Infants study published by the Ottawa group in 2012 and the recently completed RECESS study (see report at Transfusion News). While the evidence is reassuring that standard-issue red blood cells are not clinically different from fresher units, further research is needed. In particular, additional clinical situations must be studied.

While current evidence suggests there is no need for blood operators to shorten the shelf life for red blood cells, Canadian Blood Services investigated the impact a decrease in the storage time for red blood cells would have on its inventory and its distribution network. Dr. John Blake, from the product and process development group, completed modelling work and presented at various venues. His work shows that a shelf life of 14 days or less is likely to cause significant challenges for hospitals and for blood operators. With this work, Canadian Blood Services is well prepared should a change in the storage time for red blood cells become necessary. Dr. Blake received the Best Paper Award at the 2014 Industrial and System Engineering Research Conference for this work.

To meet the demand for red blood cells locally, Canadian Blood Services regularly transfers red blood cell units between its distribution sites. Dr. Blake developed a model to evaluate policies for transferring red blood cells between sites. Based on his analysis, he identified simple rules that could potentially lower transport costs while ensuring product availability. With no studies in the literature tackling this type of problem, Dr. Blake’s work is novel and will inform the optimization of Canadian Blood Services’ inventory network.

Canadian standards require that red blood cells must not be exposed to room temperature for more than 30 minutes with each removal from storage. This “30-minute rule” is meant to minimize chances of bacterial growth and limit hemolysis (or degradation of the red blood cells). Drs. Sandra Ramirez-Arcos and Jason Acker have extensively evaluated the effect of room temperature exposure of more than 30 minutes on bacterial growth and the quality of red blood cells. Their work, conducted in collaboration with Dr. Louis Thibault of Héma-Québec, led to the amendment of the Canadian Standard Association standard. The new standard, which will be published later this year, will permit the uncontrolled temperature exposure time for red blood cells to be increased to 60 minutes. This amendment will minimize red blood cell discards, especially at hospitals, without compromising the quality or safety of the product. This standard change is expected to lead to savings for the blood system.

Regulatory quality standards for red blood cell products include the requirements to have less than 0.8 per cent hemolysis in the bag, to have sufficient volume and red cell mass, to be leukocyte reduced, to be sterile, and to limit storage to a period of 42 days at 1–6°C. However, as our understanding of red blood cell products evolves, so does our thinking on how to evaluate the quality of the product. Canadian Blood Services implemented the Quality Monitoring Program. Led by Craig Jenkins, this unique program developed a series of biological markers associated with each of our blood products to better understand their quality parameters, going beyond regulatory requirements. Through the program, Jenkins and Dr. Acker were able to compare the quality of red blood cell components produced before and after the implementation of semi-automated component production at Canadian Blood Services. While the overall quality of the components was similar before and after the change in production method, the results indicate that red blood cell products manufactured by different methods are not equivalent. To further evaluate the effects of different manufacturing processes on red blood cell quality, Drs.
Acker and Dana Devine, with collaborators from Blood Systems Inc. (U.S.) compared the characteristics of red blood cell concentrates produced by nine different processing methods and showed significant differences among products. This data suggests that further research is required to evaluate the impact manufacturing processes may have on the clinical outcomes of transfusion. These studies also raise the importance of controlling for differences in manufacturing processes when performing clinical studies. Canadian Blood Services’ Centre for Innovation is currently partnering with the University of Ottawa Centre for Transfusion Research and the McMaster Transfusion Research Program to investigate the impact of manufacturing processes and donor characteristics on transfusion recipient outcomes.

In collaboration with Dr. Mark Scott. Dr. Hongshen Ma (University of British Columbia) funded through an operating grant has developed a device to determine red blood cell deformability changes that occur during storage in blood bags. This device could be used to identify high-quality and low-quality units, using a very small volume sample. Such technology may change the way red blood cells are assessed prior to transfusion. In a similar approach, Dr. Devine collaborated with Drs. Robert Turner and Michael Blades (University of British Columbia) to apply Raman spectroscopy to develop a method to measure changes in red blood cell units during storage without entering the unit and breaking sterility. Although presently at proof of concept, these technologies are being adapted to hand-held instruments that would be adaptable to the hospital blood bank environment. Drs. Acker and Michael Kolios (Ryerson University) are developing new approaches that would allow for the assessment of red blood cell structure and their oxygen carrying capacity. Although preliminary, their research suggests that photoacoustic imaging combined with spectroscopy may be useful in assessing these parameters without entering the red blood cell unit.

While red blood cell transfusions are considered to be safe, some patients exhibit mild to severe reactions. These reactions arise as the patient’s immune system recognizes one or more of the more than 300 minor blood group antigens present on the donor red blood cells, leading to the production of antibodies (alloantibodies). Patients who are chronically transfused can develop so many alloantibodies that it is impossible to find red blood cell units that can be transfused without causing harm. Researchers funded through the Centre are exploring several approaches to address this challenge. In 2014, Dr. Jayachandran Kizhakkedathu (University of British Columbia) described the development of a robust and universal technique that efficiently converts A, B, and AB red blood cells to universal (O) donor red blood cells. While this technique has been described before, Dr. Kizhakkedathu’s research team reduced the amounts of enzyme required for such conversions by more than 400-fold. This enhancement will facilitate the translation of this technology to the clinic. This work was highlighted in Transfusion News. Dr. Scott’s approach to the alloimmunization challenge is to identify ways to fool the immune system by camouflaging the non-ABO red blood cell antigens. In the last year, Dr. Scott worked with Canadian Blood Services’ Centre for Innovation to develop a strategy to facilitate the emergency use of this innovative product in these rare clinical situations described above.

New curative therapies, instead of symptomatic treatment offered through transfusions, would be advantageous to alloimmunized patients. Dr. Marie Trudel (Université de Montréal), with funding from an operating grant, is examining the molecular mechanisms involved in red blood cell differentiation. Understanding the genes involved in the transition between fetal (in the fetus) to adult hemoglobin will allow the development of therapeutic approaches that may genetically correct diseases such as thalassemia and sickle cell disease.

Researchers funded through the 2014 operating grant competitions are exploring alternative approaches to red blood cell transfusion. Alternatives that would no longer require collection from blood donors, such as synthetic hemoglobin molecules, could provide a safe and unlimited supply for patients in need. Dr. Ronald Kluger (University of Toronto) is altering human hemoglobin to develop a universal stable and sterile oxygen carrier. His team developed methods to efficiently produce the oxygen carrier. In the coming year, they will evaluate the compound in animal models with collaborators at Harvard. Dr. Thomas Ming Swi Chang (McGill University) is also exploring the development of a human hemoglobin complex. They have tested their compound in an animal model and demonstrated its efficacy in the treatment of hemorrhagic shock. In the coming year, they will develop methods to produce the compound efficiently.

In an effort to improve product quality and patient safety, Canadian Blood Services produces washed red blood
cell concentrates for transfusion recipients who have a history of severe transfusion reactions. In 2013, the ACP-215 cell processor was implemented at Canadian Blood Services to wash red blood cell concentrates, replacing the COBE 2991 processor. In the past year, Dr. **Acker**, in collaboration with Dr. **Barbara Hannach** and investigators at University Health Network, performed an observational clinical study to examine the efficacy and safety of transfused washed red blood cell concentrates produced using the COBE 2991 processor compared to those produced using the ACP-215 processor. The study found no differences on patient outcomes between the two red cell products. However, because ACP-215 processed cells can be stored for longer than those processed with the COBE 2991, the change in process has led to improved inventory management by Canadian Blood Services and the hospital. Furthermore, the study found that fewer units were transfused per transfusion episode, reducing patient exposure to red blood cell products and thus improving patient outcome.

**Platelets**

Platelets are small, circulating blood cells that play a key role in the formation of blood clots. A number of medical conditions are associated with a decrease in platelet counts. To manage the symptoms of these conditions, patients are transfused with platelets.

Unlike other blood products, platelets must be stored at room temperature. This requirement increases the risk of bacterial growth if the unit is contaminated. While transfusion reactions due to contaminated platelets are rare, they remain a challenge for the industry as they can be fatal.

Dr. **Sandra Ramirez-Arcos** is an expert in bacteria and bacterial biofilms. Her development group supports Canadian Blood Services in developing appropriate processes to minimize bacterial contamination. The first line of defense against bacterial contamination of platelets is disinfection of the donor’s skin before donation. However, her group has shown that biofilm-forming skin bacteria are more resistant to skin disinfection than free-floating bacteria. This finding suggests that current procedures for disinfecting donor skin may be inadequate and may explain why, despite current efforts, a proportion of platelets (~1:5,000) are contaminated with bacteria. This research may lead to the development of new skin disinfection products that would effectively kill biofilm-forming skin bacteria.

From the early days of platelet transfusion therapy, aggregates were observed in manufactured platelet products. Preventive measures were developed during the manufacturing process to limit the formation of these aggregates. Dr. **Dana Devine** and our supply chain contributed to an international forum that gathered information on the experiences of 25 blood operators with aggregates in platelet concentrates. This survey provides additional information to a phenomenon for which causes remain poorly understood.

The quality of platelets declines during their short storage time. This phenomenon is known as the platelet storage lesion, and is much studied but not yet fully understood. The platelet storage lesion affects everything from platelet shape to the platelet’s ability to metabolize and involves changes in the platelet’s proteins. Dr. **Devine**’s group explored platelet storage lesion from a new perspective. Her group focused on what happens to proteins, and, specifically, which proteins get cut, where they get cut, and how these protein changes might affect protein and platelet function. The study showed widespread proteolysis in platelets during storage. Importantly, the results showed that proteolysis in stored platelets does not just shred proteins. Instead, much of the proteolysis is tailored, that is, it specifically processes proteins that results in stable proteins that may function differently from the original parent protein. With the advent of new technologies to reduce the risk of bacterial contamination of platelets comes the possibility of longer storage times for platelets. For this to become a reality, a better understanding of the platelet storage lesion is needed.

Pathogen inactivation (PI) technologies reduce or eliminate pathogens that may be present in blood products. PI treatment may be an alternative to testing of blood for specific infectious agents and may increase safety by destroying unknown pathogens. While PI treatment of blood products reduces infectious risks, the technology
may reduce platelet quality. Dr. Devine’s group investigates the changes in proteins within platelets following PI treatment. Her group found that PI induces platelet degradation through activation of the apoptosis pathway.\textsuperscript{48} Her group also demonstrated that PI treatment of whole blood prior to buffy coat manufacturing reduces the quality of all blood products, including platelets.\textsuperscript{49, 50} Dr. Patrick Provost (Laval University), supported through an grant, has also observed a negative effect of PI on platelet quality. His group has shown that PI activates platelets through the involvement of microRNAs.\textsuperscript{51} These findings can help in the development of strategies to improve platelet quality and minimize the negative effects of PI treatment.

Understanding the relationship between reduced platelet quality resulting from PI and clinical outcomes is essential. The international PREPAReS clinical trial will contribute to the evaluation of a PI technology developed by Terumo BCT. In partnership with Sanquin (the Netherlands blood operator), Norwegian investigators and Terumo BCT, Canadian Blood Services is contributing to the Canadian arm of this trial by providing Mirasol-treated platelet products to Canadian patients enrolled in the trial. The McMaster Transfusion Research Program, supported by the Centre, coordinates patient enrollments at five Canadian hospitals. This trial is a first step toward licensure of this technology in Canada.

Controversies surround the use of platelets clinically. The development of rigorous clinical guidelines for the use of platelets is therefore needed. Dr. Alan Tinmouth, from the University of Ottawa Centre for Transfusion Research, contributed to a systematic review on the use of platelet transfusions in various clinical settings.\textsuperscript{52} Following up from this systematic review, the AABB published clinical guidelines, to which Drs. Tinmouth and Kathryn Weber both contributed, that provided recommendations on the use of platelets.\textsuperscript{53} The International Collaboration for Transfusion Medicine Guidelines, led by Dr. Nadine Shehata, with funding from the Centre for Innovation, published clinical guidelines for platelet transfusion in patients with hypoproliferative thrombocytopenia.\textsuperscript{54}

**Plasma, plasma products and plasma product replacement**

Plasma is the protein-rich liquid component of blood that supports the immune system and controls excessive bleeding. Plasma may be directly used for transfusion in patients, or it can be processed into cryoprecipitate and cryosupernatant plasma. These two plasma derivatives are enriched in different factors needed by different patients.

Dr. William Sheffield’s team advanced the understanding of plasma quality. With Drs. Heyu Ni and Ed Pryzdial, they developed a new mouse model in which plasma transfusion reduces bleeding. Using this model, they demonstrated that levels of fibrinogen in transfused plasma, but not coagulation factor VIII, were important in controlling bleeding.\textsuperscript{55} These findings question the adequacy of factor VIII, mandated by Health Canada, as a quality control measure for plasma. The team is currently investigating prothrombin complex concentrates in this animal model and translating their findings into human in vitro clotting assays. This work could lead to a better understanding of the key factors in plasma that are critical to its transfusion efficacy. It could also lead to more appropriate standards for plasma quality.

Dr. Sheffield used another mouse model to test a novel antidote to a new drug increasingly used by Canadian patients to protect them from strokes. Called dabigatran etexilate, this drug is safer than older agents like warfarin. However, there is no approved antidote; if a patient suffers bleeding side-effects, clinicians have few options. With Dr. Donald Arnold, the team previously showed that plasma protein products like recombinant factor VIIa, distributed by Canadian Blood Services, were not effective in reversing bleeding caused by dabigatran etexilate in mice. The new antidote, a recombinant inactive clotting factor produced in the Sheffield laboratory, was fully effective at reversing drug effects in the test tube and partially effective in reversing drug effects in mice.\textsuperscript{56} This work could improve the effectiveness of this potential antidote and reduce wastage of plasma protein products that are not effective in reversing dabigatran.
Dr. Ni also made a new fundamental contribution to scientific understanding of how plasma proteins and platelets work together to stop bleeding. Using both genetically engineered mice and mice treated with blood-thinning drugs, his team showed that a plasma protein called fibronectin plays an important role in stitching platelets together at the site of a blood vessel injury to stop bleeding.\(^{57}\) The same effect was seen in human plasma. This work could lead to the development of a new plasma protein product and to new insights into the optimal timing of platelet and plasma transfusions to patients in need.

Plasma can be pooled and fractionated to provide purified and virally inactivated plasma protein products, such as albumin and intravenous immunoglobulin (IVIg). Clinical demand for IVIg rises every year. Through its Centre for Innovation, Canadian Blood Services is working to improve the evidence base both for plasma transfusion and for IVIg utilization and replacement to ensure the best use of the national resource of donated plasma.

Drs. Don Branch and Alan Lazarus, working with Australian and Swiss collaborators, published a study that countered previous paradigms for the mechanism of IVIg. In a murine model of arthritis, they confirmed the therapeutic benefit of IVIg and IgG Fc in antibody-induced arthritis, but failed to support the significance of sialylation and basophil involvement in the mechanism of action of IVIg therapy.\(^{59}\) Another study by Dr. Branch showed that the mechanism of IVIg, at least in part, may be due to its ability to induce high levels of interleukin-11 (IL-11) and that IL-11 can reduce IL-17 production, resulting in the amelioration of disease in a mouse model of multiple sclerosis.\(^{59}\) This work is consistent with a role for IL-11 in IVIg mechanism. It suggests a role for recombinant IL-11, which is commercially available, as a potential replacement of IVIg.

Dr. Lazarus is also developing safe substitutes for IVIg. His laboratory has developed CD44 antibodies and has demonstrated their similarity to IVIg in that they both improve immune thrombocytopenic purpura (ITP) in an animal model.\(^{60}\) In both cases, they are able to improve disease activity in a manner not requiring the inhibitory Fc receptor. This information will allow the design of a CD44 antibody that does not have to interact with this receptor. Dr. Branch is also continuing his efforts to develop IVIg substitutes. In collaboration with Dr. Lakshmi Kotra (University of Toronto), Dr. Branch has identified a class of compounds called pyrazoles that are potent inhibitors of phagocytosis in vitro and in vivo.\(^{61}\) His group is now screening additional similar compounds with improved potency and solubility. IVIg only works in ITP but not in other diseases that involve phagocytosis. These new drugs have the potential to not only replace IVIg in the treatment of ITP, but also in other diseases where phagocytosis is implicated, such as rheumatoid arthritis and immune hemolytic anemias.

Anti-D is a product derived from pooled donor plasma. In the case of hemolytic disease of the fetus and newborn (HDFN), the prophylactic use of anti-D has been highly successful in preventing immunization of the mother to the D antigen on fetal red blood cells. Because of its limited supply, and the presence of other antibodies that can cause problems, many attempts have been made to make anti-D in vitro. However, a successful monoclonal anti-D has not yet been approved for human use. Dr. Lazarus tested various monoclonal antibodies in a murine model to provide insight into the mechanism of action of these antibodies and further the design of monoclonal antibodies to replace donor-derived anti-D in the prevention of HDFN.\(^{62}\) This paper was highlighted as being among the top 10 per cent of papers published in the *Journal of Immunology*.

### Hematopoietic stem cells

Hematopoietic stem cells (HSCs) are cells that can renew themselves and differentiate into the various mature blood cells. HSCs have been used in clinical practice since the 1960s to treat numerous malignant or non-malignant blood disorders. Canadian Blood Services manages a registry of adult HSC donors, the OneMatch Stem Cell and Marrow Network. Canadian Blood Services also provides autologous HSC collection, manufacturing and storage services to a few hospitals. In 2013, Canadian Blood Services launched the national public cord blood bank. Through the activities of the national public cord blood bank, Canadian Blood Services collects, processes and

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**Hematopoietic stem cells are manufactured from peripheral blood or cord blood collections and stored in liquid nitrogen prior transplantation.**
In 2014, Canadian Blood Services reviewed its strategy for its HSC programs. Contributing significantly to this review was the work performed by Ken McTaggart and Dr. John Blake from the product and process development group. Dr. Blake’s process engineering expertise was leveraged to develop a series of mathematical models to characterize Canadian transplant patients and HSC donors. The models identified an optimal ethnic composition for the Canadian adult stem cell registry (OneMatch) and determined optimal recruiting targets for adult donors. Recommendations were instrumental in the development of Canadian Blood Services’ refreshed stem cell strategy.63

Similar to blood products, autologous and cord blood HSC products must be tested for bacterial pathogens prior to transplantation in patients. Dr. Sandra Ramirez-Arcos, our microbiologist expert, worked closely with our stem cells manufacturing facility to validate a microbial culture system. In 2014, the results of their cord blood study were published to inform others in the industry.64 They continue to collaborate to understand the impact of the presence of antibiotics in cord blood on the detection of pathogens and on patient outcomes.

The product and process development group is establishing a Stem Cell Quality Monitoring Program (QMP). Similar to its blood counterpart, this new QMP will provide in-house knowledge of stem cell products. In 2014-2015, initial work has focused on acquiring equipment and identifying flow cytometry-based quality assays to evaluate stem cell viability in pre- and post-thaw cord blood samples.

Canadian Blood Services used Pentaspan in the manufacturing of its autologous and cord blood stem cell products. However, with the market removal of Pentaspan in 2014, we needed to implement a new process for red cell depletion of cord blood stem cell samples and for cryopreservation of autologous stem cell samples. As part of this extensive operational process change, Dr. Jason Acker provided scientific support to ensure the efficacy and safety of introducing Hepsan as a replacement for Pentaspan.65

Stem cell transplantation from cord blood is associated with slow cell engraftment leading to long delays in the recovery of mature blood cells, such as platelets. As a result, patients transplanted with stem cells from cord blood require more blood transfusions and may have an extended hospital stay. Recent trials have shown that the expansion of stem cells from cord blood before transplantation could accelerate recovery of mature blood cells. However, recovery of platelets remains problematic. Dr. Nicolas Pineault, in collaboration with Héma-Québec, identified novel culture conditions that efficiently improved the expansion of HSCs in vitro and enhanced their response to a low-platelet environment in a murine model.66 Dr. Pineault is investigating the molecular mechanisms responsible for this effect. Improving stem cell transplantation from umbilical cord blood would lead to better patient outcomes by reducing patients’ dependency on blood transfusion and limiting their hospitalization.

Organ and tissue transplantation
The Centre for Innovation, in consultation with Canadian Blood Services’ organ and tissue donation and transplantation group, supports research that furthers our knowledge in this area.

The Centre contributes some funding to the Canadian National Transplant Research Program led by Dr. Lori West (University of Alberta). This national initiative is designed to increase organ and tissue donation in Canada, improve survival rates of Canadians who receive transplants and enhance their quality of life.

Through its James Kreppner Fellowship program, Canadian Blood Services supported Jennifer Chandler (University of Ottawa) to explore an ethical and legal framework for Canada’s organ donation system. She conducted a study to identify the emerging neuroscientific research in brain injury and its possible impact on public attitudes to brain death and organ donation. Chandler also examined the state of knowledge on the topic of how to ask families to consent to donation of the organs and tissue of their deceased loved ones. This study informed decisions by Canadian Blood Services’ organ and tissue team.67 She is now contributing her expertise in health law and ethics to tackling some of the issues faced in this area. She co-leads the Ethical, Economical, Legal and Social Platform of the Canadian National Transplant Research Program. Recently, she was honoured...
Also through its James Kreppner Fellowship program, Canadian Blood Services recently granted an award to Meaghan Toews to identify and evaluate legal and policy strategies to increase organ donation in Alberta. Most recently, she examined the “family veto” issue and published an op-ed in the Edmonton Journal.68 “Family veto” refers to the opportunity given to families to override their loved ones’ consent to donate and contributes to the poor rate of organ donation in Alberta and elsewhere. Toews currently works closely with the Canadian National Transplant Research Program network and, like Chandler, has developed ties with Canadian Blood Services’ organs and tissues team. Both researchers participate in the Donation Legal Research and Health Policy Group facilitated by Canadian Blood Services.

Building capacity in transfusion and transplantation

An important role for Canadian Blood Services’ Centre for Innovation is to build long-term capacity in the field of transfusion and transplantation sciences and medicine. To do this, the Centre focuses on three main areas:

- salary support through competitive training award programs
- education and training through knowledge dissemination initiatives
- networking opportunities

Salary support

Through the Centre, Canadian Blood Services administers four training award programs to attract professionals to the field by providing salary support. These training programs are designed to attract professionals who are at various stages of their research careers, from undergraduate to new investigator.

In the 2014–2015 fiscal year, we granted 17 new awards and renewed four (Fig. 3). All professionals receiving our training awards are affiliated with one of the research intensive Canadian academic institutions, where, for example, the graduate students are working toward a PhD. While most of them complete their training research project under the mentorship of a Canadian Blood Services scientist or adjunct scientist, six are currently conducting their training with an external group or as independent researchers (in the case of New Investigator program awardees). Through these programs, the Centre extends its research capacity by supporting external laboratories with a research focus that is aligned with the organization’s mandate. When possible and appropriate, the Centre seeks partnerships to administer these programs. For example, the New Investigator program is administered in partnership with the Canadian Institutes for Health Research.

In addition to administering its own training programs, the Centre for Innovation, through its Program Support Award, contributes to the Centre for Blood Research (University of British Columbia) training programs. With its research focus on transfusion medicine and blood-related diseases, the Centre for Blood Research is ideally aligned with the mandate of the Centre for Innovation. In 2014–2015, with support from the Centre for Innovation and other partners, the Centre for Blood Research supported 30 students from the University of British Columbia conducting research in 15 Centre for Blood Research laboratories (Fig. 3).

In collaboration with Canadian Blood Services medical directors, the Centre for Innovation facilitates the
training of transfusion medicine specialists by supporting medical fellows who are enrolled in one of the five Transfusion Medicine Diploma Programs. These medical school-based Diploma Programs are accredited by the Royal College of Physicians and Surgeons of Canada and they are delivered in partnership with Canadian Blood Services medical directors. In 2014–2015, Canadian Blood Services awarded one new Transfusion Medicine Residency Fellowship to a fellow who is completing his Transfusion Medicine Diploma at McMaster University and renewed one for a fellow also at McMaster University. Also for the first time since the inception of this program, a fellow from Laval University in Québec received a fellowship from Héma-Québec to complete her Diploma at the University of Toronto. This new collaboration with Héma-Québec will strengthen the national impact of this program.

**Figure 3: Number of training awards and completed degrees in 2014–2015**

<table>
<thead>
<tr>
<th>Program</th>
<th>New</th>
<th>Ongoing (including renewals)</th>
<th>Completed training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centre for Innovation training programs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summer internship</td>
<td>8</td>
<td>n/a</td>
<td>8 internships</td>
</tr>
<tr>
<td>Graduate fellowship</td>
<td>4</td>
<td>15</td>
<td>2 graduate fellowships</td>
</tr>
<tr>
<td>Post-doctoral fellowship</td>
<td>4</td>
<td>6</td>
<td>4 post-doctoral fellowships</td>
</tr>
<tr>
<td>New Investigator program</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Centre for Blood Research training programs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summer internship</td>
<td>20</td>
<td>n/a</td>
<td>Not recorded by the Centre</td>
</tr>
<tr>
<td>Graduate fellowship</td>
<td>6</td>
<td>3</td>
<td>Not recorded by the Centre</td>
</tr>
<tr>
<td>Post-doctoral fellowship</td>
<td>0</td>
<td>1</td>
<td>Not recorded by the Centre</td>
</tr>
<tr>
<td>Transfusion Medicine Diploma program</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion medicine residency fellowship</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

While the number of training programs and awards distributed indicates the Centre’s success in administering relevant programs and in engaging trainees, it does not demonstrate the impact of the programs in building capacity. To this end, the Centre for Innovation recently reviewed its training programs and found good evidence for such impact.

From 2000 to 2013, the Centre's training programs supported 71 graduate students leading to the completion of 10 MSc and 38 PhD degrees, 33 post-doctoral fellows and five new investigators. A number of these trainees have since secured positions in areas related to transfusion or transplantation science and medicine in academia, health care, not-for-profit organizations, industry, at Canadian Blood Services or Health Canada (Fig. 4).

**Education and training**

The Centre for Innovation also builds capacity in transfusion and transplantation science and medicine through education and training initiatives. These initiatives are designed to share knowledge and influence practice within and across various stakeholder communities such as researchers, health-care providers (e.g., physicians, nurses, and medical laboratory technicians), industry representatives, regulators, and Canadian Blood Services staff. Education and training initiatives include a transfusion medicine education website, as well as the delivery of education events, including conferences, symposiums, workshops and seminars.
Education website

The Centre manages www.transfusionmedicine.ca, an education website for health-care professionals involved in the transfusion of blood products. The site provides original educational resources and links to reliable resources developed by other organizations. In the last year, the site’s pages were viewed more than 150,000 times (unique page views) by more than 50,000 unique visitors.

The Clinical Guide to Transfusion is the most downloaded resource on the website with approximately 12,600 downloads in the last year (compared with 9,100 the previous year). Written in collaboration with Canadian Blood Services medical directors and Canadian experts, and co-edited by Drs. Gwen Clarke and Sophie Chargé, this 18-chapter guide provides a practical summary of our current knowledge of blood components and transfusion medicine practices. Two chapters were updated last year. The guide is published in English and French.

Another unique resource available on www.transfusionmedicine.ca is the Adverse Reaction Report prepared annually by Dr. Dale Young. This report provides information about the number and type of transfusion adverse reactions reported to Canadian Blood Services (~630 downloads in 2014–2015). Complementing the Adverse Reaction Report, the Centre for Innovation developed A Guide to Reporting Adverse Transfusion Events. This guide was revised during the year (~565 downloads in 2014–2015).

Original articles are also published regularly. The following articles were published in the last year:

- "Phenotype Matching for Sickle Cell Patients: A Review and Recommendations for Transfusion Practice"
• eight ResearchUnits10, 35, 44, 47, 50, 72–74; these provide clear summaries of results and impacts of research conducted at Canadian Blood Services (~2,000 downloads in 2014–2015). Written by Canadian Blood Services’ researchers in collaboration with the Knowledge Mobilization group, these summaries help in further disseminating research findings to facilitate informed decision-making.75

Education events
In 2014–2015, the Centre for Innovation delivered, on its own or in partnership, 81 education events. These events attracted an estimated 7,000 professionals (Fig. 5).

One of the key events is the Canadian Blood Services Annual International Symposium. This year’s theme was “Plasma: Transfuse It, Fractionate It, or Forget It?” Co-chaired by Drs. William Sheffield and Kathryn Webert, the symposium updated physicians, technologists, nurses and researchers on current knowledge in this complex and sometimes controversial field. Delivered by international and national experts, the program aimed to:
• Improve clinical utilization of plasma, plasma products and recombinant proteins.
• Improve understanding of the coagulation process and how new plasma proteins and recombinants may potentially increase safety and efficacy.
• Improve understanding of methodologies available in the clinical coagulation laboratory.

A panel discussion on the future of plasma transfusion highlighted the need for better evidence upon which to base clinical practice. This Continuing Medical Education accredited event was well-received by attendees, and the majority (98%) agreed that the event enhanced their knowledge in a manner that was applicable to their work or practice. To further disseminate the knowledge shared at this live event, the presentations are available on www.transfusionmedicine.ca. A symposium report was also published in Transfusion Medicine Reviews.76

In 2014, the Centre had the opportunity, with the leadership of Dr. Donald Branch, to co-organize and sponsor the Red Cell Club Meeting. For the second time in its 67-year history, this prestigious knowledge exchange event was held outside the United States. The two-day meeting brought together approximately 75 international and national attendees representing the clinician, scientist, and trainee communities. Session topics included the production of red blood cells, red cell membrane proteins, red cell diseases and red cell antigens. The small and focused format of this event was very conducive to knowledge exchange and to the establishment of collaborative efforts.

Through the Program Support Award to the Centre for Blood Research and through the activities of the Canadian Blood Services scientists located at the Centre for Blood Research, the Centre for Innovation contributes to the Annual Norman Bethune Symposium, the Earl W. Davie Symposium, and the Centre for Blood Research Seminar Series. This year, the Norman Bethune Symposium provided insights into future therapies for hemophilia and bleeding disorders and into the mechanisms of action and use of intravenous and subcutaneous immunoglobulin therapies. The Earl W. Davie Symposium primarily focused on the coagulation pathway, and old and new drugs affecting this pathway. While attendance at these events reached close to 160 attendees, the Centre for Blood Research also broadcasted live and archived videos on its website.

With the leadership of Canadian Blood Services medical directors, the Centre for Innovation has established key partnerships with provincial blood coordinating offices to deliver educational events to health-care professionals across Canada. Again this year, Dr. Peter Lesley, co-organized with the Ontario Regional Blood Coordinating Network the Northern and Eastern Ontario Annual Transfusion Medicine Education Videoconference Symposium. In its ninth edition, the 2014 program focused on “Bleeding Issues in the Anti-coagulated Patient.” The Centre also supported the 5th Annual Blood Matters Conference, organized by the Nova Scotia Provincial Blood Coordinating Program, and the Vein to Vein Workshop, organized by the Alberta Vein to Vein Society. These events are targeted primarily at health-care professionals working in Canadian hospitals and involved in the transfusion of blood products. The events are essential for their continued learning and development as they highlight new practices and guidelines and provide access to experts, which may not be available in smaller hospitals.
Figure 5: Key education events organized by the Centre or delivered in partnership in 2014–2015

<table>
<thead>
<tr>
<th>Event (Location)</th>
<th>Primary partner</th>
<th>Number 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>170</td>
<td>Health-care providers, researchers, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>&quot;Knowledge to Munch On&quot; lunch and learn webinar series – three events (webinars)</td>
<td>n/a</td>
<td>109, 145, 195</td>
<td>Canadian Blood Services staff and volunteers, American Red Cross staff, Health Canada staff</td>
</tr>
<tr>
<td>LearnTransfusion Series – 29 events (webinars)</td>
<td>Canadian Blood Services medical directors</td>
<td>50 per event</td>
<td>Health-care professionals (physicians, technologists)</td>
</tr>
<tr>
<td><strong>Events delivered in partnership</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual Norman Bethune Symposium (Vancouver, broadcast)</td>
<td>Centre for Blood Research</td>
<td>160</td>
<td>Researchers, health-care providers, 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>160</td>
<td>Researchers, health-care providers, 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 — 27 events (Vancouver)</td>
<td>Centre for Blood Research</td>
<td>80–140 per event</td>
<td>Researchers, clinicians, basic science and clinical trainees, technicians and technologists, industry representatives</td>
</tr>
<tr>
<td>Centre for Blood Research summer seminar series — seven events (Vancouver)</td>
<td>Centre for Blood Research</td>
<td>80–140 per event</td>
<td>Researchers, clinicians, basic science and clinical trainees, technicians and technologists, industry representatives</td>
</tr>
<tr>
<td>9th Annual Transfusion Medicine Symposium (North Bay, broadcast)</td>
<td>Ontario Regional Blood Coordinating Network</td>
<td>840</td>
<td>Health-care providers primarily in northern and eastern Ontario (physicians, nurses, technologists), Canadian Blood Services staff</td>
</tr>
<tr>
<td>Vein to Vein Workshop 2015 (Edmonton)</td>
<td>Alberta Vein to Vein Society</td>
<td>100</td>
<td>Researchers, health-care providers (physicians, nurses, technologists), Canadian Blood Services staff</td>
</tr>
<tr>
<td>5th Annual Blood Matters Conference (Halifax, broadcast)</td>
<td>Nova Scotia Provincial Blood Coordinating Program</td>
<td>100</td>
<td>Health-care providers (physicians, nurses, technologists), Canadian Blood Services staff</td>
</tr>
<tr>
<td>Red Cell Club Meeting (Toronto)</td>
<td>University of Toronto</td>
<td>75</td>
<td>Researchers, clinicians, basic science and clinical trainees</td>
</tr>
<tr>
<td>Canadian Society for Transfusion Medicine Annual Meeting (Quebec)</td>
<td>Canadian Society for Transfusion Medicine</td>
<td>516</td>
<td>Researchers, health-care providers, basic science and clinical trainees, industry representatives, Canadian Blood Services staff</td>
</tr>
<tr>
<td>AABB Education Workshop — two events (Philadelphia)</td>
<td>AABB</td>
<td>254, 150</td>
<td>Physicians, scientists, technologists, managers and supervisors, CEOs and CPOs</td>
</tr>
</tbody>
</table>
Canadian Blood Services leverages national and international events to educate the community. Every year, the Centre contributes financially to the Canadian Society for Transfusion Medicine Annual Meeting and, in collaboration with Héma-Québec, develops the scientific and workshop programs. This event is Canada’s premier knowledge exchange event for the transfusion medicine community. In 2014, Drs. Sheffield, Nicolas Pineault and Mindy Goldman were members of the scientific committee that identified topics of importance. Dr. Goldman led a morning workshop on serology.

The Centre for Innovation also organized two education sessions at the 2014 AABB annual meeting in Philadelphia. The first session, led by Judie Leach Bennett, entitled “Risk-based Decision-Making for Blood Safety,” focused on the risk framework under development by an international Alliance of Blood Operators collaboration. This initial workshop, targeted at physicians, managers and supervisors, and CEOs and CFOs, was designed to provide attendees with an understanding of the concepts underpinning the framework, such as blood safety risk assessment, stakeholder engagement, and health economics and outcome methods for the blood safety decision-making process.” The second session, led by Dr. Sandra Ramírez-Arcos and moderated by Dr. Jason Acker, entitled “Let’s Talk About the 30-Minute Rule for Red Cells,” was designed to educate attendees about the regulatory requirements for red cell storage and transportation, to review principles of red cell quality and storage lesion, and to disseminate the findings from Drs. Ramírez and Acker’s research projects around the 30-minute rule for red blood cells. Targeted at physicians, scientists, technologists, managers and supervisors, this education session equipped attendees with the knowledge they need to make decisions on the merits of retaining, modifying or extending the 30-minute rule, which currently leads to unnecessary discards of red blood cells. Finally, Dr. Branch received the 2014 Sally Frank Memorial Award and Lectureship from the AABB and presented the named lecture at the 2014 AABB Annual Meeting. His lecture provided a detailed account of the monocyte-macrophage assay he developed as a medical laboratory technologist and how it influenced the field of immunohematology. Several other Canadian Blood Services experts also gave invited lectures at this annual international meeting.

The Centre for Innovation administers the BloodTechNet competition to fund innovative projects aimed at delivering educational resources that support the development of skills, knowledge, and expertise of health professionals in the transfusion, transplantation and cell therapy community. Three projects were funded in 2014 and are ongoing. Dr. Christopher Ward’s team, from the University of Alberta, is developing a self-directed, self-paced online learning module for participants to explore transfusion-related issues from bench to bedside using an interprofessional approach. Mrs. O’Reilly’s team, from the Children’s & Women’s Health Centre of British Columbia, is creating educational resources for health-care providers specific to blood transfusion in neonatal and pediatric patients. The resources will include an e-learning course and a safe blood product ordering tool. Mrs. Kenny, from the Winnipeg Regional Health Authority, is developing “snippets” to support professionals with critical information in the moment of need, thus supporting these professionals beyond the classroom or eLearning module setting. Finally, the Nova Scotia Provincial Blood Coordinating Program, received a BloodTechNet award to broadcast the 2014 Blood Matters Conference.

Internally, the Centre for Innovation continues to provide educational opportunities to Canadian Blood Services’ staff across the organization by holding "lunch and learn" webinars. These events showcase presentations by Canadian Blood Services’ research groups and highlight the impact of ongoing research projects on the blood system and operators. In its third year, the program receives positive feedback from attendees and has now been opened to our colleagues at the American Red Cross and Health Canada, and to Canadian Blood Services volunteers.

**Networking opportunities**

Promoting networking between professionals is an essential component of a strategy aimed at building capacity, in particular to retain junior professionals to a specific field of expertise. In addition to the many educational events described above, which promote networking, the Centre for Innovation undertakes activities specifically aimed at enhancing the networking opportunities for junior professionals.

In 2014, the Centre for Innovation Research Day was opened to trainees and professionals working within the
laboratories of the Centre's core investigators. Twelve trainees attended this two-day event to discuss, with investigators and the management team, key research projects and blood operators’ operating issues. Such face-to-face events are essential when considering the dispersed geographical locations of our research laboratories, which span from Vancouver to Halifax. Over the coming year, the Centre for Innovation will leverage existing networking opportunities, such as the monthly Canadian Blood Services scientific calls, to further engage junior professionals within our internal network.

Externally, through its training programs, the Centre for Innovation provides travel funds to its graduate and post-doctoral fellows to attend and present at national and international conferences. Trainees working within the laboratories of Canadian Blood Services investigators are also encouraged to present at conferences where they have the opportunity to develop collaborations.

**Leveraging expertise through collaborations**

The Centre for Innovation leverages internal expertise and the knowledge of the external stakeholder community through formal and informal collaborative activities. In the last year, 31 formal partnerships were established or renewed. This network approach allows the Centre to access external expertise, promotes the engagement of stakeholders, and ultimately facilitates the translation of the knowledge created and provides access to additional funding.

**Research and Education Network**

The Centre includes 11 permanent Canadian Blood Services research laboratories. The Centre also engages closely with the 28 Canadian Blood Services medical directors and an epidemiologist in the delivery of research and education activities. While these groups constitute the central node of the Centre’s research and education network, they are connected to the larger Canadian research community through the cross-appointments of the majority of them to Canadian academic institutions.

Complementing this central node are Canadian Blood Services adjunct scientists and Canadian research groups that receive funding from the Centre through the competitive research and training programs. Twenty-seven external principal investigators from across Canada were engaged during the last year.

Through netCAD, the Centre’s research development facility in Vancouver, and the Cord Blood for Research program, the Centre engages with numerous Canadian research groups by providing blood and cord blood research products. Working closely with Canadian Blood Services’ Cord Blood Bank, the Centre implemented the Cord Blood for Research program in August 2014 to facilitate the distribution of unbankable fresh cord blood units to researchers across Canada. The program has been well received by the community, who until now had difficulties in accessing high-quality and ethically procured cord blood for their research projects. In 2014–2015, these unique programs distributed 976 research products (810 whole blood, 119 apheresis platelet products, 47 cord blood units) to 36 research projects (16 internal and 20 external to the Centre) from across Canada.77

At an international level, the Centre’s researchers continue to build strong collaborative research projects primarily through their memberships in the Biomedical Excellence for Safer Transfusion Collaborative (BEST). In the last year, Centre researchers contributed to several BEST studies. The Centre also continues to undertake contract research for various industry partners including Terumo BCT Inc., Armour Therapeutics, Immunobiochem Corporation, and CSL Behring AG. These arrangements provide substantive research support to further technology and biologics development for the future benefit of the blood system.

In the realm of education, the Centre partners with numerous local, provincial and national organizations, as described in the previous section (Fig. 5).

**Canadian Blood Utilization Collaborative**

Upon the request of the Conference of Deputy Ministers of Health, Canadian Blood Services submitted a Proposal for the Utilization of Blood and Blood Products in March 2014. In the proposal, Canadian Blood
Services identified opportunities to improve the national utilization of blood products to improve patient outcomes and to reduce overall system costs. One of the initiatives included in the proposal was a forum through which blood utilization research and clinical program proposals could be consulted, reviewed and prioritized, along with strategies to collect relevant data and evidence, and through which diversified funding sources for such initiatives could be pursued. Taking a system-wide approach, the proposed forum was conceived to inform clinical practice, policy-making, and health-care investment decisions in the domain of blood utilization.

Over the last year, members of the Centre for Innovation worked with Canadian Blood Services' utilization group led by Dr. Kathryn Weber to bring together a group of 35 thought leaders from across Canada (Fig. 6). An initial meeting, held in Toronto in early 2015, was organized to enable the participants to describe the current state of blood utilization in Canada, articulate blood utilization objectives for the future and develop a mechanism to enable collective action on these objectives. There was a consensus that there was a need "to optimize blood utilization to improve patient outcomes in a cost-effective manner" and that this work was best accomplished collectively. Work is underway to establish a governance structure that will facilitate the activities of the collaborative while leveraging participants' expertise.

**International Collaboration for Transfusion Medicine Guidelines**

The Centre for Innovation continues to support Dr. Nadine Shehata in her leadership role in the International Collaboration for Transfusion Medicine Guidelines (ICTMG) group. In 2014, the group published new platelet transfusion guidelines to assist health-care professionals in optimizing platelet utilization during the treatment of chemotherapy or stem cell transplant patients. This publication was highlighted in *Transfusion News*. The group is now working on guidelines for the management of fetal and neonatal alloimmune thrombocytopenia. This disorder is characterized by low platelet count in fetuses and newborns, which can cause severe complications and long-term disabilities. Guidelines are also being developed for red cell specifications for patients with hemoglobinopathies, genetic defects affecting red blood cells.

**Alliance of Blood Operators**

Since 2014, the Centre for Innovation has been Canadian Blood Services’ point of contact for our collaboration with the Alliance of Blood Operators. The Alliance is a network of not-for-profit blood service providers with voluntary, non-remunerated blood donors (Fig. 7). One of the goals of the Alliance of Blood Operators is to facilitate horizontal learning across its membership to identify and promote good practice and performance improvement. The confidentiality agreement binding these organizations ensures the dissemination of valuable information. In the last year, Canadian Blood Services participated in 66 knowledge exchanges. Thirty-three of these exchanges were initiated by our organization to learn from these international members’ best practices in various areas (e.g., look-back/trace-back processes, quality management system workflows, National Contact Centre operations).
One of these activities focused on the look-back and trace-back processes implemented by blood operators to ensure product safety. Despite strict screening procedures and highly effective testing, there is the potential, in rare instances, for an infected unit of blood to be released for transfusion. A trace-back begins with a patient who may have a transfusion-related infection. A targeted search to identify which donor(s) gave that person blood is conducted. A look-back begins with an infected donor. In this case, a targeted search to identify which patients received the donor's blood is conducted. Look-back and trace-back processes are in place to limit the potential damage of an infected donation. In 2014, Canadian Blood Services reviewed its look-back and trace-back processes. Through the Alliance, we obtained information from several blood operators about the scope and limits of their programs. Many operators have made provision in their process to limit look-back procedures, and their rationales for doing so are informing our deliberations. A review of the information confirmed the opportunity for our organization to streamline our process, thereby achieving efficiencies without adding risk to recipient safety.

**Risk-Based Decision Making Framework**

The Risk-Based Decision Making Framework project, led by Judie Leach Bennett together with the members of an international Alliance of Blood Operators collaboration, was recently concluded. A final risk framework was delivered, informed by stakeholder consultation, peer review, and scenario-based feasibility testing as a tool for decision-making. A web-based, interactive version of the framework is also being developed.

**Governance**

In the last year, the Centre for Innovation continued to gain efficiencies and further integrate its Research, Knowledge Mobilization, and product and process development groups. Canadian Blood Services also established two new committees:

- **Product Innovation Operating Committee:** This committee facilitates and directs the introduction of new products, changes to products and their associated processes, and the retirement of obsolete products distributed by Canadian Blood Services. Dr. Dana Devine chairs the committee and Ken McTaggart is a member.

- **Product Development Working Group:** This working group provides ongoing advice and recommendations for minor changes to Canadian Blood Services products or processes. Dr. Jason Acker, Craig Jenkins and Ken McTaggart are members.

These groups will enhance the integration of the Centre for Innovation’s research and development efforts with the operations of our organization. They complement the already well-established Canadian Blood Services governance structure, which provides oversight to the Centre’s activities. This governance structure includes the Canadian Blood Services board of directors, the Safety, Research and Ethics Committee, the Scientific and Research Advisory Committee, and the Research Ethics Board. These committees meet throughout the year and are regularly apprised about the Centre’s activities.

In 2014, the Centre’ secretariat administered 12 funding competitions for our research and training programs, which resulted in funding 29 new projects (Appendix 1). Again this year, each competition followed strict peer-review processes that promote excellence, ensure relevance and reach a broad spectrum of Canada’s leading researchers in our field. In particular, we renewed our agreement with the Canadian Institutes for Health Research for the Canadian Blood Services/CIHR operating grant and the New Investigator programs. Through this agreement, Canadian Blood Services reviews the Relevance section of the applications for alignment with the Centre’s mission, and CIHR conducts the peer-review process and provides funding recommendations. For the intramural grant program, our management team conducts a relevance review at the Letter of Intent stage, and we convene an external grant review panel to rank the applications and make funding recommendations. The panel consists of international and Canadian experts, including a scientist from Héma-Québec.

In 2013, the Centre for Innovation, in collaboration with Health Canada, developed a performance measurement strategy for the program. Implementation of this strategy provides information for the evaluation of the program to assess relevance and performance. It is also used to support effective management and reporting requirements of Health Canada’s contribution funding. In 2014, we refined the strategy to ensure the quality of the performance information will support the program evaluation and reporting accountability requirements.
References cited
(see Appendix II for a full list of the Centre for Innovation's publications for fiscal year 2014–2015)


74. Semple J. ResearchUnit: Research into TRALI Therapies Gene Therapy Results That Are a Tad Interesting! transfusionmedicine.ca website 2014.


## Appendix I: Funded projects

### Summary of funded research projects by program

<table>
<thead>
<tr>
<th>Projects receiving funding in fiscal year 2014–2015</th>
<th>Total: 137</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research program</strong></td>
<td>51</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR Partnership Operating Grants</td>
<td>27</td>
</tr>
<tr>
<td>Blood Utilization and Conservation (21)</td>
<td></td>
</tr>
<tr>
<td>Transfusion-Related Acute Lung Injury (2)</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>7</td>
</tr>
<tr>
<td>Small projects funding</td>
<td>4</td>
</tr>
<tr>
<td>James Kreppner Fellowships</td>
<td>2</td>
</tr>
<tr>
<td>Supplementary funding</td>
<td>9</td>
</tr>
<tr>
<td><strong>Product and Process Development program</strong></td>
<td>54</td>
</tr>
<tr>
<td>Integrated Development program</td>
<td>38</td>
</tr>
<tr>
<td>Development in collaboration with external agencies</td>
<td>13</td>
</tr>
<tr>
<td>Participation in international benchmarking studies, technology evaluations, and knowledge exchange activities</td>
<td>3</td>
</tr>
<tr>
<td><strong>National training program</strong></td>
<td>29</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR Partnership Post-Doctoral Fellowships</td>
<td>1</td>
</tr>
<tr>
<td>Post-doctoral fellowships</td>
<td>9</td>
</tr>
<tr>
<td>Graduate fellowships</td>
<td>19</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

- Charaterization of Regulatory Interactions/Complex in Hemoglobin Switching
- Hydrophilic Polymer Brushes as Biocompatible Coatings: Development and Applications in Blood Handling and Platelet Storage
- Development of a Novel Method for the Surface Engineering of Red Blood Cells Comprising Chemical and Enzymatic Cell Surface Modification
- The Ability of Plasma or Plasma Replacement Products to Control Bleeding in Over-Anticoagulated Mice
- Auxiliary Cofactors in Fibrinolysis
- Cold Storage of Platelets via Membrane Pegylation
- 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
- Improving the Cryostorage of Blood Products Using Novel Small Molecule Cryoprotectants
- Small Molecule Inhibitors of Phagocytosis as Replacement Therapy for IVlg
- Development of Novel Blood Vessel and Organ Sealants for Blood Conservation in Surgical Practice
- Platelet MicroRNAs During Storage Under Blood Bank Conditions
- Transfusion of Red Cells in Hematopoietic Stem Cell Transplantation: The TRIST Study
- Tranexamic Acid Versus Placebo to Reduce Perioperative Blood Transfusion in Patients Undergoing Major Liver Resection: A Pilot Randomized Controlled Trial
- Understanding Host Mechanisms Responsible for Immune Platelet Destruction and Thrombocytopenia
- Polyhemoglobin Catalase Superoxide Dismutase Carbonic Anhydrase: A Novel Soluble Biotherapeutic with No Cardiac Toxicity for Hemorrhagic Shock and Other Uses
- Characterization of the Hematopoietic Reconstitution Enhancing Activity of Osteoblasts Derived from Human Mesenchymal Stromal Cells
- Design and Implementation of Circulatory Oxygen Therapeutics Derived from Human Hemoglobin by Improved Systematic Chemical Coupling and Cross-Linking
- Release, Delivery and Cell Programming Effects of Platelet Microparticles and MicroRNAs
- Microfluidic Devices to Measure the Deformability of Stored Red Blood Cells
- Understanding Transcriptional and Epigenetic Control by Gfi1b Towards the Development of a Therapy for Sickle Cell Disease
- Pathogenesis and Treatment of Immune Thrombocytopenia: Are There Fundamental Differences Between Anti-GP1Iba- and Anti-GpllbIIa-Mediated Thrombocytopenia?

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

- Identification of Host Immune Factors Responsible for the Initiation and/or Modulation of Transfusion Related Acute Lung Injury
- **Mechanisms of Antibody-Independent Transfusion-Related Acute Lung Injury (TRALI)**

**Purpose:** Blood supply risk

- Canada's Blood Futures: Geography, Demographic Change, and the Supply and Demand of Blood in Canada
- Transfusion-Related Epstein-Barr Virus (EBV) Infection Among Allogeneic Stem Cell Transplant Pediatric Recipients: A Multicenter Prospective Cohort Study (Treasure Study)
- **Short and Long-Term Clinical Effects of Blood Donor Characteristics in Transfusion Recipients**
- Exploratory Analyses to Determine if Method of Donor Blood Processing Affects Outcome in Transfused Recipients
**Canadian Blood Services/CIHR Partnership New Investigator Program**

<table>
<thead>
<tr>
<th>Transfusion Requirements in Cardiac Surgery II (TRICS II)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Code Sepsis: Defining and Translating Optimal Resuscitation and Care for Children with Septic Shock</em></td>
</tr>
</tbody>
</table>

**Intramural Operating Grant Program**

<table>
<thead>
<tr>
<th>Quality of Transfusable Plasma: Mouse Models and Clinical Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stealth Erythrocytes: From Bench to Bedside</td>
</tr>
<tr>
<td>Mechanism of Action of Intravenous Immunoglobulin (IVIg): Role of Dendritic Cells in Stimulating T Regulatory Cells</td>
</tr>
<tr>
<td>Antibodies to CD44 as a Potential Replacement for IVIg in ITP</td>
</tr>
<tr>
<td>Residual Risk of Transfusion-Transmitted Cytomegalovirus Infection: Incidence and Pathogenesis</td>
</tr>
<tr>
<td><em>Defining the Components of Transfusable Plasma That Reduce Bleeding</em></td>
</tr>
<tr>
<td><em>Elucidation of the Mechanism of IVIg-Associated Hemolysis</em></td>
</tr>
</tbody>
</table>

**Small Projects program**

<table>
<thead>
<tr>
<th>Use of Platelet Transfusions in Medical-Surgical Critically Ill Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trends and Predictors of Transfusion in Obstetrical Patients</td>
</tr>
<tr>
<td><em>Understanding Brain Death: A Multipurpose Educational Video Aimed to a Diverse Public and Professional Audience</em></td>
</tr>
<tr>
<td><em>Retrospective Analysis of Clinical Outcomes in Neonatal Alloimmune Thrombocytopenia (NAIT) Related to Anti-HPA-1a</em></td>
</tr>
</tbody>
</table>

**James Kreppner Fellowship in Blood System Studies**

<table>
<thead>
<tr>
<th>A Framework for Thinking Through Different Concepts of Death in Organ Donation and Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Legal and Policy Strategies to Optimize Organ Donation in Alberta</em></td>
</tr>
</tbody>
</table>

**Supplementary Funding Program**

<table>
<thead>
<tr>
<th>Purpose: External grant top-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIHR: Polymer-Grafted Allogenic Leukocytes and Systemic Immune Modulation</td>
</tr>
<tr>
<td>Heart &amp; Stroke Foundation: Auxiliary Cofactors in Fibrinolysis</td>
</tr>
<tr>
<td>Burroughs Wellcome Fund: Innovation in Regulatory Science</td>
</tr>
<tr>
<td>CIHR: Pathogenesis and Treatment of Immune Thrombocytopenia: Are There Fundamental Differences Between Anti-Gpib-α and Anti-GpIbIlla-Mediated Thrombocytopenia?</td>
</tr>
<tr>
<td>Heart &amp; Stroke Foundation: Apolipoprotein A-IV and Platelet Function: Novel Links with Thrombosis, Inflammation, and Atherosclerosis</td>
</tr>
<tr>
<td>CIHR: Pathogenesis of Fetal and Neonatal Alloimmune Thrombocytopenia and IVIg Anti-FcRn Therapies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Purpose: Bridge funding</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Small Molecule Inhibitors of Phagocytosis as Replacement Therapy for IVIg</em></td>
</tr>
<tr>
<td><em>Impact of Cord Blood Processing Delay on the Loss of Engraftment Activity and on the Release of Microparticles</em></td>
</tr>
<tr>
<td><em>Understanding the Physiological Mechanisms Responsible for the Predominance of Staphylococcus Epidermidis as a Platelet Contaminant — A Genomic Approach</em></td>
</tr>
</tbody>
</table>
**Titles of projects funded by Product and Process Development program**

<table>
<thead>
<tr>
<th>Integrated Development program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exploration of Options to Test Cord Blood Units That Contain Antibiotics for Bacterial Contamination</td>
</tr>
<tr>
<td>Product Characterization — Quality Monitoring Program for Cord Blood Derived Hematopoietic Stem Cells</td>
</tr>
<tr>
<td>Elimination of Cooling Trays</td>
</tr>
<tr>
<td>Acp-215 Closed System Cryopreservation</td>
</tr>
<tr>
<td>Non-Destructive Quality Control Testing Technique for Apheresis Products</td>
</tr>
<tr>
<td>Pentastarch Replacement Cord Blood Manufacturing</td>
</tr>
<tr>
<td>Hematopoietic Progenitor Cells Apheresis Pentaspan Replacement</td>
</tr>
<tr>
<td>Bag RFP Project</td>
</tr>
<tr>
<td>Evaluation of Alternative Skin Disinfection Kits for Donors Allergic to Chlorhexidine</td>
</tr>
<tr>
<td>The Effects of Room Temperature Exposure on Red Blood Cell Units (30-Minute Rule)</td>
</tr>
<tr>
<td>In-House Sterility Testing of Cord Blood Units</td>
</tr>
<tr>
<td>Site Inventory Model and Analysis</td>
</tr>
<tr>
<td>Paperless Clinic: Whole Blood Clinic Staffing Planning Templates</td>
</tr>
<tr>
<td>OneMatch Registry Study</td>
</tr>
<tr>
<td>Stem Cell International Benchmarking</td>
</tr>
<tr>
<td>Product Characterization — Quality Monitoring Program Database</td>
</tr>
<tr>
<td>Production Equipment Process Cycle Time Optimization: Compomat</td>
</tr>
<tr>
<td>Current State of 7-Day Platelets Whitepaper</td>
</tr>
<tr>
<td>Current State of Platelet Additive Solutions Whitepaper</td>
</tr>
<tr>
<td>Paperless Clinic: Plasma Apheresis Clinic Staffing Planning Templates</td>
</tr>
<tr>
<td>Hospital Ordering Behaviour and Management of O- Inventory</td>
</tr>
<tr>
<td>Modelling and Simulation Education and Training</td>
</tr>
<tr>
<td>Investigation of the Bactericidal Effect of the Buffy Coat Platelet Production Method</td>
</tr>
<tr>
<td>Sterility Testing — Hematopoietic Progenitor Cell — Apheresis Product</td>
</tr>
<tr>
<td>Donor Hemoglobin Instrumentation RFP</td>
</tr>
<tr>
<td>Acp-215 Cell Processor Implementation (Washed Red Blood Cells)</td>
</tr>
<tr>
<td>Feasibility Assessment of Using Stem Cell Patient Blood Product Support to Examine Changes in Blood Component Manufacturing</td>
</tr>
<tr>
<td>Impact of Donor Sex, Age and Hemoglobin Status on Hemolysis</td>
</tr>
<tr>
<td>Cryopreservation of Gerbich/Leach Donor</td>
</tr>
<tr>
<td>Impact of Sample Tube Storage (Time and Temperature) on Platelet Count</td>
</tr>
<tr>
<td>RFP — Bact/Alert System</td>
</tr>
<tr>
<td>Investigation of an Adverse Transfusion Reaction</td>
</tr>
<tr>
<td>Rinse Modification to the Platelet Pooling Process</td>
</tr>
<tr>
<td>Evaluating the Efficacy of Skin Disinfectants when Combined with Natural Oils</td>
</tr>
<tr>
<td>Support Validation of Compolab Instrument</td>
</tr>
<tr>
<td>Why Do Platelets Have a “Cell Death” Receptor?</td>
</tr>
<tr>
<td>Analyses of Riboflavin/UV Light Treatment on Blood Products</td>
</tr>
<tr>
<td>Investigation of Leukoreduction Effectiveness in B2 Whole Blood with Incomplete Filtration</td>
</tr>
</tbody>
</table>
Development in Collaboration with External Agencies

<table>
<thead>
<tr>
<th>Project</th>
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</thead>
<tbody>
<tr>
<td>Haemonetics Solx/Fenwal ESol ACP-215 study</td>
</tr>
<tr>
<td>Terumo BCT Cationization Project: Phases I, II, and III</td>
</tr>
<tr>
<td>Haemonetics in vivo study</td>
</tr>
<tr>
<td>Evaluation of Bacterial Detection in Buffy Coat Platelet Concentrates by the pH Safe System</td>
</tr>
<tr>
<td>Evaluation of the Efficacy of the Mirasol® Pathogen Reduction Technology System to Eradicate Biofilm-Forming Bacteria</td>
</tr>
<tr>
<td>INTERCEPT (Cerus) Pathogen Inactivation System</td>
</tr>
<tr>
<td>THERAFLEX (Macopharma) Pathogen Inactivation System</td>
</tr>
<tr>
<td>MIRASOL (Terumo BCT) Pathogen Inactivation System</td>
</tr>
<tr>
<td>Evaluation of DEHP-Free Pediatric Storage Bags — A Collaboration with Fresenius Kabi</td>
</tr>
<tr>
<td>Supernatant Reduction of Gamma-Irradiated RCC for pediatric transfusion — A Collaboration with the IWK Health Centre in Halifax</td>
</tr>
<tr>
<td>Short and Long-Term Clinical Effects of Blood Donor Characteristics in Transfusion Recipients</td>
</tr>
<tr>
<td>Exploratory Analyses to Determine If Method of Donor Blood Processing Affects Outcome in Transfused Recipients</td>
</tr>
<tr>
<td>Bacterial Study in Uganda</td>
</tr>
</tbody>
</table>

Participation in International Benchmarking Studies, Technology Evaluations and Knowledge Exchange Activities

<table>
<thead>
<tr>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEST 74 – Irradiation Study</td>
</tr>
<tr>
<td>BEST 76 – Donor Factors Associated with Low pH in Stored Apheresis Platelets</td>
</tr>
<tr>
<td>BEST 83 – Hemolysis Standardization</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 2014–2015.

Canadian Blood Services/CIHR Partnership Post-Doctoral Fellowship program

<table>
<thead>
<tr>
<th>Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Novel Cell Surface Engineering Method for Universal Red Blood Donor Cells Via Combination of Enzymatic Cleavage and Polymer Grafting</td>
</tr>
</tbody>
</table>

Post-Doctoral Fellowship program

<table>
<thead>
<tr>
<th>Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenesis of Fetal and Neonatal Alloimmune Thrombocytopenia and Mechanisms of IVIg Therapy</td>
</tr>
<tr>
<td>Study of the Apoptosis Mechanism in Blood Processing and Platelet Storage in Order to Improve Stored Platelet Quality After Pathogen Inactivation Treatment</td>
</tr>
<tr>
<td>Identification of a Two-Step Mechanism Responsible for Antibody-Mediated Transfusion Related Acute Lung Injury (TRALI)</td>
</tr>
<tr>
<td>CD8+CD25+ Regulatory T Cells: Unveiling New Mechanisms and Treatment of ITP</td>
</tr>
<tr>
<td>Role of fc Receptors in Antibody-Mediated Immune Suppression</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>
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Graduate Fellowship program

<table>
<thead>
<tr>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect of Polymer Size and Species on Immunocamouflage and Antigenicity</td>
</tr>
<tr>
<td>The in vivo Effects of Liposome Treatment on Minimizing Membrane Injury in Rat Red Blood Cells (RBCs) 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>Application of Microfluidic Technology to Blood Group Genotyping for Non-invasive Prenatal Diagnosis of Fetal RhD Status</td>
</tr>
<tr>
<td>Relationship of Warm Autoimmune Hemolytic Anemia to Normal Red Cell Senescence</td>
</tr>
<tr>
<td>Organ Specific Macromolecular Iron Chelators: Towards Effective Prevention of Transfusional Iron Overload</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>Novel Mechanisms of Plasma Fibronectin in Hemostasis, Cryoprecipitate Therapy and Platelet Storage: Potential Applications in Transfusion Medicine</td>
</tr>
<tr>
<td>Mechanism of Transplacental Transport of IgGs, and IVIg and Anti-FcRn Therapies in the Treatment of Fetal and Neonatal Alloimmune Thrombocytopenia</td>
</tr>
<tr>
<td>Study of the Role of Platelet microRNAs</td>
</tr>
<tr>
<td>Studies on the Development of Biocompatible Antimicrobial Platelet Storage Devices</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>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>McMaster Transfusion Research Program</td>
</tr>
<tr>
<td>University of Ottawa Centre for Transfusion Research</td>
</tr>
<tr>
<td>Centre for Blood Research Infrastructure Support for Transfusion Research</td>
</tr>
</tbody>
</table>
Appendix II: Publications

Summary of peer-reviewed and non-peer-reviewed publications from fiscal year 2014-2015

<table>
<thead>
<tr>
<th>Peer-reviewed publications</th>
<th>254</th>
</tr>
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<tbody>
<tr>
<td>Journal articles</td>
<td>113</td>
</tr>
<tr>
<td>Review articles</td>
<td>10</td>
</tr>
<tr>
<td>Clinical guidelines</td>
<td>2</td>
</tr>
<tr>
<td>Comments/Letters</td>
<td>11</td>
</tr>
<tr>
<td>Published abstracts</td>
<td>116</td>
</tr>
<tr>
<td>Canadian Blood Services Circular of Information</td>
<td>2</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-peer-reviewed publications</th>
<th>42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Blood Services website publications</td>
<td>15</td>
</tr>
<tr>
<td>Technical reports</td>
<td>24</td>
</tr>
<tr>
<td>Theses</td>
<td>3</td>
</tr>
</tbody>
</table>

Summary of h-index factor analysis

Notes: i) H-Index factors measured using GoogleScholar on April 10 2015. ii) Mean H-index calculated using H-Index factors from the 15 core investigators. 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. 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, Mark Scott, William Sheffield, and Kathryn Webert. Average overall H-index for Canadian university professors in the biological sciences is 10.6.
Publications’ details

Author Legend:

Bold – Centre for Innovation core investigators and senior staff; Canadian Blood Services medical directors; directors of transfusion medicine research programs receiving funding via the Program Support Award.

Underlined – Non-Canadian Blood Services investigators funded in part by Canadian Blood Services.


Associated with Improved 6-Month Functional Outcomes in Patients with Severe Traumatic Brain Injury. *Neurocrit Care* 2014.


56. Leontyev D, Neschatim A, Branch DR. Cytokine Profiles in Mouse Models of Experimental Immune Thrombocytopenia Reveal a Lack of Inflammation and Differences in Response to Intravenous Immunoglobulin Depending on the Mouse Strain. *Transfusion* 2014; 54: 2871-9.


**Review Articles**


**Clinical Guidelines**


**Comments/Letters**


Published Abstracts


5. Arbaeen AF, Levin E, Serrano K, Devine D. The Efficiency of Thromboelastography (TEG) to Discriminate Good Vs. Poor Quality of Buffy Coat Platelet Concentrates. Transfusion 2014; 54: 77A.


42. Gerges H, Cembrowski G, Clarke G, Yakimec J. The R\textsubscript{5\text{a,b}} \times \text{R\textsubscript{5\text{a,b}}} and 75\% \text{Ae} Rule Combination Can Efficiently Interpret Proficiency Testing (PT) Data Produced by Highly Precise Hematology Analyzers. *Int J Lab Hematol* 2014; 36: 128.


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96. Schubert P, Culibrk B, Arbaeen AF, **Devine D**. Fas Receptor Signaling in Platelets Is Involved in Platelet Clot Fibrinolysis. *Transfusion* 2014; 54: 20A.


110. Westhoff CM, **Hannon J**, **Clarke G**, Cote J, **Goldman M**, Lane D, Vege S, Lomas-Francis C, Ochoa G. A Weak D Phenotype Discovered in Nine Patients in Western Canada Due to a Nucleotide 1187c>G (Pro396Arg) Change in RHD. *Transfusion* 2014; 54: 30A.


Ruggeri ZM, Ni H. Apolipoprotein a-IV Is a Novel Ligand of Platelet Beta3 Integrins and an Endogenous Inhibitor of Thrombosis. 2nd Cardiovascular Forum for Promoting Centers of Excellence and Young Investigators Website 2014: 37.


Canadian Blood Services Circular of Information

Canadian Blood Services Website Publications
11. Semple J. ResearchUnit: Research into TRALI Therapies Gene Therapy Results That Are a Tad Interesting! transfusionmedicine.ca website 2014.

Technical Reports


**Theses**


## Appendix III: Health Canada Financial Contribution

Summary of Expenditures – April 1, 2014, to March 31, 2015

### Schedule 1: Overview

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating funds (Schedule 2)</td>
<td>1,378,895</td>
</tr>
<tr>
<td>Funding programs (Schedule 3)</td>
<td>5,508,602</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$6,887,497</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 programs administration</td>
<td>561,857</td>
</tr>
<tr>
<td>NetCAD operations</td>
<td>446,458</td>
</tr>
<tr>
<td>Intellectual property protection and other legal activities</td>
<td>362,054</td>
</tr>
<tr>
<td>Capital purchases</td>
<td>8,526</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$1,378,895</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 grants</td>
<td>2,812,091</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR new investigator program and fellowship</td>
<td>75,000</td>
</tr>
<tr>
<td>Canadian Blood Services intramural operating grants</td>
<td>840,757</td>
</tr>
<tr>
<td>James Kreppner fellowship in blood system studies</td>
<td>75,000</td>
</tr>
<tr>
<td>Kenneth Fyke award</td>
<td>89,588</td>
</tr>
<tr>
<td>Small projects funding</td>
<td>29,000</td>
</tr>
<tr>
<td>Graduate fellowship</td>
<td>398,225</td>
</tr>
<tr>
<td>Postdoctoral fellowship</td>
<td>278,128</td>
</tr>
<tr>
<td>Summer internship</td>
<td>63,472</td>
</tr>
<tr>
<td>Program Support Award for Canadian transfusion medicine and science research</td>
<td>699,905</td>
</tr>
<tr>
<td>Additional funding for research projects</td>
<td>147,435</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$5,508,602</strong></td>
</tr>
</tbody>
</table>

**Notes:**
Funding programs includes capital expenditures under $10,000.