Executive summary

Through the Centre for Innovation, Canadian Blood Services facilitates the creation, translation and application of new knowledge to support a safe, effective and responsive system of blood and related biologics for Canada. We foster and support relevant discovery and applied research, facilitate the dissemination and application of the knowledge created, and build capacity through training and collaborations. The unique integration of the Centre for Innovation within our core operations provides exceptional opportunities for cross-fertilization that enhance the efficiency and cost-effectiveness of the blood system, while the academic cross-appointments of Canadian Blood Services’ scientists promote research excellence and provide access to infrastructure.

Over the last year, we restructured the Centre to effectively respond to the system’s ever-changing needs and to leverage existing strengths. With the support of a Secretariat, the Centre’s activities are now focused on three key pillars:

- research
- product and process development
- knowledge mobilization

This new structure will enhance our innovation pipeline to ensure that Canadians benefit from one of the safest and most advanced blood systems in the world, now and in the future.

The Centre for Innovation includes 12 staff researchers and a vast network of internal and external partners. Funded primarily by Health Canada and provincial and territorial governments, the Centre undertakes a range of activities that span the translational continuum from “bench to bedside.” These activities promote the creation of new knowledge and its translation into enhanced and new practices, services and technologies, for the benefit of Canadian patients and the health-care system.

Achievement highlights

Over the last year, the Centre for Innovation:

- Published 223 peer-reviewed publications including in high impact journals such as Blood, PloSOne and Transfusion. The productivity and impact of the Centre’s core researchers’ published work is reflected by an average h-index factor of 24 — more than double the national average in the scientific field.
- Shared 41 technical reports within Canadian Blood Services and with partners. Subject-matter expertise and data included in these reports informed product and process improvement.
- Issued seven patents.
- Trained 21 professionals through its formal national training program.
- Delivered over 151 oral and poster presentations at national and international conferences, supported five major knowledge exchange events, and delivered 35 LearnTransfusion webinars.
- Formalized or renewed 25 partnerships to facilitate research with national and international private institutions (Blood Cell Storage Inc., TerumoBCT, CSL Behring), academia
(University of Ottawa, McMaster University) and not-for-profit organizations (Ludwig Institute for Cancer Research, Canadian Society for Transfusion Medicine).

- **Facilitated** three Health Canada license amendments to:
  - Implement a change in Canadian Blood Services’ whole blood manufacturing process to improve efficiency
  - Develop a new closed system process to wash red blood cells on the latest generation ACP-215 Cell Processor
  - Implement a change in donor eligibility criteria.
- **Further developed** knowledge around new technologies in key areas such as red blood cell immunocamouflage and intravenous immunoglobulins (IVIg) replacements.
- **Provided** evidence-based data to the Canadian Standards Association to inform changes in red blood cell storage and in cryosupernatant plasma regulations.
- **Contributed** to the execution of several clinical trials, including PREPAREs, and the publication of systematic reviews and clinical guidelines to influence clinical practice.
Overview

About this report

Through the Centre for Innovation, Canadian Blood Services continued to play a significant national and international leadership role in 2013–2014 in discovery, development and clinical research on blood transfusion. The organization also contributed, to a lesser extent, to the fields of cellular therapies and transplantation.

This report highlights the contributions that our highly networked programs have made to the enhancement of scientific and medical knowledge in transfusion and related fields, and to the application of this knowledge for the benefit of Canadians. It focuses on accomplishments made during the fiscal year 2013–2014, including cited work published during the same period.

Structure

Instrumental to the Centre for Innovation’s research efforts are eight discovery research laboratories and four product and process development laboratories. Led by Canadian Blood Services staff scientists, these labs are located within Canadian academic research centres or within Canadian Blood Services facilities.

The Centre’s positioning within Canadian Blood Services’ Medical Services and Innovation division enables direct cross-fertilization with the organization’s epidemiology, medical microbiology, and medical services groups and, cross-divisionally, with Canadian Blood Services’ supply chain operations. The unique academic–Canadian Blood Services model also ensures that our staff researchers are cross-appointed with academic centres, thus providing access to a network of academic colleagues and trainees, and to state-of-the-art technologies and additional funding opportunities. We have enhanced this model through the activities of our newly established Knowledge Mobilization group within the Centre for Innovation. The group aims to maximize the dissemination and uptake of the knowledge created. The group also continues to build and leverage a network of relationships with other blood operators and related industry partners across all activities of the Centre, to support objectives.

The Centre for Innovation is administered by a small Secretariat. The Secretariat leverages Canadian Blood Services’ financial, legal, IT, communication and human resources services.

Programs

Funded primarily by Health Canada and provincial and territorial governments, the Centre for Innovation undertakes a multifaceted set of activities that together span the translational continuum from “bench to bedside”. These activities promote the creation of new knowledge and its translation into enhanced and new practices, services and technologies, for the benefit of Canadian patients and the health-care system.

The Centre has established research priorities aligned with the needs of Canadian Blood Services and of the blood system, including:

- blood supply risk
• transfusion-related acute lung injury (TRALI)
• blood utilization and conservation
• improved cellular products
• product quality
• pathogen reduction/inactivation
• therapeutic immunoglobulins
• improved clinical practice.

Research projects addressing these priorities are funded through multiple Centre programs. Each program follows strict peer-review processes that promote excellence, ensure relevance and reach a broad spectrum of Canada’s leading scientists and clinicians in the field. Our researchers are also competitive at obtaining funding from other organizations leveraging further the investments of our primary funders. For example, over the last year, a Heart & Stroke grant was secured to study fibrinolysis, a Burroughs Wellcome Fund innovation award was secured for research in blood product regulatory science, and an NSERC grant was secured to study oxidative injury during cell storage.

The Centre for Innovation also leads projects that address specific operational needs of Canadian Blood Services. These are undertaken through various laboratories or via netCAD, our simulated collection and production facility in Vancouver. To build capacity in the area of transfusion science and medicine, the Centre for Innovation also supports the training of professionals through targeted salary support programs and the delivery of educational events.

**Research progress**

**Safety and sufficiency of the blood supply**

Every year, Canadian Blood Services collects nearly 900,000 units of whole blood that is processed into red blood cells, platelets, and plasma. Plasma may be further processed into cryoprecipitate and cryosupernatant plasma, or fractionated into plasma protein products.

Blood operators must develop new donor criteria policies and re-evaluate existing criteria to ensure the safety, quality and efficacy of blood products and to ensure donor safety. Donor education materials are developed to explain risk factors for transmissible diseases and donor deferral policies. Donors must also complete health questionnaires prior to donation.

Led by Drs. Margaret Fearon, Mindy Goldman and Sheila O’Brien, Canadian Blood Services carries out comprehensive surveillance of bloodborne pathogens to monitor changing trends in known infections, identify new infectious diseases and develop policies appropriately. During the last year, these surveillance data were published for the first time in a surveillance report made available publicly online.38 The report presents the prevalence rates of tested pathogens in Canadian Blood Services collections from 1995 to 2012, as well as the estimated current residual risk of tested viruses. The report also highlights risks associated with known and emerging pathogens. Such information is invaluable for our organization, and for blood operators internationally in the process of evaluating blood testing and donor eligibility criteria. Canadian Blood Services also researches the prevalence rates of certain viruses in Canadian donors to inform policy development. For example, a Human T-Cell Lymphotropic Virus (HTLV) study demonstrated that with the current testing of the blood supply, the risk from HTLV is very
Seroprevalence studies on the emerging pathogens Babesia microti and Hepatitis E are near completion. Antibody testing has shown no evidence of babesiosis in over 10,000 Canadian Blood Services blood donors tested. Hepatitis E seroprevalence is just over 5% in the same group of donors, with no evidence to date of active infection in any of the antibody positive donors. Based on these results, there is no urgency to change our current testing policies or procedures.

Formulating a donor deferral policy requires robust data, research, and analysis to achieve an optimal risk reduction approach. For example, in the course of the last year, Dr. O’Brien studied Canadian Blood Services’ temporary deferral of potential donors for travel to malaria-endemic regions. She evaluated the impact of allowing donation from travellers to states in Mexico with very low malaria risk. She concluded that deferrals for malaria risk travel are substantial, and that a careful revision and refinement of risk areas of travel could safely and significantly reduce the burden of deferral. In another blood supply risk assessment, Canadian Blood Services and Héma-Québec conducted extensive stakeholder consultations and research to evaluate the risk and impact of revising the “men who have sex with men” (MSM) deferral policy. This work led to a new policy, approved by Health Canada in 2013, to allow blood donation in Canada from men who had sex with men more than five years ago. The impact of the policy continues to be monitored and evaluated. Furthermore, a change submission is in progress with the Canadian Standards Association.

A research lens was also applied to very practical donor base considerations such as accessibility to blood collection centres. Dr. Antonio Paez, with funding from a Canadian Blood Services/Canadian Institutes of Health Research (CIHR) grant, collaborated with Dr. John Blake and Professor Nancy Heddle to analyze data from the Canadian Blood Services Toronto blood donation dataset. They demonstrated that by improving accessibility to donor clinics, the number of donors would increase. They also developed a model that can be used to investigate the impact of policy changes, namely clinic location and size, on donor turnout. As part of Canadian Blood Services’ operational planning, Dr. Blake developed a method to determine staff requirements for standard clinic models. The staffing model was used to balance the requirements of minimizing staffing costs with that of ensuring that donors do not suffer unnecessary delays.

While ensuring a sufficient blood supply is important to blood operators, this cannot be achieved at the detriment of donor health. Iron deficiency is a major aspect of donor health being investigated by blood operators worldwide. Dr. Goldman’s research group has assessed ferritin levels in Canadian Blood Services donors and has found that one-third of first-time or reactivated female donors and approximately two-thirds of repeat female donors have low or absent iron stores. The study recommended that donors and physicians need to be more aware of iron needs associated with blood donation and of appropriate treatment for low iron stores. Consequently, Dr. Goldman, working with Canadian Blood Services colleagues, has developed tools to educate donors on iron deficiency. The group is now conducting a larger study to assess the operational feasibility of ferritin testing in donors to further inform policy development.

After careful selection of donors, the process of collecting whole blood and manufacturing specific blood products requires the use of specialized closed-system blood packs (medical devices). The quality of the finished blood products depends on both the specifications of these
bags and the manufacturing processes in which they are used. As Canadian Blood Services is evaluating new blood packs for whole blood collections, netCAD was leveraged to perform pre-validation comparative quality studies to guide the selection of new blood bag vendors and ensure product quality. The results and recommendations were presented in an internal technical report. The report provided key data to help in short-listing vendors and to make decisions on proceeding to validation. netCAD is also leveraged to undertake investigations that improve Canadian Blood Services operations. For example, work done at netCAD during the year led to the elimination of a mixing step early on in the manufacturing process, as it was shown to have no impact on the quality of blood products produced. Based on the data generated at netCAD, Canadian Blood Services submitted and received a licence amendment from Health Canada for this change, and it was implemented in all Canadian Blood Services sites in 2013. The elimination of this step streamlines the process without compromising the quality of the blood products produced.

Red blood cells

Red blood cell (RBC) units are the most common blood product Canadian Blood Services distributes to hospitals, with approximately 800,000 RBC units distributed to hospitals each year. One of the challenges of RBC units relates to the potential impact of the manufacturing process and post-production storage on the product quality. Over the years, the Centre’s unique Quality Monitoring Program (QMP), led by Craig Jenkins, has developed extensive knowledge of the blood products manufactured by Canadian Blood Services. The team has developed a series of biological markers associated with each product to better understand the products’ quality parameters that go beyond the regulatory requirements. This growing product characterization dataset is an invaluable resource for our development, medical, production, and quality professionals who need to better understand “what is in the bag?” Through the QMP, the Centre partnered with Blood Systems Inc. in the United States to expand the RBC benchmarking internationally, and to begin to evaluate the impact of different manufacturing processes on RBC quality. Furthermore, applying the knowledge developed through QMP, Dr. Jason Acker worked with Canadian Blood Services colleagues to develop a new closed-system process to wash saline, adenine, glucose and mannitol (SAGM) RBC on the latest generation ACP-215 Cell Processor, replacing the outdated COBE 2991s. The new process, for which Canadian Blood Services received a license amendment from Health Canada in May 2013, was implemented in October 2013. The process is expected to increase efficiency and improve washed RBC product quality due to the use of a closed system for production and the addition of an RBC preservative. The knowledge acquired on RBC products is also being applied by Dr. Acker and collaborators to develop new processes and technologies to optimize RBC quality and storage and to test the impact of new components on RBC quality. Specifically, Dr. Acker, in collaboration with clinicians at the University Hospital Network in Toronto, recently developed a protocol to ensure that adding dextrose to RBCs had minimum impact on the blood product quality. This finding could have an important impact on neonatal clinical practice, where dextrose is sometimes co-infused with RBC.

Dr. Sandra Ramirez-Arcos and her research group also evaluated the effect of time exposure of RBC units to room temperature on RBC quality and bacterial growth. Under current Canadian regulations, RBC units are stored at 4°C for up to 42 days, and can only be removed from
refrigeration and exposed to ambient temperatures for up to 30 minutes during this period. The studies that led to the establishment of this 30-minute rule were performed in the 1970s at a time when manufacturing practices were very different from today. Dr. Ramirez-Arcos showed that, in the first two hours of room-temperature exposure, bacterial growth does not significantly increase and RBC quality is not reduced. As a result of this research, the Canadian Standards Association is considering changing the maximum time limit of uncontrolled temperature exposure from 30 minutes to 60 minutes, a decision that will reduce wastage of RBC units without compromising safety or efficacy of the product. In recognition of the international leadership Dr. Ramirez-Arcos is playing in this area, this study was selected by the International Society of Blood Transfusion (ISBT) Jean Julliard Prize Committee for the prestigious Vox Sanguinis Best Paper Prize for the best original paper published in Vox Sanguinis in 2013.

RBCs must be irradiated as an additional safety measure to inactivate residual white blood cells prior to transfusion to newborn or immunocompromised patients. Dr. Dana Devine and her research group examined how the timing of irradiation of RBC units affects the amount of damage caused to the RBCs. The study showed that the timing of irradiation has a significant impact on RBC quality, suggesting that storage times for irradiated RBC may need to be reconsidered and shortened depending on clinical impact.

The current 42-day RBC storage regulation has been challenged by preliminary clinical studies that suggest that patients transfused with “older blood” — blood that is closer to the end of its shelf life — may have poorer health outcomes. One of the thematic research areas of the University of Ottawa Centre for Transfusion Research (UOCTR), led by Dr. Alan Tinmouth and supported by the Centre for Innovation, is focused on assessing the effect of RBC storage on clinical outcomes. In 2012, UOCTR completed the first large trial to examine the effects of red cell storage in premature infants and is now conducting the Age of Blood Evaluation (ABLE) and Age of Blood in Pediatric ICUs (ABC PICU) studies to further inform this contentious area of transfusion medicine. UOCTR’s neonatal study found no difference between clinical outcomes in patients receiving newer or older red cells. UOCTR also examined the effect of RBC storage time on overall survival and cancer recurrence in cancer patients. The study found that the duration of storage of RBCs prior to transfusions is not associated with overall survival or cancer recurrence, suggesting that current guidelines on RBC storage durations are adequate for the transfusion of cancer patients.

Although there is currently no clinical evidence to support a change in RBC storage regulations, to be prepared for pending results from large randomized controlled clinical trials that could provide such evidence, process engineer Dr. Blake built a computer simulation model to evaluate the impact that shortening the shelf life of RBC would have on the supply chain. By simulating the inventory and ordering behaviours of hospitals, the group found that shortening the RBC shelf life to 28 or 21 days would not significantly affect hospital or blood product supply chains. This model can be used to inform policy development should any of the large clinical studies underway find a negative correlation between patient outcome and RBC age, and the maximum RBC storage time standard must be reduced.

RBC transfusions are the most common form of tissue transplantation. While RBC transfusions are considered generally safe, some patients develop mild or severe reactions to transfusion. These reactions arise when the blood recipient’s immune system recognizes one or more of the
more than 300 minor (non-ABO and RhD) blood group antigens present on donor RBCs and produces antibodies (alloantibodies) against them. Patients who are chronically transfused, such as those suffering from thalassemia or sickle cell anemia, can develop so many different alloantibodies that it becomes practically impossible to find transfusable red cell units that they will not reject. To address this global problem, Dr. Mark Scott has pioneered the immunocamouflage of donor RBCs. This novel technology, patented by Canadian Blood Services, relies on the chemical attachment of biologically safe polymers on donor RBCs, which camouflages the foreign blood group antigens. Efforts continue to develop this novel RBC product to meet the needs of a high-risk patient group with significantly safer product.11, 28

Another challenge relates to the poor understanding of the role of RBC transfusion on the clinical outcomes observed in patients undergoing hematopoietic stem cell transplantation. In 2013, Drs. Jason Tay and David Allan from the UOCTR were supported with a Canadian Blood Services/CIHR grant to conduct the Transfusion Requirements in Stem Cell Transplantation (TRIST) study to learn about the best transfusion practices in this high-risk population. Finally, Drs. Lauralyn McIntyre and Dean Fergusson, also from the UOCTR, completed a review to summarize the current evidence for commonly transfused blood components. The review made some recommendations for RBC transfusion for critically ill patients.35 The group also conducted a systematic review on the effect of blood donor characteristics on transfusion outcomes with a specific focus on RBC transfusion.12

Platelets

Platelets are small, circulating blood cells that play a key role in the formation of blood clots in response to bleeding. Various medical conditions are associated with a decrease in platelets for which platelet transfusions are used to manage the clinical symptoms. Canadian Blood Services manufactures approximately 150,000 transfusion doses of platelets annually. Most are derived from whole blood donations and the remaining from apheresis donations. Platelets are unique amongst blood products in that they require storage, with continuous agitation, at ambient temperature. This requirement makes platelets the most susceptible blood product to bacterial contaminants. Implementation of donor skin disinfection, first aliquot diversion, a five-day storage limit, and bacterial screening with the BacT/ALERT® culture system has improved platelet safety in Canada. However, transfusion reactions due to contaminated platelets are still reported.

Dr. Ramirez-Arcos’ research focuses on bacterial biofilms that can contaminate platelet concentrates to understand factors influencing biofilm formation.16, 26, 63 Her research has shown that these biofilms may not be detected during screening3 and have increased pathogenicity.21 Her group has also shown that anaerobic bacteria cannot replicate during platelet storage, but can survive in the presence of oxygen, likely as a result of the formation of biofilms.26 Dr. Ramirez-Arcos’ group also contributes to the development of better methodologies and technologies. A patent describing a method for detecting Staphylococcus epidermidis in platelet concentrates was issued for their work in 201462, and the group is participating in an international study, endorsed by the World Health Organization, to develop a panel of bacterial strains suitable for validation and comparison assessments. The group also completed two studies with industry partners. One study was conducted with Immunetics Inc. to evaluate the BacTx technology for bacterial detection at point-of-issue58, and one was conducted with Blood
Cell Storage Inc. to evaluate the efficacy of pH SAFE technology in identifying bacterial contamination also in platelet units.\textsuperscript{59} Contributing directly to the safety of platelet concentrates in Canada, Dr. Ramirez-Arcos' group regularly tests BacT/ALERT media, which are used for routine platelet screening\textsuperscript{49-57} at Canadian Blood Services manufacturing sites. The group also contributed to an international forum to better understand bacterial contamination in platelet concentrates and related international practices.\textsuperscript{45} Finally, the Centre for Innovation, through a licencing agreement with LightIntegra Technology, continues to support the development of the ThromboLUXTM technology. This technology was first established by Canadian Blood Services adjunct scientist Dr. Elisabeth Maurer based on discoveries funded by Canadian Blood Services. It is a quick and simple diagnostic test for platelet quality and function that will make it easy to screen platelets prior to transfusion. Several ongoing clinical studies in North America and Europe use this technology, including the PREPARES study described below.

Pathogen reduction technology (PRT) seeks to reduce or eliminate the proliferation or replication of a large range of bacteria, viruses and parasites that may be in donated blood. PRTs may be an alternative to expensive testing of blood for specific infectious agents and may increase safety by destroying emerging pathogens. Although no PRT has yet been implemented in Canada, Canadian Blood Services is contributing to the Canadian arm of the international PREPARES clinical trial. The trial aims to evaluate the Mirasol method of platelet pathogen reduction treatment as compared with Canadian Blood Services regular pooled platelets. Our manufacturing site in Ottawa prepares Mirasol treated platelet concentrates that are used by the participating Canadian sites. The McMaster Transfusion Research Program, led by Professor Nancy Heddle, and supported by the Centre for Innovation, participates and coordinates patient enrolments at five Canadian hospitals. 358 patients (64 from Canada) have been enrolled to date and completion of the study in partnership with Sanquin and Norway is anticipated by the end of 2015. Recently, the McMaster researchers searched the global literature on implementation of food irradiation technology to identify important lessons learned that could be applicable to pathogen reduction technology if a decision is made in the future to implement this technology in Canada.\textsuperscript{20} While PRTs reduce infectious risks, the technology may negatively affect platelet function. Dr. Devine partnered with TerumoBCT to study the impact of the Mirasol technology on platelet quality. Their research has shown that pathogen reduction treatment increases markers of activation in platelet concentrates, which increase during the storage period. The group is now performing proteomic profiling to identify critical changes in the treated platelet concentrates, which may provide information about product quality and inform further technology development.\textsuperscript{46} Similarly, Dr. Patrick Provost's research group, funded by a Canadian Blood Services/CIHR grant, has examined platelet microRNA levels following pathogen reduction treatment and has shown that treatment releases platelet microRNAs, possibly through the formation of microparticles, and may reduce platelet function.\textsuperscript{29} The clinical study and the group's research will ensure that PRTs are developed without compromising product efficacy and patient safety.

Another approach aimed at minimizing platelet contamination is to develop technologies that would enable platelets to be stored at 4°C or below. Currently, platelets cannot be stored at 4°C since transfusion of cold storage-activated platelets leads to rapid clearance of these cells within the recipient. Funded via a Canadian Blood Services/CIHR grant, Dr. Scott has developed a method to pegylate platelets that enables platelets to be stored at 4°C. Dr. Donald Brooks, also
funded through a Canadian Blood Services/CIHR grant, has taken a different route to increase the storage time for platelets and has developed a hydrophilic coating for the plasticized polyvinyl chloride platelet bags.\textsuperscript{18} This hydrophilic coating minimizes the adhesion of platelets and bacteria to the walls of the bags, extending the platelet storage time at room temperature, while preventing bacterial growth in the bags. If successful, these new technologies could extend platelet storage time while preventing bacterial infections associated with platelet transfusion, significantly improving product quality to the benefit of patients while reducing costs to the system.

While there has been progress in recent years in the utilization of platelets in the clinic, many controversies remain. With funding from the Small Project program, an international team led by Dr. Donald Arnold completed a systematic review on the use and impact of platelet transfusions in critically ill patients. The team found a surprising lack of evidence from clinical trials to support or refute platelet transfusion practice in the intensive care unit.\textsuperscript{33} UOCTR, led by Dr. Tinmouth and supported by the Centre for Innovation, also looked at prophylactic platelet transfusion for preventing bleeding in patients with haematological disorders after chemotherapy or stem cell transplantation. The Centre also supports Dr. Nadine Shehata to lead the International Collaboration for Guideline Development Implementation and Evaluation for Transfusion Therapies (ICTMG). The ICTMG published two systematic reviews around the utility of HLA-matched platelets and cross-matched platelets in patients with hyperproliferative thrombocytopenia.\textsuperscript{43,74} Clinical guidelines based on these reviews will be published in the coming year.

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

Plasma is the protein-rich liquid component of blood that supports the immune system and promotes the control of excessive bleeding. Plasma is routinely stored frozen, providing a longer shelf life and limited bacterial contamination risk. Plasma can be prepared from apheresis or whole blood. 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, allowing for the most benefit to be derived from donated plasma. Every year, Canadian Blood Services manufactures approximately 276,000 and 55,000 units of plasma and plasma cryosupernatants, respectively.

Plasma can also be pooled and fractionated to provide purified and virally inactivated plasma protein products, such as albumin and intravenous immunoglobulins (IVIg). We send plasma for fractionation to manufacturers under national contracts. This allows us to provide plasma protein products to Canadian hospitals at a lower cost than would otherwise be the case. Nevertheless, clinical demand for IVIg rises every year, and providing this product alone to Canadians consumes a significant part of our total operating budget. Through the Centre for Innovation, we are 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.

Many different plasma coagulation factors contribute to blood clotting, but it is not known which are the most important components to ensure the best quality transfusable plasma. Health Canada currently requires Canadian Blood Services to test plasma for only one coagulation factor, factor VIII (FVIII). Developing a better understanding of these coagulation factors and
their role in forming blood clots would provide evidence to develop more appropriate plasma quality tests. Dr. William Sheffield has created a mouse model of global plasma protein deficiency to test plasma quality. The results suggest that high fibrinogen levels, not FVIII levels, in the transfused plasma, more reliably reduce bleeding. This work complements other efforts, such as the QMP led by Craig Jenkins, which could lead to defining better standards for plasma quality. Over the last year, Dr. Sheffield and Jenkins also completed a study on the quality of frozen plasma prepared from whole blood, measuring both FVIII and seven other factor levels. They have extended this approach to cryosupernatant plasma and cryoprecipitate components to gain a better understanding of these products to enhance manufacturing methods. Given that Canadian Blood Services is considering manufacturing pooled-cryoprecipitate products, the group also surveyed the international community to assess the current practices and manufacturing processes used by other blood operators and documented the findings in an internal report.

Through its QMP, the Centre also completed a study led by Drs. Sheffield and Ramirez-Arcos to evaluate the impact of post-thaw storage on the quality of cryosupernatant plasma. Current Canadian regulations require that cryosupernatant plasma be transfused within 24 hours of thawing, a standard which leads to wastage since clinical procedures may be cancelled or postponed. The group demonstrated that thawed cryosupernatant plasma can be refrigerated for up to five days without compromising the quality or the safety of the thawed product. The study has been shared with the Canadian Standards Association in hopes of influencing cryosupernatant plasma regulations to reduce wastage in Canadian hospitals without compromising the quality of the product transfused into the patients.

As the Canadian population ages, more Canadians are put on “blood thinning” drugs to minimize the likelihood of strokes and heart attacks. However, there are situations in which the blood thinning effects must be rapidly reversed, for example if emergency surgery is required. Canadian clinicians are also using newer oral anticoagulants. There is controversy over the best way to achieve drug reversal; plasma or plasma protein products have been considered. Using animal models like those described above, Dr. Sheffield’s group, supported by a Canadian Blood Services/CIHR grant and in collaboration with Dr. Arnold, compared these alternatives. The group found that for some oral anticoagulants, a plasma protein product called a prothrombin complex concentrate (PCC) was superior to plasma transfusion to achieve reversal. For others, neither plasma nor PCCs were effective. Such findings correlate with clinical studies and provide further evidence that could reduce wastage of plasma or plasma protein products in fruitless administration, and improve patient safety.

In conceptually related work, Dr. Ed Pryzdial investigates the regulation of clot formation and dissolution and the molecular basis of clotting protein deficiency in patients. Particular emphasis is placed on novel applications of plasma proteins to transfusion science. His research has led to the development of derivatives of Factor X that promote clot lysis. In the long term, such an agent could lead to alternative treatments for cardiac surgery, a medical procedure that currently requires significant transfusion product support. In addition, Dr. Pryzdial’s research has led to the development of derivatives of Factor V that reduce blood clotting activity by reducing thrombin generation, for which a patent was issued in Canada in 2013.

It is broadly accepted that frozen plasma is frequently transfused inappropriately, putting the patient at risk with no benefit, and wasting product. To better understand current utilization
practices, the UOCTR, led by Dr. Tinmouth and supported by the Centre for Innovation, completed an audit to evaluate the clinical indications and appropriateness of frozen plasma transfusion in Ontario. The survey revealed the two most common reasons for inappropriate use of frozen plasma transfusions: they were administered to patients with an international normalized ratio below 1.5, or they were administered in absence of bleeding or emergency surgery. The investigators concluded that focusing on reducing these two inappropriate practices could significantly improve frozen plasma utilization.73

IVIg is a product that contains the antibodies from plasma pooled from up to 1,000 healthy donors. Approximately 10% of IVIg used in Canada is for the treatment of immune thrombocytopenia (ITP), a serious bleeding disorder generally caused by low number of platelets due to the production of anti-platelet antibodies. Canada is the largest user of IVIg per capita in the world, and with new indications being identified for this product, the usage may rise. However, the supply of IVIg is limited. The development of alternative therapies to IVIg and a better understanding of the mechanism by which IVIg works would benefit patients and the blood system in general. Dr. Heyu Ni conducted a retrospective study in adults with ITP and concluded that patients with autoantibodies to the platelet surface protein GpIIb/IIIa respond well to IVIg therapy, but those with autoantibodies to platelet GpIb/IX do not.44 Such studies could lead to more appropriate clinical practice. Drs. Ni, Alan Lazarus, Donald Branch and John Semple are internationally recognized for their work in elucidating the molecular mechanisms through which IVIg works. Using a mouse model of ITP, Dr. Semple’s group has shown that IVIg treatment produces cytokines. Preliminary evidence indicates that the cytokines have an effect on the number of T regulatory cells — cells important in autoimmunity. However, more work is required to fully understand the effects of IVIg treatment on the immune system.64

With funding from a Canadian Blood Services/CIHR grant, Dr. Lazarus explores the potential for monoclonal antibodies against CD44 to be used as replacements for IVIg in ITP. Through the identification of the region of the antibodies necessary to elicit the required effect, Dr. Lazarus’s group has shown that the antibodies against CD44 can mimic the effects of IVIg, at least in mouse models.13, 37 Dr. Lazarus holds several patents in this area, one of which was issued in 2014.31 Dr. Branch’s efforts in the development of IVIg alternatives have focused on the development of small molecule inhibitors of phagocytosis. Supported by a Canadian Blood Services/CIHR grant, the group in collaboration with Dr. Lakshmi Kotra and in partnership with the University Health Network and the MaRS Discovery District, used proven drug design methods to develop first- and second-generation drugs that can reverse platelet destruction in a mouse model of ITP.48 This drug development effort, which has been filed for patent protection, provides hope for a new class of drugs for the treatment of ITP.

**Hematopoietic stem cells**

Hematopoietic stem cells (HSCs) are cells that can renew themselves and differentiate into the various mature blood cells. HSCs are normally found in the bone marrow and peripheral blood of adults and in umbilical cord blood. HSCs have been used in clinical practice for many years to treat numerous malignant or non-malignant blood-related disorders. The demand for HSC transplants is increasing for both Canadian and international patients.
In 2013, Canadian Blood Services launched the National Public Cord Blood Bank (NPCBB) to collect, process, test and store cord blood units for use by any Canadian or international patient in need of a HSC transplant, with a focus on supporting Canada’s ethnic diversity. The Centre for Innovation has been instrumental in facilitating the establishment of the NPCBB. Dr. Ramirez-Arcos has developed and executed a validation protocol to evaluate the sterility of cord blood collected by the NPCBB and Dr. Acker has validated the colony-forming unit assay used by the NPCBB to assess the quality of the stored stem cells. This work also lays the foundation for a stem cell QMP which will provide in-house knowledge of stem cell products. Recognizing the increasing need for knowledge in this area to support Canadian Blood Services’ operations, the Centre has recruited Dr. Nicolas Pineault, an expert in cord blood stem cells. His expertise will prove essential as we further develop our activities in this emerging field of research and clinical practice.

Building capacity through training and knowledge mobilization

An important role of the Centre for Innovation is to build long-term capacity in the field of transfusion and transplantation sciences and medicine. To do this, the Centre facilitates the training of professionals and develops knowledge mobilization tools and best practices.

Training program

The Centre for Innovation administers a competitive Canadian Blood Services National Training Program to attract, train and retain promising young scientists. Through the Canadian Blood Services Summer Internship, the Centre attracted nine undergraduate students in 2013 to carry out four-month research projects in a Canadian Blood Services laboratory, providing a valuable first step into a research lab and the field of transfusion and transplantation sciences. Four new graduate students were awarded a Canadian Blood Services Graduate Fellowship, complementing the 12 ongoing awardees. These trainees are completing research studies toward a PhD in nine laboratories affiliated with Canadian universities. The training program also supports scientists during their post-doctoral training to promote their retention and advancement in the field. One new post-doctoral fellow received a Canadian Blood Services Post-doctoral Fellowship, and one fellowship was renewed, complementing the six ongoing fellowships in four Canadian Blood Services laboratories and two external laboratories across Canada. In partnership with CIHR, the Centre also runs a Canadian Blood Services/CIHR New Investigator competition. Two physicians are currently funded. Finally, through a Program Support Award, the Centre for Innovation contributes to the Centre for Blood Research (CBR) Training Program led by Dr. Ed Conway. The program includes a CBR Summer Studentship Program and a CBR Collaborative Research Award Program. Ten CBR Summer Studentships and three Collaborative Awards were awarded in the last year, providing research opportunities for undergraduates and graduates to perform research projects in CBR laboratories in Vancouver.

Of the 46 trainees directly supported by the Centre’s National training program, 21 completed their training in 2013–2014. These trainees are complemented by the numerous students who are pursuing their research studies in Canadian Blood Services laboratories and supported by other sources of funding. Together, this cohort will continue to lead research excellence in
Canada in transfusion and transplantation science and medicine. This leadership is already demonstrated by the achievement of Dr. Jayachandran Kizhakkedathu, a Canadian Blood Services/CIHR New Investigator awardee who won the 2013 Distinguished Achievement Award for Excellence in Basic Science Research award from the University of British Columbia faculty of medicine.

In addition to developing capacity in transfusion and transplantation sciences, the Centre for Innovation also facilitates the training of transfusion medicine specialists by offering fellowships to medical fellows. Following completion of their medical degree and specialties, these fellows are accepted in the Transfusion Medicine Residency program. The Transfusion Medicine Residency program is accredited by the Royal College of Physicians and Surgeons of Canada and is developed and delivered in partnership by Canadian Blood Services medical directors and five Canadian medical schools. In 2013–2014, seven fellows completed the diploma. One of the fellows, Dr. Cindi Jacques from the University of Ottawa, received a Canadian Blood Services Transfusion Medicine Residency fellowship. Also in 2013–2014, the residency program was modified to align with the new Royal College of Physicians and Surgeons Diploma Program.

Finally, through the Canadian Blood Services James Kreppner Award, the Centre attracts researchers who conduct legal research in the field of transfusion and transplantation. In 2013, Dr. Jennifer Chandler at the University of Ottawa was awarded the James Kreppner award to address three issues of importance in the functioning of Canada’s organ donation system. The research conducted by Dr. Chandler is being leveraged by other groups within Canadian Blood Services.9, 10

Disseminating knowledge

In addition to having published over 280 peer-reviewed and non-peer-reviewed publications, Centre for Innovation staff presented over 150 oral and poster presentations at national and international conferences over the last year.

The Centre also organizes symposiums to mobilize knowledge and influence practice while nurturing national and international collaboration. One of these key events is the Annual Canadian Blood Services International Symposium, held in Toronto. The symposium is designed to bring together professionals in the fields of transfusion medicine, cellular therapy and transplantation to share the latest clinical and discovery research around a specific topic. This year’s program was chaired by Dr. Sheffield and medical director Dr. Kathryn Webert, and included five Canadian and four international speakers. It focused on platelets, their clinical utilization and inventory management, as well as the novel technologies being developed to manipulate them to increase safety and efficacy. For the first time, the event was accredited by the Royal College of Physicians and Surgeons as a continuing medical education (CME) event. The 159 attendees included mostly health-care professionals, such as speciality physicians, medical lab technologists and scientists. They were highly satisfied and agreed that the event enhanced their knowledge in an area that was applicable to their work or practice. To further disseminate the knowledge shared at this live event, a report was published in Transfusion Medicine Reviews.76
Via a partnership with the Canadian Society for Transfusion Medicine, the Centre provides funding and human resources toward the organization of the society’s annual meeting. Held in Edmonton in June 2013, the event attracted over 350 participants.

Through its Program Support Award to the CBR, the Centre also contributes to the Annual Norman Bethune Symposium and the CBR Seminar Series in Vancouver. Held in April, the symposium was chaired by Drs. Pryzdial and Ross MacGillivray and provided to over 150 attendees a series of clinical and research talks to promote excellence in research, education, training and clinical care. The symposium was also broadcast online. The Seminar Series is delivered each week at the CBR and is attended by 80 to 120 individuals who are primarily CBR scientists, clinicians and trainees.

Canadian Blood Services medical directors also deliver regular educational events (including “Hospital Rounds”). One key event is the ORBCoN/Canadian Blood Services Annual Transfusion Medicine Education Videoconference Symposium organized by medical director Dr. Peter Lesley in partnership with the Ontario provincial blood coordinating office. This year’s event was focused on the needs of transfusion in the female population and was hosted at the Queensway-Carleton Hospital in Ottawa. Eighty-three hospital sites registered for the videoconference, representing 53 per cent of the hospital sites in Ontario. A total of 810 professionals attended, including medical lab technologists, nurses and physicians.

As part of the national Transfusion Medicine Residency Program, medical director Dr. Robert Skeate organizes CME-accredited LearnTransfusion Webinars for health-care professionals. Over the last year, 35 one-hour webinars were delivered on topics ranging from serology testing to ethical aspects of transfusion and were attended by on average 60 health care professionals.

In an effort to promote knowledge exchange within Canadian Blood Services, the Centre organizes Knowledge to Munch On Lunch & Learns. The Centre facilitated eight presentations during two events attended by 116 and 147 Canadian Blood Services staff members, respectively, from across Canada. The presentations were carefully selected to provide staff with a snapshot of the organization’s ongoing research projects and their impact on the organization. To further disseminate Canadian Blood Services’ research achievements internally, conference reports are posted on the intranet to share staff presentations made at key international conferences. The 2013 conference reports and associated presentations were downloaded 747 times.

Finally, the Centre published eight ResearchUnits to provide clear summaries of results and impacts of research conducted by the Program.

**Best practices**

The Centre publishes the Clinical Guide to Transfusion Medicine. This 18-chapter online guide, co-edited by Drs. Gwen Clarke and Sophie Chargé, is an excellent and practical summary of our current knowledge of blood components and transfusion medicine practices. The guide contributes to improved patient safety and greater confidence for those who provide services. Over the last year, the 18 chapters were downloaded more than 9,000 cumulatively (unique events) and four chapters were updated.
Recognizing the need for evidence-based clinical guidelines to optimize transfusion care, the Centre supports Dr. Nadine Shehata’s leadership in the ICTMG. In 2013, this international group published two systematic reviews on platelet transfusion therapy in hypoproliferative thrombocytopenia and has submitted the related clinical guideline for publication. Such collaborative efforts, and the application of consistent, up-to-date methodology, enable a more timely and cost-effective approach to the creation of transfusion medicine guidelines, while increasing the credibility of guideline development for transfusion medicine.

With its extensive knowledge of Canadian Blood Services blood products, the Centre oversees the development of Canadian Blood Services circulars of information (COIs). The COI is an extension of the component label and provides information on component composition, packaging, storage and handling, indications, warnings and precautions, adverse events, dose and administration. The COI conforms to the applicable regulations issued by Health Canada. The COI is a knowledge mobilization tool that promotes the safe transfusion of all Canadian Blood Services blood products. In 2013, the Centre revised the RBC COI and developed a new COI for hematopoietic progenitor cells, which will be distributed with cord blood units manufactured by the NPCBB.

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, 25 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.

The Centre includes 12 permanent Canadian Blood Services research laboratories. While these groups constitute the central node of the Centre’s research pillar, they are complemented by numerous research groups enabled through formal partnerships. The Centre for Innovation’s Program Support Award (previously named Transfusion Medicine Research Programs in Canadian Academic Institutions) provides funding to Canadian centres that have an established track record in transfusion medicine or transfusion science research. The three recipients of this award for 2010–2014 were:

- the McMaster Transfusion Research Program led by Professor Nancy Heddle
- the University of Ottawa Centre for Transfusion Research led by Dr. Alan Tinmouth
- the Centre for Blood Research in Vancouver led by Dr. Ed Conway.

As described earlier in this report, the Ottawa and McMaster teams provide extensive expertise in the areas of clinical research, while the Vancouver group complements the Canadian Blood Services discovery research activities and provides further training and knowledge mobilization.
activities. The program was reviewed in 2013 and a competition was held to identify the 2014–2017 recipients and their areas of activities.

Another important partnership is one established with CIHR. Through this formal partnership, which was renewed in 2013, the Centre partners with the Institute of Circulatory and Respiratory Health to issue calls for CIHR/Canadian Blood Services Priority Announcement operating grants and New Investigator awards from the greater Canadian research community. Through this partnership, the Centre leverages the expertise of CIHR in the area of peer-review process, facilitates the dissemination of identified priorities for the blood system, and leverages CIHR funding as some of the higher-ranked projects are directly funded by CIHR (e.g. two new projects were funded by CIHR in 2013). Also in partnership with CIHR, the Centre has partnered with multiple organizations to fund (for 2013–2018) Dr. Lori West who leads the Canadian National Transplant Research Program: Increasing Donation and Improving Transplantation Outcomes project.

At an international level, Dr. Devine is team lead, and Drs. Acker and Goldman are associate members of the Biomedical Excellence for Safer Transfusion (BEST) organization. BEST is an international research organization that works collaboratively to explore ways to improve transfusion-related services through standardization of analytic techniques, development of new procedures, systematic review of evidence, and execution of clinical and laboratory studies. A number of our researchers contribute to the 21 ongoing BEST international studies.

Through netCAD, the Centre for Innovation research development facility in Vancouver, 105 blood and apheresis clinics were conducted for deferred donors in the last year. These clinics resulted in the distribution of 1,086 whole blood and 131 apheresis platelet products for research. This unique service supported 15 internal research projects, as well as 10 external research teams across Canada. Leveraging netCAD expertise in delivering blood products for research, the group worked closely with the National Public Cord Blood Bank to establish the Cord Blood for Research Program to distribute unbankable cord blood to researchers across Canada for cord blood and stem cell research.

Finally, the Centre for Innovation worked in partnership with several international companies such as Immunetics Inc., Blood Cell Storage Inc. (BCSI), and Mirasol, to provide substantive research support to further technology development for the future benefit of the blood system.

In addition to establishing partnerships that expand and leverage the Centre’s research activities, Centre for Innovation staff actively contribute expertise to a variety of committees. Their solicited participation is a testimony to their recognized leadership in the field. Furthermore, they allow Canadian Blood Services to remain informed of the latest developments affecting the blood system and to influence it. A few examples of participation on external committees include membership on editorial boards of scientific journals and review boards for granting agencies. Of note:

- Dr. Devine is editor-in-chief of the journal Vox Sanguinis.
- Dr. Blake is a member of the Blood Shortage Working Group of the National Advisory Council on Blood, which advises on operations, strategy and metrics for dealing with blood distribution in the event of a shortage.
• Dr. Ramirez-Arcos is a member of a bacteria subgroup for the International Society for Blood Transfusion-Transfusion-Transmitted Infectious Diseases (TTID), intended to drive development of the next generation of basic and clinical research with interest in transfusion-transmitted bacterial infections from all regions of the world.

• Dr. Acker was elected president-elect of the International Society for Cryobiology, a field highly relevant to cellular therapies and tissue/organ banking.

Since early 2014, the Centre for Innovation has been Canadian Blood Services’ point of contact for our collaboration with the Alliance of Blood Operators (ABO). The goal of this international collaborative effort is to facilitate horizontal learning across its membership to identify and promote good practice and encourage performance improvement. The collaboration focuses on research program management and collaborations, and horizon scanning in the area of new scientific and product developments. The other members include NHS Blood and Transplant (United Kingdom), Australian Red Cross Blood Service, America’s Blood Centres, American Red Cross, Blood Systems Inc. and the European Blood Alliance. As part of this ABO network, Canadian Blood Services participated in 42 knowledge exchanges over the course of the year. Such knowledge exchanges included the establishment of an R&D Leadership group led by Dr. Devine and focused on research program operation and management, international research collaborations, increasing research efficiency and productivity, and horizon scanning in the area of new scientific developments. Surveys were also conducted to understand how other blood services validate and monitor activities to minimize bacterial contamination and how others forecast demand, especially with the recent decline in RBC demand. Canadian Blood Services conducted a survey on the level of hemolysis in SAGM RBC and on other blood services’ quality control programs to understand why the level of hemolysis is observed in whole blood units produced through top/top whole blood filtration blood packs. This information will be incorporated in Canadian Blood Services decision documents to develop best practices that help minimize the incidence of hemolysis.

Also as part of the ABO network, Judie Leach Bennett provides leadership for developing an integrated and internationally applicable risk-based decision-making framework focused on donor safety and optimal patient outcomes. The framework is intended to optimize the safety of the blood supply by enabling the proportional allocation of finite resources to mitigate the most serious risks, recognizing that the elimination of all risk is not possible. A second objective is to analyze and account for a series of contextual, often qualitative, factors that affect decision-making in the management of blood risks: social, economic, and ethical perspectives, which go beyond quantitative calculations of risk and which can alter risk tolerability. Another example of the Centre’s work with international groups is the leadership provided to the ICTMG.

**Governance**

In 2013, Canadian Blood Services established the Centre for Innovation to gain further efficiencies and increase integration across our research, knowledge mobilization and product and process development teams. Our research team is led by Dr. Sheffield, our knowledge mobilization team is led by Dr. Chargé, and our product and process development team is a
newly configured team led by Ken McTaggart. The product and process development team focuses on the nexus between research and Canadian Blood Services’ supply chain operations. A secretariat was also established to enable these three pillars. It provides support by managing grant funding competitions and associated disbursement of funds, in accordance with the programs’ guidelines and controls. Over the last year, the secretariat facilitated eight competitions for the Centre’s various research and training programs resulting in the funding of 19 new projects (see Appendix 1). The secretariat supports technology transfer activities as well as performance evaluation. During the year, a new performance management framework was established in collaboration with Health Canada. Processes and databases were also developed to capture and report the data in compliance with this framework. The Performance Management Framework is being leveraged to report on our activities to Canadian Blood Services corporate performance reporting.

Residing in Canadian Blood Services’ Medical Services & Innovation division, the Centre is integrated within Canadian Blood Services’ overall governance structure (see chart below). In the last year, the memberships of both the Canadian Blood Services Scientific and Research Advisory Committee (SRAC) and Canadian Blood Services Research Ethics Board (REB) were enhanced. The SRAC meets twice a year to review the Program content and performance obligations. It is comprised of international experts with scientific, medical, and ethics expertise and experience in the administration of large research programs. The membership was analyzed and was expanded to include new subject-matter experts based on Canadian Blood Services’ expanded scope of activity. The Canadian Blood Services REB meets at least three times per year to provide guidance on the research ethics of projects and ensures projects supported by the organization adhere to the Tri-Council Policy statement on ethical conduct for research involving humans. It is comprised of external members and was also expanded to include a new community representative to strengthen that perspective. Over the last year, the Canadian Blood Services REB was instrumental in guiding the development of the research donor consent and project approval process for the Cord Blood for Research Program.
References cited (See Appendix II for a full list of Centre for Innovation’s publications for fiscal year 2013–2014):


30 D Lane, 'Pre-Transfusion Testing', in Clinical Guide to Transfusion, ed. by G Clarke and SB Charge (transfusionmedicine.ca: Canadian Blood Services, 2014).


32 P Lesley, and G Clarke, 'Preoperative Autologous Donation', in Clinical Guide to Transfusion, ed. by G Clarke and SB Charge (transfusionmedicine.ca: Canadian Blood Services, 2013).


37 PJ Mott, and AH Lazarus, 'Cd44 Antibodies and Immune Thrombocytopenia in the Amelioration of Murine Inflammatory Arthritis', PloS One, 8 (2013), e65805.
68. 'The Testing of Frozen Cryoprecipitate Thawed and Stored at Ambient Temperature for up to 24 Hours', Internal report submitted to Canadian Blood Services, Craig Jenkins, Director, Quality Monitoring Program, Research & Development (2013).
74. RR Vassallo, M Fung, P Reulla, R Duquesnoy, CL Saw, SJ Slichter, S Tanael, N Shehata, and International Collaboration for Guideline Development Implementation Evaluation for


### Appendix I: Funded Projects

<table>
<thead>
<tr>
<th>Projects Receiving Funding in Fiscal Year 2013/14</th>
<th>92</th>
</tr>
</thead>
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<td><strong>Research Program</strong></td>
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<tr>
<td>CBS/CIHR Partnership Operating Grants</td>
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<tr>
<td>Blood Utilization and Conservation</td>
<td>17</td>
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<tr>
<td>Transfusion Related Acute Lung Injury</td>
<td>1</td>
</tr>
<tr>
<td>Blood Supply Risk</td>
<td>2</td>
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<tr>
<td>CBS/CIHR New Investigator Program</td>
<td>2</td>
</tr>
<tr>
<td>Intramural Operating Grants</td>
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</tr>
<tr>
<td>Small Projects Funding</td>
<td>3</td>
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<tr>
<td><strong>Product and Process Development Program</strong></td>
<td>33</td>
</tr>
<tr>
<td>Integrated Development Program</td>
<td>20</td>
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<tr>
<td>Development in Collaboration with External Agencies</td>
<td>8</td>
</tr>
<tr>
<td>Participation in International Benchmarking Studies, Technology Evaluations, and Knowledge Exchange Activities</td>
<td>5</td>
</tr>
<tr>
<td><strong>National Training Program</strong></td>
<td>24</td>
</tr>
<tr>
<td>James Kreppner Fellowship</td>
<td>1</td>
</tr>
<tr>
<td>CBS/CIHR Postdoctoral Fellowship</td>
<td>1</td>
</tr>
<tr>
<td>Postdoctoral Fellowship Program</td>
<td>6</td>
</tr>
<tr>
<td>Graduate Fellowship Program</td>
<td>16</td>
</tr>
<tr>
<td><strong>Transfusion Medicine Research Program</strong></td>
<td>3</td>
</tr>
</tbody>
</table>
Research Program

CBS/CIHR Partnership National Operating Grant Program

Purpose: Blood Utilization and Conservation
- Fanconi Anemia Proteins as Regulators of Genes Involved in Hematopoietic Stem Cell Function
- Characterization of Regulatory Interactions/Complex in Hemoglobin Switching
- 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
- Mechanism of Action of Anti-CD44 Antibodies in Murine ITP
- Preservation of Red Cells from Cord Blood as a New Blood Product for Intrauterine and Neonatal Transfusions
- Improving the Cryostorage of Blood Products Using Novel Small Molecule Cryoprotectants
- Small Molecule Inhibitors of Phagocytosis as Replacement Therapy for IVIG
- 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
- Age of Blood in Children in Pediatric Intensive Care Units (SBC-PICU): a Multicenter International Pragmatic Double Blind Randomized Clinical Trial on the Efficacy of "Short Storage" Red Blood Cell Units to Decrease the Incidence of New or Progressive Multiple Organ Dysfunction Syndrome in Critically Ill Children
- Hydrophilic Polymer Brushes as Biocompatible Coatings: Development and Applications in Blood Handling and Platelet Storage

Purpose: Transfusion Related Acute Lung Injury
- Identification of Host Immune Factors Responsible for the Initiation and/or Modulation of Transfusion Related Acute Lung Injury

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)

CBS/CIHR Partnership New Investigator Program

- Transfusion Requirements in Cardiac Surgery II (TRICS II)
- Five Percent Albumin vs. Normal Saline as Fluid Resuscitation Strategies for the Management of Early Suspected Septic Shock (PRECISE Trial)

Intramural Operating Grant Program

- Application of Liposomes to Improve Hypothermic Storage of Red Blood Cells
- Immunocamouflage of Blood Group Antigens
- Quality of Transfusible Plasma: Mouse Models and Clinical Samples
- Stealth RBC: From Bench to Bedside
- Mechanism of Action of Intravenous Immunoglobulin (IVig): Role of Dendritic Cells in Stimulating T Regulatory Cells
- Antibodies to CD44 as a Potential Replacement for IVig in ITP
- Residual Risk of Transfusion-Transmitted Cytomegalovirus Infection: Incidence and Pathogenesis

Small Projects Program

- Use of Platelet Transfusions in Medical-Surgical Critically Ill Patients
- IVIG vs. Prednisone for Pregnant Patients with ITP
- Trends and Predictors of Transfusion in Obstetrical Patients

Note: Projects that are bolded and italicized are those for which funding was initiated in fiscal year 2013/14.
### Integrated Development Program

<table>
<thead>
<tr>
<th>Project</th>
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<tbody>
<tr>
<td>Support Evaluation of Pooled Cryosupernatant Project</td>
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<tr>
<td>Support Blood Packs and Platelet Pooling Set Replacement Project</td>
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<tr>
<td>The Effect of Room Temperature Exposure on Red Blood Cell Units</td>
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<tr>
<td>Validation of Bact/ALERT System to Detect Microbial Contamination in Cord Blood Units</td>
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<tr>
<td>Gerbich Negative Red Cell Concentrate Cryopreservation</td>
</tr>
<tr>
<td>Paperless Clinic Flow</td>
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<tr>
<td>Site Inventory Model and Analysis</td>
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<tr>
<td>Age of Red Blood Cell Studies</td>
</tr>
<tr>
<td>Support the Development of the Colony Forming Unit Assay for the National Umbilical Cord Blood Bank</td>
</tr>
<tr>
<td>Pre- and Post-Implementation Monitoring of the ACP-215 Cell Processor for Red Cell Concentrate Washing</td>
</tr>
<tr>
<td>Validation of the Process to Follow-Up Positive Bacterial Cultures</td>
</tr>
<tr>
<td>DOP for Preparation of Bacterial Frozen Stocks for Master Lot Test Results of BacT Cultures</td>
</tr>
<tr>
<td>Microbial Viability During Umbilical Cord Production and Storage</td>
</tr>
<tr>
<td>Bag RFP Project</td>
</tr>
<tr>
<td>Modeling Blood Product Inventory in Support of Atlantic Facilities Consolidation</td>
</tr>
<tr>
<td>Development of Non-Destructive Quality Control Processes</td>
</tr>
<tr>
<td>Evaluation of Skin Disinfection Kits</td>
</tr>
<tr>
<td>Residual Storage Plasma in Red Blood Cell Concentrates and the Association with Post-Storage Hemolysis</td>
</tr>
<tr>
<td>Study to Model the Composition of the One Match Registry</td>
</tr>
<tr>
<td>Pentaspan Replacement for Processing of Umbilical Cord and Autologous Hematopoietic Stem Cells</td>
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</tbody>
</table>

### Development in Collaboration with External Agencies

<table>
<thead>
<tr>
<th>Project</th>
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<tbody>
<tr>
<td>Evaluation of Bacterial Detection in Buffy Coat Platelet Concentrates by the pH SAFE System</td>
</tr>
<tr>
<td>Evaluation of Bacterial Detection in Buffy Coat Platelet Concentrates by the BacTx Rapid Assay System</td>
</tr>
<tr>
<td>Co-Infusion of Dextrose Solutions and Packed Red Blood Cells</td>
</tr>
<tr>
<td>Pathogen Reduction Technologies (Mirasol)</td>
</tr>
<tr>
<td>Donor-Product-Recipient Database Development with McMaster University and Ottawa Hospital Research Institute</td>
</tr>
<tr>
<td>In Vitro Quality of Red Blood Cells Stored in DEHP-free Pediatric Storage Bags Produced by Fresnius Kabi</td>
</tr>
<tr>
<td>TerumoBCT Cationization Project</td>
</tr>
<tr>
<td>Evaluating the Efficacy of Skin Disinfectants when Combined with Natural Oils</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Project</th>
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</thead>
<tbody>
<tr>
<td>Evaluation of Bacterial Standards. International Project by the International Society of Blood Transfusion and the World Health Organization</td>
</tr>
<tr>
<td>Irradiation of Red Cell Concentrates (a Biomedical Excellence in Safer Transfusion Study)</td>
</tr>
<tr>
<td>Evaluate the Correlation between in Vivo Red Cell Concentrate Survival and in Vitro Quality Parameters</td>
</tr>
<tr>
<td>International Comparison of Red Cell Concentrate Manufacturing Processes</td>
</tr>
<tr>
<td>Study to Detect Bacterial Contamination in Platelets in Uganda</td>
</tr>
</tbody>
</table>
# National Training Program

## James Kreppner Fellowship in Blood System Studies

A Framework for Thinking Through Different Concepts of Death in Organ Donation and Transplantation

## CBS/CIHR Partnership Postdoctoral Fellowship Program

A Novel Cell Surface Engineering Method for Universal Red Blood Donor Cells via Combination of Enzymatic Cleavage and Polymer Grafting

## Postdoctoral Fellowship Program

Dengue Virus Persistence in Blood Products and Hemostatic Effects on Infection

Mechanism of Action of Anti-D-Like Antibodies in the Prevention of Immune Responses to Allogeneic RBC

Identification of a Two-Step Mechanism Responsible for Antibody-Mediated Transfusion Related Acute Lung Injury (TRALI)

**CD8+CD25+ Regulatory T Cells: Unveiling New Mechanisms and Treatment of ITP**

Pathogenesis of Fetal and Neonatal Alloimmune Thrombocytopenia and Mechanisms of IVIG Therapy

Study of the Apoptosis Mechanism in Blood Processing and Platelet Storage in Order to Improve Stored Platelet Quality After Pathogen Inactivation Treatment

## Graduate Fellowship Program

Towards the Impact of Protein Synthesis in Human Platelets to Transfusion Medicine

Studies on the Development of Bioincompatible Antimicrobial Platelet Storage Devices

The Mechanism of IVIG Involves Induction of IL-10

Effect of Polymer Size and Species on Immunocamouflage and Antigenicity

The in Vivo Effects of Liposome Treatment on Minimizing Membrane Injury in Rat Red Blood Cells (RBCs) During Hypothermic Storage

Identification of Protein Biomarkers for Red Cell Quality

**MRI Guided Focused Ultrasound Facilitated IVIG Immunotherapy as a Therapeutic Approach for Alzheimer’s Disease**

Application of Microfluidic Technology to Blood Group Genotyping for Non-Invasive Prenatal Diagnosis of Fetal RhD Status

Relationship of Warm Autoimmune Hemolytic Anemia to Normal Red Cell Senescence

Ice Recrystallization Inhibitors (IRIs) as Cryoprotectants for Hematopoietic Stem Cells (HSCs)

Organ Specific Macromolecular Iron Chelators: Towards Effective Prevention of Transfusional Iron Overload

**Characterization of the Role of MS12 in Human Hematopoietic Stem Cell Self-Renewal**

Role of Skin Disinfection and Buffy Coat Platelet Production on Residual Bacterial Contamination in Platelet Concentrates and Cord Blood Stem Cells

Novel Mechanisms of Plasma Fibronectin in Hemostasis, Cryoprecipitate Therapy, and Platelet Storage: Potential Applications in Transfusion Medicine

**Mechanism of Transplacental Transport of IgGs, and IVIG and Anti-FcRn Therapies in the Treatment of Fetal and Neonatal Alloimmune Thrombocytopenia**

**Study of the Role of Platelet MicroRNAs**

Note: Projects that are bolded and italicized are those for which funding was initiated in fiscal year 2013/14.

## Transfusion Medicine Research Programs in Canadian Academic Institutions (Program Support Award)

MacMaster Transfusion Research Program

University of Ottawa Centre for Transfusion Research

Centre for Blood Research Infrastructure Support for Transfusion Research
Appendix II: Publications

Summary of peer-reviewed and non-peer-reviewed publications from fiscal year 2013/14

<table>
<thead>
<tr>
<th>Publication Type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peer-Reviewed Publications</td>
<td>223</td>
</tr>
<tr>
<td>Journal Articles</td>
<td>82</td>
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<tr>
<td>Review Articles</td>
<td>14</td>
</tr>
<tr>
<td>Clinical Guidelines</td>
<td>1</td>
</tr>
<tr>
<td>Comments/Letters</td>
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<tr>
<td>Books/Book Sections</td>
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<tr>
<td>Published Abstracts</td>
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<tr>
<td>Issued Patents</td>
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<tr>
<td>CBS Circular of Information</td>
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<tr>
<td>Non-Peer-Reviewed Publications</td>
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<tr>
<td>CBS Website Publications</td>
<td>14</td>
</tr>
<tr>
<td>Technical Reports</td>
<td>41</td>
</tr>
<tr>
<td>Theses</td>
<td>6</td>
</tr>
</tbody>
</table>

Summary of h-index factor analysis

Notes: i) H-Index factors measured using GoogleScholar on April 15 2014. ii) Mean H-index calculated using H-Index factors from the 16 senior staff researchers. 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.


**Publications’ Details**

**Author Legend:** Bold – Centre for Innovation Scientists and Senior Staff; Directors of Transfusion Medicine Research Programs; Underlined – Non-Canadian Blood Services Researchers funded in part by Canadian Blood Services; Canadian Blood Services Medical Directors.

**Journal Articles**


**Review Articles**


**Clinical Guidelines**


**Comments/Letters**

Books/Book Sections

Published Abstracts


137. Branch DR. Leontyev D. Cytokine Profiles in Mouse Models of Experimental Immune Thrombocytopenia Reveal a Lack of Inflammation and Differences in Response to IVlg Depending on the Mouse Strain. 9th International Congress on Autoimmunity Website. 2014.


165. Lane DJ. Hemolytic Disease of the Newborn Due to Antidiego(B) - Review of Four Cases from One Institution. Vox Sang. 2013;105(S1):248-249.


200. Simon AY, Sutherland MR, **Pryzdial EL**. Direct Dengue Virus-Platelet Binding: Replication of the Positive-Strand Ribonucleic Acid (RNA) Viral Genome. *Transfusion.* 2013;53(S2):26A.


Issued Patents


CBS Circular of Information


CBS Website Publications


**Technical Reports**


275. **Sheffield W.** The Testing of Frozen Cryoprecipitate Thawed and Stored at Ambient Temperature for up to 24 Hours. *Internal report submitted to Canadian Blood Services, Craig Jenkins, Director, Quality Monitoring Program, Research & Development 2013.*


**Theses**

280. Li J. Anti-GP Ibα Mediated Desialylation and Activation: A Novel Fc-Independent Platelet Clearance Mechanism and Potential Therapeutic and Diagnostic Target in ITP. Department of Laboratory Medicine and Pathology. MSc in Medical Sciences. Supervisor: Ni H. University of Toronto; 2014.


282. Scott BM. Applying Phage Display to Screen a Library of Alpha-1 Proteinase Inhibitor Mutants for Improved Thrombin Binding Activity. MSc in Medical Sciences. Supervisor: Sheffield W. McMaster University; 2013.


# Appendix III: Health Canada Financial Contribution

## Summary of Expenditures – April 1, 2013 to March 31, 2014

### Schedule 1: Overview

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating Funds (Schedule 2)</td>
<td>1,280,670</td>
</tr>
<tr>
<td>Funding Programs (Schedule 3)</td>
<td>4,236,932</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$ 5,517,602</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>486,739</td>
</tr>
<tr>
<td>NetCAD Operations</td>
<td>418,848</td>
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<tr>
<td>Intellectual Property Protection and Other Legal Activities</td>
<td>304,531</td>
</tr>
<tr>
<td>Capital Purchases</td>
<td>70,552</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>$ 1,280,670</strong></td>
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</tbody>
</table>

### Schedule 3: Funding Programs

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
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</thead>
<tbody>
<tr>
<td>CBS/CIHR Partnership Operating Grants</td>
<td>2,165,712</td>
</tr>
<tr>
<td>CBS/CIHR New Investigator and Fellowship Programs</td>
<td>165,000</td>
</tr>
<tr>
<td>CBS Intramural Operating Grants</td>
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</tr>
<tr>
<td>Small Projects Funding</td>
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<tr>
<td>Graduate Fellowships</td>
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</tr>
<tr>
<td>Postdoctoral Fellowships</td>
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<tr>
<td>Transfusion Medicine Research Program</td>
<td>635,915</td>
</tr>
<tr>
<td>Additional Funding for Research Projects</td>
<td>148,773</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$ 4,236,932</strong></td>
</tr>
</tbody>
</table>