2017 Report Card on Canada's Blood System

Marking the 20th Anniversary of the Final Report of the Commission of Inquiry on the Blood System in Canada

Prepared by the Blood Safety and Supply Committee of the

Canadian Hemophilia Society
Help Stop the Bleeding

November 2017

November 26, 2017 marks the 20th anniversary of the final report of the Commission of Inquiry on the Blood System in Canada, commonly known as the Krever Commission. The Commission was set up in 1993, following Canada's worst public health tragedy in which 1200 people were infected with HIV and many thousands with hepatitis C through infected blood and blood products, transfused in the 1970s and 1980s.

This Report Card constitutes the sixth time in the last 20 years that the Canadian Hemophilia Society has reported to Canadians on the state of the country's blood system. Previous reports can be found at: **www.hemophilia.ca/en/safe--secure-blood-supply/report-cards-on-canada-s-blood-system**.

This report was prepared by the Canadian Hemophilia Society Blood Safety and Supply Committee. The CHS would like to thank Canadian Blood Services, Héma-Québec and the patient organizations of the Network of Rare Blood Disorder Organizations for their collaboration and input.

The Krever Commission has had a profound impact on Canada's blood system; several key recommendations remain to be implemented.

It is widely accepted that the Krever Commission has had a profound impact on the blood system in Canada and beyond our borders. Justice Krever's findings are still frequently quoted in publications and at conferences around the world. The large majority of his 50 recommendations have been acted upon. Several key recommendations, however, remain unimplemented.

1. **Recommendation 2b** states: *Donors of blood and plasma should not be paid for their donations, except in rare circumstances*.

   Recommendation 2c states: *Whole blood, plasma and platelets should be collected in sufficient quantities in Canada to meet domestic needs for blood components and blood products*.

   While Canada's blood suppliers, Canadian Blood Services and Héma-Québec, have been extremely successful in fulfilling the needs for fresh components (red cells, platelets and plasma for transfusion) from Canadian donors, the rapidly expanding use of plasma-derived products, most importantly immune globulins, has made self-sufficiency an unattainable, and even undesirable, goal. (See "Plasma protein products" below.)

2. **Recommendation 3** states: *It is recommended that Canada have a national system for the collection and delivery of blood components and blood products*.

   Following the withdrawal of the Canadian Red Cross as the national supplier in 1999, two blood operators were established: Héma-Québec for the Province of Québec, and Canadian Blood Services (CBS), for the remaining nine Provinces and three Territories. They have both proven to be extremely effective in serving their populations, and work collaboratively. A single national service, as recommended, has not been necessary.

3. **Recommendation 15** states: *It is recommended that the national blood service be funded by payments from hospitals for the blood components and blood products supplied to them by the blood service*.

   The goal of this recommendation was to put blood components on an equal footing with alternative therapies or technologies (blood recuperation devices during surgery, red cell or plasma exchange equipment, non-blood pharmaceutical products …). Because all blood components are paid through provincial budgets and no cost is borne by individual hospitals, hospitals may in some cases choose blood components over alternative therapies or technologies, even when the latter are preferable from a health perspective and cheaper for the overall health system. Implementation of

Recommendation 15 could lead to less use of blood components, more use of alternatives, overall cost savings and better outcomes for patients.

In the case of blood products for rare diseases, for example, primary immune deficiency, hereditary angioedema and inherited bleeding disorders, where care is delivered by a very small number of specialized centres (as few as one per province), provincial reimbursement is the ideal model and should be retained.

4. **Recommendation 24** states: *It is recommended that an amount equal to 10 percent of the annual operating budget be allocated to research and development*.

   In 2016-17, Héma-Québec invested $8 million in R&D, or 5% of its $150 million in expenses for fresh blood components. CBS invested $13 million, or just over 4% of its $300 million budget for the fresh components it manufactures. Federal/Provincial and Territorial governments are falling short of the target of 10 percent in research and development.

5. **Recommendation 33** states: *It is recommended that the federal Minister of Health appoint an advisory committee to assist the Bureau of Biologics and Radiopharmaceuticals in its assessment and management of risk.*

   The National Blood Safety Council was created by Health Canada in the wake of the Krever Commission but ceased to be active in 2003. Health Canada's secretive Expert Advisory Committee on Blood Regulation quietly ceased to operate in 2015. It is concerning that, while new risks to blood safety arise every year, Health Canada appears to be becoming complacent.

Canada's blood system continues to be extremely safe.

Fresh blood components

The combination of rigourous donor selection and testing of each donation continues to result in a very low risk of infection in fresh blood components.

Estimates for 2017 indicate that the risk regarding the historically most serious blood-borne infections in Canada are:

- one in 21.4 million donations for HIV
- one in 12.6 million donations for hepatitis C
- one in 7.5 million donations for hepatitis B

In practice, none of these viruses has been transmitted by fresh blood components in recent years.

The most recent challenge to safety was the Zika virus epidemic in South and Central America and the Caribbean in winter 2016. Rapid implementation by both CBS and Héma-Québec of a 21-day waiting period for donors who had visited endemic areas was successful in avoiding any transmission by blood. This temporary deferral has been maintained to protect recipients against other tropical mosquito-transmitted infectious diseases such as dengue fever, chikungunya and yellow fever.

Two other pathogens have emerged in recent years. Babesia microti, a tick-borne parasite, is affecting people in New England. A recent joint study by CBS and Héma-Québec showed no positive donations out of 14,000 people tested. Hepatitis E, transmitted by water and food, is prevalent in parts of Europe. A large study in Canada found that, while six percent of donors had been exposed to hepatitis E in the environment, very few were viremic, and the risk of transmission to recipients is extremely low.

Both CBS and Héma-Québec have adopted an additional strategy to protect platelet recipients from bacterial infection, currently the most serious transfusion risk. Platelets are tested at 36 or 48 hours after donation, rather than 24, increasing the ability to detect bacteria. Shelf life was safely extended from five to seven days so as not to increase outdating.

Both blood operators introduced an electronic self-administered health history before donation to decrease the risk of errors.

CBS and Héma-Québec continue research into pathogen inactivation technologies for fresh blood components. It is hoped that this technology will allow the operators to move from reactive strategies, where deferrals or tests are introduced for each new threat, to a proactive strategy that is able to intercept a wide range of pathogens, including those not yet identified. A 2007 CBS/Héma-Québec Consensus Conference recommended that such technology be introduced in Canada as soon as it became available. It remains to be seen if the Provinces and Territories, who fund CBS and Héma-Québec, will pay to introduce this paradigm-shifting technology.

Plasma protein products and their alternatives

Plasma-derived products to treat diseases such as primary immune deficiency, hereditary angioedema and inherited bleeding disorders continue to be extremely safe from pathogen contamination. This has been made possible by the combined strategies of donor selection, testing of each donation, testing of plasma pools and multiple methods of pathogen reduction (heat treatment, filtration and chemical inactivation). No case of HIV, hepatitis B or hepatitis C infection has been observed with products manufactured in this way since the late 1980s. This is true whether the products are manufactured from plasma donated by compensated or uncompensated donors.

Patient organizations consulted by the Canadian Hemophilia Society have expressed a high level of confidence in the safety of both fresh blood components and plasma protein therapies.

MARKS FOR SAFETY	
Canadian Blood Services	**A**
Héma-Québec	**A**

Canadians continue to have access to a secure supply of blood components and plasma-derived products and their alternatives … with some exceptions … and some questions about the future.

Fresh blood components

Blood operators around the developed world have seen a drop in the demand for fresh blood components, for reasons that are not perfectly understood. Over the last five years, Héma-Québec reports decreases of 13%, 5% and 32% in the delivery of red cells, platelets and plasma for transfusion respectively.

Both CBS and Héma-Québec have been very successful in filling hospital orders for red blood cells, platelets and plasma. In 2016-17, CBS reports that it filled orders for 99.4% of red cells, 98.3% of platelets and 99.6% of plasma within one day. The rare delays were not associated with compromises in patient care.

On the other hand, demand for phenotyped blood, needed notably for the treatment of sickle cell disease, more common in the Black community, has doubled. Both CBS and Héma-Québec have worked closely with the Black community and the sickle cell patient associations to recruit donors whose phenotypes more closely match the needs of these recipients.

MARKS FOR SUPPLY OF FRESH BLOOD COMPONENTS	
Canadian Blood Services	**A**
Héma-Québec	**A**

Plasma protein products

The cost of plasma protein products and their recombinant alternatives represents 60% of the budgets of CBS and Héma-Québec. Generally, CBS and Héma-Québec provide a sufficient supply of safe, efficacious products to patients with diseases such as primary immune deficiency, hereditary angioedema and inherited bleeding disorders, including hemophilia A and B. Importantly, these expensive therapies are available at no cost to the end user through the CBS and Héma-Québec distribution systems. This “mini-pharmacare” plan merits being copied for all essential drugs.

The demand for some of these 30 plasma protein products is increasing rapidly. For example, deliveries by Héma-Québec of immune globulins, prescribed to treat immune deficiencies and neurological conditions, have increased more than six percent per year for the past four years.

Plasma protein products are manufactured by American and European pharmaceutical companies from recovered plasma (the excess plasma after red cell donation) and from source plasma, collected through plasmapheresis donations.

In 2016-17, CBS collected only 15 percent of the plasma needed for the manufacture of immune globulins; Héma-Québec only 21 percent. The balance of the plasma is supplied by compensated donors in the U.S. CBS has proposed to the Provinces and Territories a business plan to increase the volume of plasma collected from non-compensated Canadian donors from 180,000 litres per year to 600,000 litres per year (866,000 donations), which would meet 50 percent of the demand for plasma for immune globulin production. In recent years, Héma-Québec has opened three PLASMAVIE centres to exclusively collect plasma. Expansion of this program is hoped to increase plasma volume from 100,000 litres currently to 150,000 litres by 2020, which would result in a level of plasma sufficiency of 30 percent.

Both blood operators rely on compensated donations from U.S. donors for the balance. Meanwhile, legislation in Quebec, Ontario and Alberta prohibits compensation for plasma donation to private pharmaceutical companies.

The Canadian Hemophilia Society has been critical of CBS' and Héma-Québec's record in plasma collection in every Report Card since 1999. While we certainly hope that the current plans to raise collection levels are successful, it is clear that a system based entirely on non-compensated donation will leave Canada over-reliant on U.S. plasma donors. A fresh approach is needed.

Following the direction of the Provinces and Territories, competitive tender systems have been put in place by both CBS and Héma-Québec in recent years where comparable products in the same therapeutic category are available in the Canadian market. They have been very successful in reducing per unit prices, which is of course desirable. For some products, however, for example extended half-life factor VIII and IX for the treatment of hemophilia, this has come at the cost of limiting access to the most innovative and efficacious products. This raises a number of questions. How far can we go in procuring the least expensive product even if they are not of the highest value for patients? What impact will this "race to the bottom" have on companies' willingness to innovate and bring these products to the Canadian market? How can the procurement process evolve so that value for patients is not overwhelmed by desires for cost containment?

In addition, short-sighted financial considerations have prevented access to a number of blood-and plasma-derived therapies for certain rare conditions. For example:

- The distribution of Solvent Detergent Plasma, a virally inactivated plasma product widely used in Europe to treat patients who need multiple plasma transfusions, is severely restricted across Canada, making access impossible in urgent situations such as thrombotic thrombocytopenic purpura (TTP).
- Normosang and Panhetin, red cell-derived products to treat porphyria, are not distributed via CBS, making access uneven and often impossible. The product is routinely available in Quebec through Héma-Québec.

- Alpha-1-antitrypsin, a plasma-derived product to treat alpha-1-antitrypsin deficiency which is licensed in Canada and recommended by expert physician groups, is not distributed by either CBS or Héma-Québec, again greatly complicating access.
- Importantly, the CHS and other patient associations have grave concerns about early signals that some Provinces are considering moving plasma derivatives and their alternatives from the CBS national blood budget to provincial drug formularies. This would have disastrous consequences for patients with serious, rare and chronic disorders. Equitable and affordable access to life-saving therapies could be jeopardized.

MARKS FOR SUPPLY OF PLASMA PROTEIN PRODUCTS

Canadian Blood Services	**C**
Héma-Québec	**C**
Provinces and Territories	**D**

CBS and Héma-Québec have made great efforts to be accountable and transparent … but the wider health system is more opaque.

Both CBS and Héma-Québec have implemented the Krever Commission's recommendations with regard to accountability and transparency. The CBS National and Regional Liaison Committees and Héma-Québec's Recipient Representatives Advisory Committee provide recipients of blood and blood products an opportunity to learn about developments in the blood system and provide input. True representatives of recipients sit on the Board of Directors of Héma-Québec. CBS holds open board meetings twice a year at which the public can raise issues and voice concerns.

An example of excellent public engagement is CBS' interaction with community, student and patient groups over the controversial policy of donor deferral of men who have had sex with men. Since 2012, that deferral has been reduced from lifelong to one year. A research agenda has been implemented by CBS and Héma-Québec, with funding from the federal government, to explore alternative donor selection strategies that could reduce unnecessary discrimination while maintaining recipient safety.

Both blood operators include representatives of patient organizations in providing advice on the procurement of plasma protein products and their recombinant alternatives during competitive tenders. This ensures greater understanding of patient needs and product value, on one side, and appreciation for system challenges, on the other. Some of the recent CBS tenders for plasma derivatives, however, have taken place with little or no expert patient or physician involvement. This is not conducive to the best results.

Despite these excellent initiatives, it can be very difficult, if not impossible, for a patient organization to navigate the different institutions—blood operators, Provincial/Territorial payers, health technology assessment (HTA) bodies and medical/scientific advisory groups—in an effort to gain access to an existing blood product or present the patient perspective when a new therapy has the potential to be introduced.

MARKS FOR LEVEL OF ACCOUNTABILITY AND TRANSPARENCY	
Canadian Blood Services	**B**
Héma-Québec	**A**
Provincial and Territorial payers and HTA bodies	**D**