



Canadian Hemophilia Society
Help Stop the Bleeding
Société canadienne de l'hémophilie
Arrêtons l'hémorragie

Submission to the Expert Panel on Immune Globulin Product Supply and Related Impacts in Canada

Submission of the Canadian Hemophilia Society, 301-666 Sherbrooke St. West, Montreal, Quebec, H3A 1E7. Contact person: David Page, national executive director, Canadian Hemophilia Society, dpage@hemophilia.ca, 1-418-884-2792.

The Canadian Hemophilia Society (CHS) is a patient organization representing people with inherited bleeding disorders, namely: hemophilia A and B, von Willebrand disease (VWD), rare factor deficiencies and inherited platelet disorders. While most patients with hemophilia A and B are now treated with recombinant clotting factors, many with other bleeding disorders continue to be treated with plasma-derived medicinal products.

The number of patients with inherited bleeding disorders areⁱ: hemophilia A and B: 3,822; von Willebrand disease: 4,180; rare factor deficiencies (I, II, V, V&VIII, VII, X, XI, XIII); and other hereditary bleeding disorders including platelet disorders: 1,899.

Immune globulin products are not used to treat inherited bleeding disorders. Recombinant therapies are available for hemophilia A and B, and factor XIII deficiency, but are not available for VWD, most rare factor deficiencies or platelet disorders. Recombinant factor VIII is the standard treatment for hemophilia A and represents more than 90% of the products infused. Plasma-derived factor VIII containing von Willebrand factor is, however, used for specific indications, notably immune tolerance induction to treat inhibitors to factor VIII, a serious treatment complication. In hemophilia B, recombinant factor IX is used in 90% of cases; plasma-derived factor IX in the balance. Serious bleeding in VWD is treated with plasma-derived von Willebrand factor, less serious bleeding with desmopressin. Rare factor deficiencies are treated with plasma-derived factor concentrates and/or fresh frozen plasma. Platelet function disorders are treated with a number of therapies including platelets.

The key factors in clinician/patient choice in clotting factor concentrates are efficacy and the risk of developing an inhibitor (neutralizing antibody) to the infused treatment, not the origin of the plasma used in manufacturing.

Of the 11 plasma-derived clotting factor concentrates used in Canada, only two (Humate P[®] for VWD and Riastap[®] for fibrinogen deficiency) are manufactured from plasma from unpaid donors collected by Canadian Blood Services and Héma-Québec. The remaining nine clotting factors are made by a number of multi-national pharmaceutical companies using plasma from paid U.S. donors.ⁱⁱ Because many of these companies are unlikely to have fractionation contracts with CBS and Héma-Québec, collecting more plasma from Canadian donors is unlikely to change this situation significantly.

The cost of the products described above, whether recombinant or plasma-derived, is reimbursed through the plasma protein budgets managed by Canadian Blood Services and Héma-Québec and made available to patients at no direct cost.

The CHS closely follows clinical trials of innovative therapies for inherited bleeding disorders and regularly updates this information in a section of its website called *Products in the Pipeline*.ⁱⁱⁱ

The CHS Policy on Paid Plasma Donations was approved by the CHS Blood Safety and Supply Committee on March 11, 2013, and adopted by the CHS Board of Directors on May 26, 2013. It is an addition to the complete CHS Policy on Blood, Blood Products and their Alternatives, adopted in 2003 and reviewed annually.^{iv} The Policy on Paid Plasma Donations states:

- Given that 80% of the Canadian and world supplies of plasma-derived products are manufactured from the plasma of paid donors, mainly from the U.S.;
- Given that Canadian Blood Services and Héma-Québec are increasingly dependent on U.S. source plasma from paid donors for the supply of plasma-derived products and that they have no plans to become, at best, more than 30% sufficient in plasma for immunoglobulin (Ig) supply from Canadian non-paid donors;
- Given the worldwide shortage of plasma-derived products;
- Given that many plasma-derived products used in the treatment of bleeding disorders (von Willebrand disease, rare clotting factors, inhibitors) are already manufactured from U.S. source plasma from paid donors;
- Given that plasma-derived products are life-saving therapies for a number of other rare blood diseases that affect thousands of Canadians;
- Given that, with the exception of factors VIII, IX and XIII, there are no recombinant alternatives for these products;
- Given that effective donor selection and testing technologies are applied to both paid and non-paid donations;
- Given that, in addition, highly effective viral elimination/reduction steps are applied to plasma-derived products;
- Given that plasma-derived products from paid donors have not been shown to transmit HIV, HBV or HCV in more than 20 years;
- Given that plasma collection sites in Canada where donors are paid have operated under Health Canada and U.S. FDA regulation and oversight for many years;

The Canadian Hemophilia Society takes the position that ...

1. Plasma-derived products in adequate supply from both paid and non-paid sources are essential to the health of thousands of Canadians and, indeed, hundreds of thousands of people around the world;
2. Plasma-derived products manufactured following Standard Operating Procedures and Good Manufacturing Practices are of equally high quality from both paid and non-paid donors;
3. The collection of source plasma from paid donors in a properly regulated environment is not a patient safety issue;
4. CBS and Héma-Québec should make all reasonable efforts to increase the quantity of Canadian plasma for fractionation from non-paid donors and the number and quantity of plasma-derived products made from this plasma;

5. In the absence of any realistic strategy to significantly increase the Canadian contribution to the world supply from non-paid donations, and when Canada relies almost entirely on paid donors from the U.S. for life-saving plasma-derived products, it is not defensible to reject paid donor practices on ethical grounds;
6. Any endeavour to collect plasma for plasma-derived products from paid donors in Canada must respect the highest regulatory standards. Health Canada should make these standards known to Canadians and report to Canadians on a regular basis the results of their collection site inspections, including transfusion-transmissible infection rates among donors. CHS will monitor these reports and endeavour to hold the regulator to account;
7. Any endeavour to collect plasma for plasma-derived products from paid donors must not affect the ability of Canadian Blood Services or Héma-Québec to collect whole blood, platelets and plasma from non-paid donors to meet the needs for fresh blood components. Canadian Blood Services and Héma-Québec should report to Canadians on a regular basis the impact of paid plasma collections on their ability to meet the needs of Canadian patients;
8. The health of donors should not be compromised by their donations, paid or non-paid. Donors should not be exploited by any individual or organization. Measures and initiatives taken to encourage blood and plasma donations should not overwhelm the capacity of the donor to make an informed decision about whether to donate;
9. Patients whose continued health is dependent on the use of blood components or plasma-derived products have a right, through their representative organizations, to be consulted on any issue which may have an impact on the safety, efficacy or supply of the treatment they receive. Health authorities should ensure that robust mechanisms are in place to ensure that this happens.

More information is available from the CHS Policy on Paid Plasma Donations, Background Document.^v The Canadian Hemophilia Society is a signatory to *The Dublin Consensus Statements* of 2011 and 2012.^{vi vii}

Conclusion

The CHS recognizes that the pain and suffering caused by the tainted blood tragedy of the 1970s and 1980s are not forgotten. The issue of payment for plasma donation remains a controversial and emotional one; however, the CHS stands by its evidence-based positions. Plasma-derived medicinal products (PDMPs) are of equivalent safety, whether manufactured from paid or unpaid donations. In a perfect world, all donations of plasma would be unpaid; realistically, however, payment for plasma donation is essential to the Canadian and world supply of these medicines. It is no more or less ethical to pay Canadian donors than it is to pay American donors. Indeed, what would be unethical is any action that would deny an adequate supply of essential medicines to patients. Evidence from the United States has shown that two systems—one to collect fresh blood components from unpaid donors and a second to collect source plasma for subsequent manufacturing into PDMPs—can co-exist. They should work cooperatively. Public-private collaboration between reputable companies in the plasma collection/fractionation field and the two Canadian Blood Establishments, CBS and Héma-Québec, should be explored and expanded.

ⁱ World Federation of Hemophilia Global Survey 2015. www1.wfh.org/publications/files/pdf-1669.pdf.

ⁱⁱ Clotting Factor Concentrates. Website of the Canadian Hemophilia Society. www.hemophilia.ca/en/bleeding-disorders/clotting-factor-concentrates.

ⁱⁱⁱ Products in the Pipeline. Website of the Canadian Hemophilia Society. www.hemophilia.ca/en/safe--secure-blood-supply/products-in-the-pipeline.

^{iv} CHS Policy on Blood, Blood Products and their Alternatives. www.hemophilia.ca/en/about-the-chs/public-affairs/chs-policy-on-blood--blood-products-and-their-alternatives.

^v CHS Policy on paid plasma Donations, Background document. www.hemophilia.ca/files/Background%20document%20for%20policy%20on%20paid%20plasma%20donations%2029-05-2013.pdf.

^{vi} The Dublin Consensus Statement 2011. *Vox Sang.* 2012 Feb;102(2):140-3. doi: 10.1111/j.1423-0410.2011.01528.x. Epub 2011 Aug 1.

^{vii} The Dublin Consensus Statement 2012. *Blood Transfus.* 2013 Oct; 11(4): 623–626. doi: 10.2450/2013.0044-13.