November 27, 2017

Ms. Judy Hoff, Chair Provincial/Territorial Blood Liaison Committee
Saskatchewan Disease Control Laboratory (formerly Provincial Laboratory)
5 Research Drive
Regina, SK Canada S4S 0A4
Fax: (306) 787-1525
Email: judy.hoff@health.gov.sk.ca

Dear Ms. Hoff:

The Association of Hemophilia Clinic Directors of Canada (AHCDC) would like to provide you with comments on the results of the recent Canadian Blood Services (CBS) Request for Proposal (RFP) for Plasma Protein Products. As outlined in the Customer Letter (2017-42) representatives of our Association participated in the advisory committee struck by Canadian Blood Services to review the submissions. Extensive discussion about these results has occurred within our Association and amongst various stakeholders since the announcement was made on October 31, 2017. We have already provided feedback directly to CBS, who are also copied on this letter.

Our members highly value the provision of an effective, secure and safe supply of plasma derived and recombinant factor replacement products funded through our Provincial health budgets. We agree with published evidence that tender or procurement processes that include involvement of patients, physicians and nurses greatly improve outcomes and contribute to cost reductions (O'Mahoney et al. Haemophilia (2015), 21, 436–443).

The continued provision of the category of extended half-life (EHL) products is valued by patients and clinicians because of the potential of an EHL product to improve health outcomes in selected patients and contribute towards value based health care. However, we do not consider the transition from an EHL product based on Fc-fusion to one based on PEGylating to be a simple switch between biosimilar products. We have three specific areas of concern about how the results of this RFP will negatively impact patients and hemophilia treatment centers.

First, in an internationally unprecedented type of switch, Canadian hemophilia patients younger than 12 years of age who are currently treated with Fc-fusion EHL products (Eloctate or Alprolix) will be left with no EHL alternatives approved for use in their age range. Neither PEGylated nor EHL product has been approved for this age group and this situation will likely continue until more safety data of PEGylating exists, which may take several years. As a result, patients, parents and hemophilia treaters will be facing the difficult choice of using PEGylated products off-label or switching back to a standard half-life (SHL) product. Since the current NAC EHL criteria allow switching to EHL for the intent of improving quality of life, decreasing bleeding rates or increasing compliance, a switch to SHL would potentially return those children to a product previously associated with inferior outcomes. **We therefore request that patients under 12 years of age continue to have full access to both FVIII-Fc and FIX-Fc EHL products for the duration of this agreement and until the PEGylated products are approved for prophylaxis in that age group.**

Second, measuring accurate FIX levels for patients on PEGylated FIX will be a major challenge for all coagulation laboratories in Canada. Accurate factor assays are critical for evaluating pharmacokinetics, and are the foundation of assessing efficacy of treatment and providing

appropriate dosing regimens and modification for the specific clinical situation. Current FIX assays in clinical use are based on a clotting time assay, with a variety of instruments employed throughout Canadian coagulation laboratories. PEGylated FIX can only be accurately measured with an alternate chromogenic assay. This assay cost is approximately 3-fold higher than the current FIX assay, and requires appropriate instrumentation systems and additional technical time in each laboratory for initiation and validation. For coagulation laboratories associated with hemophilia treatment centers, funding for the FIX chromogenic assay will need to be secured, and we are therefore unlikely to have an assay in place for clinicians by April 1, 2018. Fortunately, the PEGylated FVIII product does not share this same laboratory challenge. **We request that a mechanism to compensate coagulation laboratories for the additional cost of implementing and performing these assays for FIX be put in place.**

Lastly, four Canadian research studies specifically evaluating patient outcomes on Fc-fusion EHL will be adversely affected by the lack of EHL product availability, and represent a lost opportunity to fully understand the impact of introduction of the EHL category on health outcomes in Canada. ***We request that patients enrolled on these research studies continue to have access to the Fc product for the duration of the ongoing studies and that important outcomes from these studies be considered in future RFP processes for the EHL category.***

Maintaining a safe, secure and effective supply of plasma-derived and recombinant factor replacement products for hemophilia patients in Canada is a fundamental goal for all stakeholders. As a community, we value the consultation that occurred with AHCDC during the RFP process. However, it is evident that the final decision by CBS was made with the belief that physicians and patients would continue to have product choices that would provide similar or better outcomes. As outlined, there are several clinical and laboratory dilemmas that our patients and treatment centers must now face because of this decision. It is our position that the effort to generate substantial cost savings has created a situation where some patients, especially in the pediatric age group, may be effectively deprived of access to EHL products because of labeling criteria, safety concerns, and challenges with laboratory monitoring, leading to compromised outcomes.

We appreciate the opportunity to communicate with the Provinces and Territories from our perspective as an expert medical group, and welcome further dialogue around patient outcomes in the context of future EHL availability.

Sincerely,

Dr. Shannon Jackson
President, AHCDC

Dr. Jayson Stoffman
Chair, AHCDC Provincial Working Group

Cc: Dr. Graham Sher, Canadian Blood Services
Mr. David Page, Canadian Hemophilia Society
Mr. Peter Saunders, Canadian Blood Services

Association of Hemophilia Clinic Directors of Canada | 70 Bond Street, Basement, Toronto, ON M5B 1X3
Tel: 416-864-5042 Fax: 416-864-5251 | E-mail: ahcdc@smh.ca | www.ahcdc.ca