Delegate Overview: Australian Red Cross Lifeblood proposed changes to the deferral of donors in relation to sexual activity-based deferrals

Background and Context

The TGA received a submission in June 2020 from Australian Red Cross Lifeblood seeking a reduction in the donor deferral period for some high-risk sexual activity donors from 12 months to three months. This submission complements the Lifeblood submission from January 2020, where an identical reduction in donor deferral period was sought for whole blood donors only.

The previous Lifeblood submission for whole blood donors was approved in April 2020. The decision letter for that approval is in TRIM D20-359363.

The scope of this current (June 2020) Lifeblood submission includes donors of plasma for fractionation and donors for plateletpheresis and plasmapheresis. Those donor groups were outside the scope of the previous (January 2020) Lifeblood submission.

The current Lifeblood submission to the TGA included prevalence data for transfusion-transmissible infections (TTI) relevant to sexually transmitted TTIs (HIV, HBV, HCV, HTLV and syphilis), a risk analysis including mathematical modelling for these TTIs; analysis of international practice; and the predicted impact on the donor base in Australia if the changes were made to the deferral period. The submission also contains information from CSL Behring indicating that changes to donor deferral criteria for Australian sourced plasma from Lifeblood do not have an impact on final product risk assessments on CSL Behring's plasma-derived medicinal products as the controls and procedures ensure the required level of safety for product and patients.

The Lifeblood submission suggested that the proposed changes would yield a minimal sufficiency gain for clinical blood components without affecting patient safety.

Scope of the proposal

The current Lifeblood submission proposes a change to the donor deferral period from 12 months to three months for whole blood and plasma donors reporting the following activities:

- for male donors: male-to-male sex
- for female donors: sex with a man who has ever had sex with a man
- for transgender donors: sexual contact with a male
- sex work
- sexual contact with a sex worker (male or female)
- overseas sexual contact with a resident of a HIV high prevalence country
- sexual contact with an injecting drug user (current or past)
- sexual contact with a partner known to be infected with a blood-borne virus (HIV, HBV, HCV or HTLV)

Donors currently receiving pre-exposure prophylaxis HIV prevention (PrEP) treatment are outside the scope of this submission, and the deferral period for those donors remains unchanged at 12 months post PrEP. Lifeblood has submitted a proposal for donors receiving PrEP treatment that will be the subject of a separate TGA approval process.

Lifeblood proposes that the deferral period for donors with new partners from HIV risk areas remains at 12 months as the deferral only applies for the first 12 months of an ongoing sexual relationship. This allows donors who are in an ongoing relationship with a person from a HIV risk area to regain eligibility to donate without the need for deferral for a set period after every sexual contact with their long-term partner. After 12 months the sexual partner is no longer defined as 'new' and the deferral will no longer apply.

The scope of any change in donor deferrals resulting from this submission is restricted to Lifeblood and does not apply to other sponsors/products.

Advisory Committee for Biologicals (ACB) considerations.

The submission from Lifeblood on proposed changes to the deferral of donors in relation to sexual activity –based deferrals was referred to ACB for advice on several occasions, most recently in February 2020. Advice from ACB is included in the April Delegate Overview in TRIM D20-329479

Questions previously raised by the ACB have been addressed and evidence provided by Lifeblood supported the requested change for whole blood donors.

Considerations

From the Lifeblood submission:

- The prevalence of transfusion transmissible infections (TTI) in first time blood donors is low but not zero.
- TTI-infected donors donating during the testing window period constitute the majority of the TTI residual risk. To minimise this risk the donor deferral period should adequately cover this window. The TTIs considered relevant to MSM include HIV, HCV, HBV, HTLV and syphilis. The window period for the current tests for these TTIs is longest for HTLV (51 days) and syphilis (serological window is ill defined but suggested to be ~30 days). The proposed deferral period of 90 days is approximately two times these window periods.
- Mathematical risk modelling focussed on HIV among MSM, given that this constitutes the largest risk for any TTI in any group subject to sexual activity based deferrals (prevalence of HIV in MSM is 56 times higher than the general population and the per contact risk is higher for anal than vaginal sex). Modelling was presented for four 'scenarios' where the major risk factors of the non-compliance rate and the HIV incidence rate of 'newly eligible' donors are varied. The most likely scenario (scenario 3 in the Lifeblood submission) assumes a HIV incidence midway between blood donors (low) and MSM attending STD clinics (high) and a non-compliance rate 5x that measured in a 2013 Australian compliance study of existing blood donors. A 'worst case' scenario (scenario 1 in the submission) included a non-compliance rate 10x that measure and a HIV incidence rate that is equal to the general incidence of HIV among Australian MSM.
- The estimated risk is considered against the 'tolerable risk' level in Lifeblood's risk tolerability framework. According to this framework the risk for HIV transmission per unit transfused should be below 1 in 5 million (as it is the TTI of highest concern based on societal, political and clinical concerns, with a tolerable risk of 1 in 1 million for other TTIs). It is noted that the UK's SaBTO uses a similar tolerability cut off of 1 in 1 million (UK SaBTO, Donor Selection Report (2017) Version 2, clause 1.6, page 4).
- Risk modelling by Lifeblood indicated that the proposed changes in the 'most likely' scenario would result in an increased risk for HIV from less than 1 in 37 million per unit transfused in 2017/18 to 1 in 20 million. In the 'worst case' scenario the estimate was 1 in 5 million. While the modelled risk increases, both estimates are below the 'tolerable risk' level in Lifeblood's risk tolerability framework.
- Lifeblood has calculated that for fresh frozen plasma that is sent for plasma fractionation, if the risk reduction attributed to CSLB pathogen reduction steps is

rounded down to 10^6 (a highly conservative estimate used in historical risk modelling), then the HIV residual risk for fractionated plasma is reduced by a factor of 10^6 or 1 million. The Lifeblood submission makes reference to CSLB internal data that indicates that, as of March 2017, the lowest validated virus reduction (VVR) claim for any CSLB plasma product was >=$10^{6.3}$ for PROTHROMBINEX-VF: a figure that has since improved to >=$10^{12.6}$.

- The Lifeblood submission provides confirmation from CSL Behring that the impact on pathogen safety and quality for plasma-derived medicinal products (PDMPs) in relation to proposed changes to donor selection and deferral criteria for Australian sourced plasma can be considered as negligible with regard to product and patient safety based on the following rationale:
  • Viral marker testing of plasma donations (performed by the plasma supplier) remains unchanged.
  • Plasma pool virus marker testing performed by CSL Behring of each manufacturing pool remains unchanged. Only plasma pools which are non-reactive as defined in the PMF, are released for further manufacturing.
  • Manufacturing processes of CSL Behring's PDMPs contain validated pathogen reduction steps that can efficiently remove a broad range of blood borne viruses and TSE agents. These pathogen reduction steps also minimize the risk for unknown or emerging blood borne viruses to be present in the final product for which plasma screening is not performed and remain unchanged, therefore ensuring adequate safety margins.
  • Furthermore, in accordance with the EMA PMF requirements, the epidemiological rates are monitored and provided annually in the PMF annual update.
- The UK NHS Blood Service introduced a similar three month deferral for high risk sexual behaviours in 2017 and preliminary data from them suggests no significant change in HIV incidence in blood donors since that change.
- The proposed changes are not expected to yield a significant sufficiency gain.

Conclusion:

The proposed change to a three-month donor deferral period for donors with sexual activity based risk factors is supported, based on the evidence provided in the Lifeblood submission and the advice received from the Advisory Committee on Biologicals including:

- the proposed donor deferral of three months is approximately two times the longest test window period for relevant TTIs (HTLV and syphilis) and considerably longer for other relevant TTIs (HIV, HCV, HBV)
- the results of mathematical modelling suggest the risk of HIV transmission remains acceptable, noting that HIV transmission constitutes the largest risk for any TTI in any group subject to sexual activity based deferrals and has the highest concern based on societal, political and clinical concerns
- changes to donor deferral criteria for Australian sourced plasma from Lifeblood do not have an impact on final product risk assessments for CSL Behring's plasma-derived medicinal products, as the controls and procedures ensure the required level of safety for product and patients
- the proposed donor deferral of three months is also approximately three times the incubation period of HAV infection prior to symptom onset and is acceptable

- experience from other jurisdictions such as the UK where similar deferrals have been implemented have not lead to significant changes in HIV incidence in blood donors.

Conditions should be applied to the decision to reflect the advice received from ACB including:

- Should new information become available in the future that indicates the risk of transmission of infectious diseases from donors has increased, Australian Red Cross Lifeblood must submit this information to the TGA and obtain approval to continue with this consent.
- Due to uncertainty regarding the impact of this change on the rate of non-compliance to donor selection questions for Australian donors, Lifeblood should assess the non-compliance rate of high-risk donors and monitor the return rate for donors and provide this information to the TGA for review within two years of the date of approval