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RE: Italian policy around the collection of plasma for manufacture

The Italian policy around the collection of plasma for manufacture is based on two fundamental imperatives:

1. The assurance of the security of supply.

In this context, it is noted that the global supply of plasma for manufacture is dominated by the contribution of the population of paid source (apheresis) plasma donors from the USA. This donor population is relatively small, and consists of ca 1.5 million donors (1) who, because of the high donation frequency, are able to contribute ca two thirds of the plasma available for fractionation to the fractionation industry (2).

The Italian system shares the concerns, expressed by various authorities, which can arise from this global dependence on a relatively small and concentrated population of donors. The Italian policy of national self-sufficiency is intended to counter the risk posed by this global situation, by generating, to the greatest extent possible, the products required by patients from the national blood and plasma supply. The

Italian system recognises that this strategic imperative (3) depends on the generation of plasma by plasmapheresis as this generates higher volumes than is possible from extracting plasma from whole blood donations, which are increasingly limited by the appropriate use of red blood cells for transfusion and PBM programmes. Hence the Italian system concurs with the current EDQM which establishes a maximum frequency of 33 donations yearly. The Italian system is confident of attaining its goals through collecting a maximum of 20 plasma donations yearly to a maximum volume of 12 Litres.

Collecting at levels greatly in excess of these Italian targets would result in concentrating the Italian plasma supply in fewer donors and would generate an excessive dependence on a relatively small population, similar to the current global dependence on the small population of the US source donor population. For this reason, Italy will focus her efforts on increasing the number of donors willing to donate plasma, to a level which will ensure the security and sustainability of supply without risking concentrating the supply in an excessively small donor population.

2. Safety for donors and patients.

The Italian transfusion service is part of the national health system and, in this instance, exists to serve patients and the donors who give their blood for the benefit of patients. Any factors which affect the wellbeing of these two groups is of fundamental interest and concern.

The frequency of plasmapheresis donation is known to influence a number of physiological parameters which are related to the health of donors. The most important of these is the amount of immunoglobulin (Ig) in the donor's plasma. Ig is a protein which is crucial in ensuring the body's capacity to fight infection. Ig purified from donated plasma is the main product of plasma fractionation and is administered to patients who suffer from a deficiency in this protein or who can profit of its immune-modulation properties.

Increased frequency of plasmapheresis decreases the concentration of Ig in donor plasma. This has two consequences:

a) This drop in Ig level is known to be too steep for some donors and they would suffer consequences if it happens. Hence, donors who are subjected to high frequency plasmapheresis need to be monitored strictly with clinical and laboratory tests, with consequent resource implications for the health care system. In addition, the long-term effect of highly intensive plasmapheresis is not known, as many of the intensively plasmapheresed donors of the US system do not stay in the system long enough for their health to be monitored, even if the cursory health examinations in the donors were to be sufficient to detect any problems¹.

Hence, the Italian system considers that the long-term effects of intensive plasmapheresis are not enough documented. The Italian system seeks long-term, repeat plasma donors, in order to generate a safe and sustainable supply, and will protect the health of these donors. In the context of the unknown effects of long-term intensive plasmapheresis, the Italian system considers that the policy towards donors needs to be governed by the established *Precautionary Principle* which underpins blood safety policy globally. The application of this principle requires a conservative approach and a restriction of plasmapheresis frequency to the currently applied rates while pursuing the extension of plasmapheresis donation to a wider number of repeat donors.

b) Another consequence of the depletion in donor Ig resulting from intensive plasmapheresis is its effect on the yield of Ig in the manufacture of IG products for therapeutic use. It is known that the yield is dependant, amongst other things, on the Ig level in the plasma and hence, plasma from pools derived from

¹ In the USA, unlike in Italy, it is not mandatory to retain a doctor to examine and advise donors who attend blood establishments.

intensively plasmapheresed donors results in a lower Ig yield. Increasing Italy's dependence on donors with low Ig would hence decrease Italy's ability to acquire self-sufficiency in Ig.

The Italian blood system is also concerned that increasing the frequency of donations may pose a risk to the safety of products derived from the plasma. The safety of blood is always under threat from infection by pathogenic agents, including viruses. Many of these agents, emerging from the natural environment through human intervention, enter the blood supply before their epidemiology is well understood and before testing and donor selection measures have been developed to exclude their presence. In these circumstances, donors infected with these agents may contribute to the pool of plasma for manufacture infected donations able to compromise the safety of products. Thus, if hepatitis B virus may be used as an example, the current state of knowledge of the life history of this virus shows that infective donations may possible be collected two weeks after the donor has been infected and remain undetected by current tests (4). Hence, during this period, collecting plasma at the rate of 60 donations per annum will pose twice the risk of an infective donation entering the manufacturing environment than collecting at half that rate (i.e. the current approved rate). The Italian blood system has a number of robust measures designed to eliminate such a risk to patients, and the actual risk of Hepatitis B transmission from blood and plasma products is vanishingly small. However, it is the case that for a hypothetical agent possessing qualities as described, this risk may increase. The Italian blood system prefers to exercise precautionism in this aspect as will, and to limit the number of donations to that which is manageable.

Conclusions

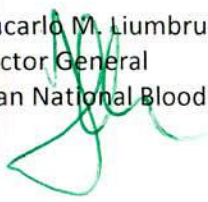
The Italian National Blood Centre and the National Coordinating Committee of voluntary Italian Blood Donors' Associations/Federations (CIVIS), representing more than 1,700,000 voluntary non-remunerated blood donors, maintain that the proposed increase in the donation frequency for plasmapheresis donors in Italy poses additional and unnecessary risks for the management of the Italian blood supply and the provision of plasma products for Italian patients. Maintaining the current EDQM standard of 33 donations yearly will suffice abundantly for the Italian system to fulfil its mandate without these risks.

References

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