Urgent Need to Regulate Convalescent Plasma Differently from Thawed Plasma

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Dear Editor,

Observational pieces of evidence, still awaiting confirmation through randomized clinical trials, support the use of plasma collected from donors who have recovered from COVID-19 infection (convalescent plasma – CP) in treating the infection [1]. In the European Union, the current regulatory basis for plasma for transfusion is based on the requirements of the European Department of Quality in Medicines (EDQM) [2]. These requirements are based on ensuring the preservation of labile coagulation factors, and, by specifying strict limits on the conditions for the collection and storage of the plasma, pose strict limitations to the manufacturing and usage of CP. It may be argued that the preservation of these factors is irrelevant for this product and may well be harmful [1].

It is a matter of urgency to specify CP in terms of the relevant therapeutic entity, in this instance neutralizing antibodies specific to SARS-CoV-2. In this regard, experimental data indicates that the antibodies in plasma are stable and retain activity after multiple cycles of freezing and thawing [3]. Hence, the manufacture of CP may be delayed pending transportation to centralized processing facilities, which may be distant from the initial collection points, which can then prepare the CP in a form that is best suited to its purpose. This could include qualifying the plasma through the relevant screening tests, performing tests to ensure adequate levels of anti-SARS-CoV2 antibodies, and subjecting the CP to pathogen inactivation. Imposing limits on the acceptability of this material through rigid time requirements for separation, freezing

and storage will only impede its availability in a form which is fit for its purpose.

Similarly, evidence is mounting about the stability of antibodies at refrigerator temperatures, which could allow storage after thawing or as an alternative to thawing [4]. Pending studies on the preservation of PRNT titer, surrogate ELISA assays have shown no decline in antibody titer for up to 95 days [5]. This will allow facilities to produce CP for treatment even in the absence of freezers, or where not all of the three 200-mL aliquots typically produced during the pathogen inactivation process can be transfused within 24 h. The latter scenario is common since aliquots are typically transfused 12 h apart but can also occur where less than 3 aliquots are clinically needed (e.g., for pediatric patients). However, the freezing and storage requirement of the EDQM would negate this possibility, decreasing access to CP.

We therefore encourage regulatory authorities, including the EDQM, to rapidly develop a specification for CP, which includes conditions rendering it fit for its purpose, and excise the current measures which are incorporated for irrelevant clinical considerations. In the absence of such a measure, a significant amount of this precious resource could be wasted, to the detriment of patient care.

Conflict of Interest Statement

We declare we have no conflict of interest to disclose related to the manuscript.

References

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