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LETTER TO THE EDITOR

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Reply to Farrugia: Appropriately specifying the quality of plasma for fractionation

We are grateful to Albert Farrugia for sharing his additional considerations with regards to our work and would like to take the opportunity to address these [1].

He asks – aside from the well-described and efficient, but sparse, characteristics defined so far for plasma fractionation – the fundamental question, whether other biochemical characteristics could contribute to a better understanding of this valuable raw material for life-saving therapies? We would like to clarify this.

There is no doubt that immunoglobulins (IgG) are one of the main drivers for plasma procurement globally [2] as emphasized by Farrugia. However, plasma fractionation is a complex procedure by which a variety of therapeutic proteins are separated. This comprises not only albumin and the coagulation factors VIII and IX but also a substantial number of therapeutically important and life-saving coagulation proteins, such as fibrinogen, factor VII or protein C, to give just a few examples. Of course, alternative non-factor therapies have become available as substitutes for plasma-derived coagulation factor VIII, but it is only conditionally true that classical plasma-derived preparations are completely or mostly superseded [3]. Currently, an increasing amount of plasma is needed by the pharmaceutical industry to meet the global demand and patients' needs for all plasma-derived therapies [4]. For example, in India, one of the most populous countries in the world, the need for plasma has strongly increased during the last few years [5], and this is for all fractions, not just IgG.

Farrugia explained in his letter that detailed process and product-relevant plasma criteria for a fractionation company should be directly defined between a fractionation company and a plasma supplier. This is common practice in the plasma industry. For such a complex starting material, it would never make sense to include all possible criteria in a general specification as these strongly depend also on the processes and the combination of different products within those processes that come from the same starting material. However, the collection of plasma to manufacture therapeutic products has substantially changed from how it has typically been performed in the past. Besides the use of plasma recovered from whole blood, source plasma – where plasma is separated from blood through plasmapheresis – is now being increasingly used [6]. This is because new cost-effective plasmapheresis systems have become available, and the fractionation industry is investing more in developing the infrastructure to meet the growing patients' need. In addition, plasma for fractionation is prepared using multicomponent collection systems with different equipment design compared to established plasmapheresis systems. With the advent of the coronavirus disease 2019 pandemic, plasma supply has become even more critical and more challenging [7]. Therefore, we propose consideration that is given to defining universal plasma-quality parameters, which can be used for characterization of all these new 'plasma flavours' in the future [8]. These concepts are even more necessary when plasma is fractionated according to the 'product for plasma' methodology or in the plasma tender business.

Our investigation to define plasma-quality parameters was triggered by the fact that each, even slightly different, method of obtaining plasma might be influenced by the interactions of the plasma proteins with soluble and cellular components of whole blood and the potent anticoagulantly acting endothelium during collection processes. Different methods of plasma preparation could, therefore, be expected to result in different activation levels of major plasma protein systems, including contact activation, coagulation and complement system. Rather than proposing the introduction of mandatory standards and restrictions for plasma quality with regard to these activation levels, the data presented in our work – which do not claim completeness – are intended to provide a baseline evaluation in order to increase our knowledge on this irreplaceable, unique raw material.

As plasma derivatives usually undergo multi-step, effective purification procedures, the probable impact of differences in the starting material obtained with plasma preparation technologies used today is reduced to a minimum. In addition, established quality control testing contributes to maintaining standardized safety and efficacy of plasma derivatives. Nevertheless, introducing new technologies for plasma preparation might call for a more in-depth analysis of the resulting plasma for fractionation. In this context, the data provided by our study will be supportive and could be used as a starting point for further efforts in this direction without any intent to limit plasma availability, be it recovered or source plasma.

CONFLICT OF INTEREST

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Jürgen Siekmann[1]
Alfred Weber[1]
Christoph Bauer[2]
Peter L. Turecek[1]

[1]*Baxalta Innovations GmbH, part of Takeda, Vienna, Austria*
[2]*Baxter AG, part of Takeda, Vienna, Austria*

Correspondence
Peter L. Turecek, Baxalta Innovations GmbH, part of Takeda, DC-Tower, Donau-City-Straße 7, A-1220 Vienna, Austria.
Email: peter.turecek@takeda.com

ORCID

Alfred Weber https://orcid.org/0000-0002-0423-3851
Peter L. Turecek https://orcid.org/0000-0002-6161-1556

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