PPTA
Plasma Protein Therapeutics Association

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Dr. Anneliese Hilger
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To: Anneliese.Hilger@pei.de
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Dear Dr. Hilger,

On behalf of PPTA and its member companies, the PPTA would like to request your support as Chair of EMA's Blood Products Working Party in the following important matter:

We would like to draw your attention to the fact, that following a public consultation by the European Chemicals Agency (ECHA) in 2012 and ECHA response to comments by stakeholders in February 2014 substances belonging to the class 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated - (also known as '4-tert-OPnEO'), including Triton-X 100 are considered as substances of very high concern (SVHC). Thus, their general use is restricted as meeting the SVHC criteria set out in Article 57 of the REACH Regulation (Art. 57(f)).
Currently, the use of Triton-X is only unlimited if it is part of a formulation of a pharmaceutical substance. The restriction will be extended to its use in or as part of a manufacturing process, such as in plasma fractionation.

This restriction is of concern for PPTA and its associated member companies since Triton-X is widely used and a well-recognized agent in the solvent/detergent (SD) treatment process for plasma fractionation (1). In fact, current applicable guidelines by EMA and the WHO specifically refer to the use of solvents such as tri-n-butyl-phosphate (TNBP) combined with a non-ionic detergent such as Triton X-100 or Polysorbate 80 to effectively inactivate enveloped viruses or similar agents during the virus inactivation process (2), (3), (4).
Therefore, Triton-X is a crucial agent for the plasma fractionation industry; its use is paramount in assuring the high virus safety margins of plasma-derived products as afforded by their manufacturing processes.

In addition, for the plasma fractionators this would increase the complexity and time needed to address identification of chemically-based candidate substitutes (animal-origin substitutes would need to be avoided due to a potential biological risk) to ensure no change in virus inactivation performance as well as regulatory obstacles to have these validated and approved. Furthermore, the restriction would lead to the divergence between USA and Europe in quality and safety requirements – whilst global supply of these life-saving PDMPs must be maintained at the same time.

We therefore consider that any restriction of Triton-X in the manufacturing process may potentially have serious detrimental effects and unintended consequences on the safety and availability of plasma-derived medicinal products (PDMP) in Europe.

Consequently, we would like to request your support in exempting Triton-X from the REACH restriction and maintain its unlimited use for the manufacturing processes for our industry.

We thank you in advance for your consideration, and if you have any questions, we would welcome a discussion of the subject at your convenience.

Yours sincerely,

Dominika Misztela

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Manager, Regulatory Policy Europe PPTA

References:

1. Dichtelmüller HO, Biesert L, Fabbrizzi F, Gajardo R, Gröner A, von Hoegen I, Jorquera JI, Kempf C, Kreil TR, Pifat D, Osheroff W, Poelsler G: Robustness of solvent/detergent treatment of plasma derivatives: a data collection from Plasma Protein Therapeutics Association member companies. Transfusion. 2009 Sep;49(9):1931-43.
2. Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products; WHO Technical Report series no. 924, 2004.
3. Guideline on plasma-derived medicinal products (EMA/CHMP/BWP/706271/2010)
4. Draft Reflection paper on viral safety of plasma-derived medicinal products with respect to hepatitis E virus (EMA/CHMP/BWP/723009/2014) and Workshop on Viral safety of plasma-derived medicinal products with respect to hepatitis E virus (EMA/CHMP/BWP/196177/2014)