Plasma Protein Therapeutics Association

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Human Parvovirus PARV4 and plasma protein therapies

Parvoviruses are small, non-enveloped DNA viruses that infect both vertebrate and invertebrate hosts.

The human Parvovirus PARV4 has first been described in 2005 by Jones et al. For PARV4 no associated disease or specific symptoms have been observed.

In hemophilia patients anti-PARV4 antibodies have been detected (Simmons et al. 2007). Recently, Sharp et al. (2009) demonstrated high frequency of exposure to PARV4 in hemophiliacs treated with non-virally-inactivated Factor VIII/Factor IX in the late 70s to early 1980s. In two other studies, PARV4 DNA was detected in 16 – 33% non-virally-inactivated coagulation factors (Factors VII, VIII, and IX) (Fryer et al. 2007 and Schneider et al. 2008).

In recent products 1.7 to 9 % of the batches tested were PARV4 DNA positive by NAT, but most of them at trace levels since they were under the limit of quantification. These findings may raise concerns among the patient communities pertaining to the possible transmission of PARV4. PPTA takes these concerns very serious and would like to reassure the patient community about the safety of plasma protein therapies manufactured by PPTA members.

Extensive research with relevant model non-enveloped viruses have demonstrated that certain procedures, for example virus filtration using small pore size filters is able to remove viruses as small as parvoviruses (Stucki et al. 2008). Human Parvoviruses have been also shown to be removed in partitioning and/or precipitation methods and to be inactivated by heat treatment. Human Parvovirus B19 is effectively inactivated by wet and dry heat (Blümel et al. 2002 and 2008). If PARV4 shows a similar sensitivity against heat treatment can be presumed, but has not been tested yet.

Fryer et al. (2007) and Schneider et al. (2008) detected PARV4 DNA in 1.7 to 9 % of solvent- or heat-inactivated concentrates. This scenario is compatible with the application of removal/inactivation methods in the manufacturing process. The authors also acknowledge that the presence of genomic material is not necessarily associated with infectivity. DNA or fragments thereof from disrupted and inactivated virus particles might be present in the final product especially when inactivation procedures (for example heat treatment) rather than removal procedures are applied in the manufacturing process.

Conclusion: PARV4 is a recently described small non-enveloped DNA virus. Available data with relevant model viruses indicate that PARV4 is removed/inactivated by established removal/inactivation methods implemented in the manufacturing process of plasma protein therapies. PPTA is committed to further substantiate the existing evidence of effective removal/inactivation of PARV4.

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