## Zika Virus and Plasma Protein Therapies

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Recent scientific and public press reports have heightened awareness of the emergence of Zika virus (ZIKV) in the Americas (1, 2) and the causal relationship between prenatal ZIKV infection and microcephaly and other severe fetal brain defects (3, 4). ZIKV infection has also been associated with an increased incidence of Guillain–Barré syndrome (GBS). PPTA is aware that persons who use plasma protein therapies are understandably concerned about whether these therapies remain safe with respect to the ZIKV.

ZIKV is a Flavivirus that is primarily transmitted by infected *Aedes* mosquitoes (5), however, transmission may also occur by sexual contact, from a pregnant woman to her unborn child during pregnancy or during birth (6, 7, 8), or by transfusion of infected blood (9, 10).

ZIKV is of intermediate size (approximately 40–60 nm in diameter), has a lipid envelope and is therefore similar to other Flaviviruses such as West Nile (WNV), Dengue (DENV), Yellow Fever (YFV) and Japanese Encephalitis (JEV) viruses. This group of viruses is highly susceptible to manufacturing steps with virus inactivation and removal capacity as typically used in the production of plasma derived medicinal products, such as caprylate- or solvent-detergent (S/D) treatments, low pH incubation, pasteurization, dry-heat treatments, nanofiltration or plasma fractionation processes. The effectiveness of these processes has been clearly demonstrated using closely related lipid-enveloped model viruses belonging as ZIKV to the *Flavivirus* family, e.g. Bovine viral diarrhea virus (BVDV), or Tick-borne encephalitis virus (TBEV), or WNV (11-16).
In addition, donor screening procedures make it highly unlikely that any person showing disease symptoms typical of ZIKV would be accepted for donation.

PPTA member companies have established convincing evidence to support the capacity of their plasma product manufacturing processes to effectively eliminate Flaviviruses, in case they would be present in the plasma. **Given the scientific data, and aligned with guidance from European (17, 21) and US (18) health authorities, PPTA is assured that existing**

**manufacturing methods are also fully effective against ZIKV, and consequently, the safety of plasma protein therapies is not affected by ZIKV.**

PPTA is aware that there are recommendations by regulatory agencies and blood collection organizations to defer potential donors of blood components (3, 17-20) who are at risk for ZIKV infection and, in some cases, to halt blood collections in ZIKV risk areas (1, 17-20). In August 2016, the FDA revised its earlier recommendations to advise that all states and U.S. territories screen individual units of donated whole blood and blood components with a blood screening test authorized for use. Alternatively, steps with pathogen reduction or inactivation capacity can be used for some components (18).

According to recommendations from US and European health authorities (17, 18, 21) measures such as halting collections, donor deferral or testing are not necessary for plasma, which is further manufactured into plasma protein therapies as these are safe with regard to ZIKV.

**Conclusion:**

**Based on robust virus clearance capacity during manufacturing of plasma-derived products, and current regulatory guidance in Europe and the USA PPTA does not consider that deferral of donors or donation testing is necessary for plasma used for further manufacturing into plasma-derived therapies.**

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