Plasma Protein Therapeutics Association

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Ebola Virus and Plasma Protein Therapies

The recent outbreak of Ebola virus has caused great concern among many people. We read stories about isolation, experimental therapies and many deaths. It is understandable that this raises questions for persons who are more vulnerable to infections such as persons with immunedeficencies. We have seen questions and concerns expressed by various persons and would like to provide information about the safety of immune globulins.

With the occurrence of the first confirmed case of Ebola in the US, it becomes obvious that Ebola, as many other viruses originally confined to certain regions, can be introduced into other geographic areas through travelers who have visited countries where the virus is endemic. In response the U.S. Centers for Disease Control (CDC) has taken measures to assist health care facilities and professionals to more accurately identify and diagnose cases of Ebola virus infection after the misdiagnosis of a patient later discovered to have Ebola. Since Ebola infection initially presents with non-specific flu-like symptoms such as fever, myalgia and malaise, patients need to be tested before a final diagnosis can be made about the cause of the illness.

PPTA members are committed to providing safe and effective therapies. PPTA understands that people who rely on plasma protein therapies may have concerns about the possible transmission of Ebola virus through these therapies.

Ebola virus is a genus of the family of *Filoviridae* within the order of *Mononegavirales*. Filoviruses are enveloped negative strand RNA viruses with a diameter of 80 nm. The viruses originate from the tropical rain forests of Central Africa and Southeast Asia. In response to the Ebola outbreak in West Africa, the EU Center for Disease Prevention and Control (ECDC) recommends that travelers or residents returning from an Ebola Virus Disease (EVD) affected areas should be deferred for donation of plasma for fractionation two months after return (1). The longest incubation period for Ebola virus has been estimated at 25 days (2). On the basis of this information, PPTA's voluntary Inventory Hold of all incoming plasma for fractionation of 60 days would be adequate to allow for removal of a unit in question if necessary. It is unlikely that the Ebola virus would ever be introduced into a plasma pool for fractionation because individuals are rejected for donation if they have symptoms of viral infection (e.g. fever). In the highly unlikely event that a donor subsequently developed an Ebola infection, the inventory hold period would allow ample time for donations to be identified, removed from inventory and destroyed prior to the beginning of manufacturing. On 13 October 2014 the PPTA Source Board endorsed a recommendation for implementing a voluntary deferral of 60 days for donors returning from Ebola virus disease affected areas as an additional safeguard.

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Over the years, PPTA member companies have generated considerable data regarding the inactivation of enveloped viruses, either with the specific virus of concern, or with relevant model viruses, and the equivalence of the results obtained have provided support for the validity of the model virus concept (3). The viruses tested include a broad variety of different RNA viruses, such as Vesicular stomatitis virus (VSV), another virus of the order *Mononegavirales*. At least two effective virus inactivation/removal steps are in place for the manufacturing of plasma-derived products. Regardless of taxonomical differences of Ebola virus to other enveloped RNA or DNA viruses used as model viruses in virus validation studies, the data collected in those studies support the assertion that the clearance level for Ebola virus is comparable. In 2009, PPTA published a collection of PPTA members' data on the inactivation of enveloped viruses by solvent detergent (S/D) treatment (4). These data collectively demonstrated the high robustness, reliability, and efficacy of this virus inactivation method. Additional investigations also demonstrate that enveloped viruses are efficiently inactivated by commonly used inactivation methods (5, 6, 7). Moreover, filtration of intermediates through 35 nm or 20 nm filters is a common manufacturing step for plasma-derived products and is able to remove any potential virus with the size of the Ebola virus (diameter: 80 nm) (8).

PPTA considered relevant information on Ebola virus and the available data indicate that plasma protein therapies manufactured by PPTA member companies provide high margins of safety against Ebola transmission.

References:

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