Virus Validation for Plasma Derivatives

Hye Na Kang

Blood Products Team, Biologics Headquaters, Korea Food & Drug Administration

Plasma is the non-cellular part of blood, and derivative products, such as albumin, immunoglobulins, clotting factors, are manufactured from the plasma by fractionation process. There is always transmission risk of blood-borne viruses in receiving plasma derivatives. A several layer system of overlapping safeguards forms the safety of the derivative products established by National Authorities and manufacturers. The system starts from blood establishments, extends to manufacturers, and reaches to the National Authorities. Firstly, potential donors who have blood-borne agents are excluded through donor screening and testing of donations and of plasma pools. Secondly, validated viral inactivation and/or removal steps should be applied to manufacturing process of the products. Finally, the batch release tests, which are the quality control by the National Authorities, are performed in final products.

Virus validation studies are showed how much virus infectivity is eliminated during manufacture. According to EMEA guideline (CPMP/BWP/268/95: August, 1996), aims of virus validation studies is "to provide evidence that the production process will effectively inactivate/remove viruses which are either known to contaminate the starting materials, or which could conceivably do so, and to provide indirect evidence that the production process might inactivate/remove novel or unpredictable virus contamination." To achieve the virus validation studies, several things are considered for performing the steps. The scaling down process for the studies is designed with comparability with the manufacturing scale process. In the downscaling model, physical parameters (e.g. temperature, column heights, flow rates, filtration condition) and chemical parameters (e.g. pH, ionic strength, concentration) should be considered where possible. Also, appropriate virus inactivation and/or removal steps are considered during manufacture. Lastly, the viruses should be chosen to resemble viruses which may contaminate the product and to represent a wide range of physico-chemical properties to test the ability of the system to eliminate viruses in general. Select the viruses to encompass all of the viral types, including viruses with a DNA or RNA, with and without a lipid membrane, and ranging in size from the smallest, such as parvovirus, to the middle range, such as HBV.

To enhance the safety margin of plasma derivates, more sensitive methods to detect blood-borne viruses in donations will be adapted, and simpler and more inexpensive viral reduction methods should be encouraged to use. To achieve the high level safety though the virus validation studies, interpretation of viral clearance/reduction and limitations of the studies should be well-recognized.