

## 5. VIRAL INACTIVATION

Specification for the validation of virus inactivation procedures used during the manufacture of clotting factor concentrates

The demonstration that HIV can be transmitted by Factor VIII and Factor IX products has led to the requirement that fully validated virus inactivation procedures must be included in the processes used to manufacture each type of coagulation factor concentrate. This specification outlines the minimum requirements for the virus validation of a particular product.

It should be emphasised that the inactivation of viruses in blood products involves a complex interaction of a number of factors, including product type, product concentration, product formulation, presence of stabilisers and type and conditions of inactivation process. For this reason, each manufacturer must validate each product and cannot rely on data from other products or other manufacturers.

### 5.1 Source plasma

In order to minimise the virus challenge to the manufacturing process, each individual plasma donation used for the manufacture of coagulation factor concentrates must be tested for the presence of hepatitis B surface antigen and for antibody to the human immunodeficiency virus, type 1 (HIV-1). In future, it may become necessary to test for other viral contaminants. The assay methods used must comply with the minimum requirements defined in the appropriate specification for each product.

### 5.2 Process validation

#### 5.2.1 Validation of formal virus inactivation step

- i) Data should be generated which demonstrate that at least one single stage in the manufacturing process is capable of inactivating at least  $10^7$  infectious particles of HIV per ml of solution (i.e. a 5 log reduction in the concentration of viable virus.)
- ii) It is widely recognised that the transmission of non-A, non-B (NANB) hepatitis is a major potential problem. The agent(s) of NANB hepatitis have not yet been cultured and it is, therefore, recommended that data are generated on the ability of the process to inactivate a range of other 'model' viruses to include RNA and DNA viruses, both enveloped and non-enveloped. It is suggested that these might include Vaccinia and Semliki Forest Virus as these have both proved fairly resistant to heat inactivation.