

Joint UKBTS / NIBSC Professional Advisory Committee (*)

UKBTS General Information 06

Evaluation of Efficacy of Prion Removal Filters

February 2007

Prepared by: Standing Advisory Committee on Transfusion Transmitted Infections (SACTTI), vCJD Working Group.

This document will be reviewed whenever further information becomes available. Please continue to refer to the website for in-date versions.

The vCJD Working Group of SACTTI has been asked to provide a specification around efficacy for the prion reduction devices currently being brought to market by several manufacturers.

This document is supplementary to the specification on blood component quality and safety produced by the Standing Advisory Committee on Blood Components and the Standing Advisory Committee on Immunohaematology, and the operational specification produced by the Prion Removal Working Group.

- ◆ The threshold prion reduction beyond which the technology should be effective in reducing the risk of secondary transmissions.

Although the concentration of infectivity per ml in peripheral blood of patients with clinical or sub-clinical vCJD is likely to be low, the total amount of infectivity present may be quite high due to the large volume of blood transfused. The current risk evaluation produced by ESOR based on assumptions agreed by SEAC suggests that a 3 log reduction in the concentration of prion infectivity in peripheral blood across the device would be required to reduce the number of individuals infected through secondary transmission by blood components by around 95%. Further improvements above this level of prion reduction are predicted to make a small further positive impact on transmission rates.

It is recognised that it is not possible to evaluate the prion reduction devices on infected human blood, partly because large volumes of blood from patients with vCJD are not available and partly because at the present time neither PrP^{TSE} nor infectivity can be detected within the peripheral blood of such patients. Data will therefore be generated using infected brain homogenates and endogenous animal infectivity studies. It is recognised that whilst the brain homogenate studies should be capable of demonstrating a 3 log or more reduction in infectivity, there will be questions over the relevance of the physico-chemical nature of the infectivity. In comparison, endogenous infectivity studies are likely to represent a more relevant form of infectivity but are unlikely to be able to demonstrate more than 1 log reduction in infectivity.

Recommendation: devices should demonstrate a minimum of 3 log reduction in infectivity in brain homogenate spike studies and >1 log reduction (to the limit of detection) in endogenous infectivity studies.

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◆ Independent evaluation of data and relevance of animal experiments to blood transfusion.

SEAC and MSBTO have requested an independent evaluation be carried out

- to demonstrate reproducibility of experimental results by an independent laboratory.
- to ensure that data from prototypic devices is translated to the clinical device.
- to allow comparative data to be generated using different devices / systems.

It is proposed that this should be a 3 step process:

- 263k hamster brain (crude brain homogenate) spiked into peripheral blood using both an immunoassay for abnormal prion (such as Western blot) and infectivity bioassays in triplicate.
- 263k hamster brain as a sonicated microsomal preparation spiked into normal human peripheral blood using immunoassay and infectivity bioassay end points.
- 301V homogenised murine brain in sonicated microsomal form spiked into normal human peripheral blood using immunoassay and infectivity bioassay end points.

◆ Assessment of filtration variables.

The companies should demonstrate the efficacy of the process under two sets of conditions, blood which has been stored at 4°C and at ambient temperature.

◆ Process control.

The companies should propose suitable surrogate markers to apply statistical process control over the prion reduction devices.

◆ Extension of study to plasma and platelet concentrates.

At present prion reduction devices are only applicable to red cell concentrates. The extension of this work to whole blood, platelet and plasma concentrates is encouraged.

(*) **Joint United Kingdom Blood Transfusion Services and National Institute for Biological Standards and Control Professional Advisory Committee**