CSM/Biols 94 7th Mat
Tabled Paper 1V

NIBSC
Assuring the quality of biological medicines

Blanche Lane
South Mimms
Potters Bar
Hertfordshire EN6 3QG
United Kingdom

FAX

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Mrs Glenda Silvester
Department of Health
Medicines Control Agency
Market Towers
1 Nine Elms Lane
London SW8 5NQ

To MRS G SILVESTER
Company
From T HARROWCLIFFE
Company
Tel No.
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Dear Glenda

Re: Viral Safety of Blood Products

I am sorry I have been unable to attend either of the two recent meetings on this topic, but I have been keeping in close touch with Robin and Phil and have also looked through the documents you have circulated.

I think the draft paper that you circulated on 11 October, for eventual submission to Langen, is excellent, and I only have comments in one area.

In 3.1 it is proposed that two specific, complementary viral inactivation/removal steps be employed, and this seems eminently sensible. However, in 3.2 it is stated that fractionation and chromatography, which are the only practicable production methods for blood products, should not be considered as virus removal steps. This seems to me a little unrealistic, since it is almost certain that alcohol fractionation (albumin and immunoglobulins) and chromatography, especially immunoaffinity chromatography (coagulation factors) do make a real contribution to virus elimination in these products. I accept that these parts of the process are more difficult to control, but it seems to me that if the virus validation data is good and reproducible and if there is long-term evidence of clinical safety then these processes should be accepted as one of the two complementary steps.

Otherwise the implication of 3.1 is that all products should be subject to both heating and solvent detergent steps. This may be most desirable virologically but we have to be aware that product safety in other aspects could be affected. Albumin would probably be all right, but heating immunoglobulins would be difficult and for FVIII and FIX products the concerns would be enhanced inhibitor development and thrombogenicity, both of which are virtually impossible to predict from pre-clinical data.

I think one of the most important points is the one you state in the second paragraph of 1, ie all aspects of blood product safety need to be addressed,

especially pharmacovigilance, since the only way that product safety can be determined is from clinical data.

I hope these comments are helpful.

Yours sincerely

GRO-C

Trevor W Barrowcliffe
Head, Division of Haematology

Copy to Dr G C Schild, NIBSC
Dr R Thorpe, NIBSC
Dr P Minor, NIBSC