SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE

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FACSIMILE

FOR THE ATTENTION OF: PROFESSOR JD CASH

BTS CENTRE/COMPANY NAME: HQ

FROM: DR R STEWART

DATE: 17. MARCH 1992

REFERENCE:

DESTINATION FAX NUMBER:

PAGES TO FOLLOW: TWO

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MESSAGE:

MINUTES OF FAC VIII. W.P OF 15 NOV 1990. - THE ONLY REFERENCE I CAN FIND - BUT IT IS CLEAR THAT WE PRESENTED A 'TERMINAL VIRUCIDAL STEP' OPTION AS ONE OF THE ADVANTAGES OF A MODIFIED LILLE PROCESS, LEADING THE HAEMOPHILIA DIRECTORS TO SUPPORT THIS PROCESS.

GRO-C

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Dr Mayne felt that we should not rush to follow the FDA and that there was evidence from the UK to suggest that heat treatment was a valuable and effective virucidal process.

Dr Prowse was invited to comment on scientific aspects of the process options. He stated that there was considerable discussion taking place with NIBSC, who seemed to be concerned that some high purity Factor VIII concentrates were partially activated and that this could affect the label potency. He also reviewed the protein content of a likely ion exchange product versus an immuno purified product which would require to have albumin added back to it, these are shown in Appendix 4.

Professor Cash outlined a proposal to use a modified version of the process used in Lille. Under this option an upstream component of the S8 process would be added onto the column. The target product would have the following specification:

specific activity of >100 IU per milligram
a dispensing volume for 500 IU of < 20 ml
viral inactivation by solvent detergent

He pointed out that current experience with a non-modified Lille process was 130 batches made in France since July 1988, and a total use of 200 million international units. In addition other countries were using this type of technology and these include Norway, Denmark, Australia, Republic of Ireland, Luxembourg, Belgium, Israel and Germany.

The Haemophilia Directors enquired about the likely licence position of this process and it was pointed out that Bio-Transfusion have committed to apply for a product licence which will cover the European community in 1991.

Professor Cash described additional advantages to using a modified Lille process, these were

a. an option for a further terminal virucidal step
b. agreement for a further licence of other products, processes for example von Willebrand factor or a high purity IX.

Dr Mayne enquired exactly what modifications to the Lille process were needed. Dr Perry replied that through collaboration with Lille it was intended to alter the cryoprecipitate stage to that which had been used in S8 and both Centres would thereafter produce the modified Lille process ie PFC and Lille would both be producing the same product.

Dr Ludlam commented that Dr Savidge had said that his early experience with Lille product had been excellent but that recent batches had experienced solubility problems. He further commented that he was aware of similar problem occurring with the Octapharma product.

Professor Cash replied that this was not a universal problem with Bio-Transfusion and while the Company had been aware of some problems they said that it had not occurred in a significant number of batches.

Dr Mayne said that solubility was a very important feature and in her opinion once she had experience with a monoclonally purified Factor VIII product which went into solution quickly it was extremely difficult to go back to using products which were more difficult to solubilise. However, she commented that she was unaware of any problem with the Octapharma product having been experience in Dublin.

Professor Cash said in discussion with Bio-Transfusion it was suggested that it may be important that the dissolution water is at room temperature and not a 4°C and that Bio-Transfusion were looking at altering their packaging to allow the water to be stored separately from the Factor VIII. They also are developed an alternative needle which assists in solubilisation.

Dr Lowe asked if this product and process are so good why did BPL take it up? Professor Cash and Mr McIntosh agreed that they were not in a position to respond for BPL. However, when they had done a full option appraisal on the likely benefits of the various processes including additional costs, the modified Lille process appears to be the best choice.

It was agreed that the Haemophilia Directors should be left for a period of time to discuss the various options before making any recommendation to the SNBTS on which fractionation procedure they should adopt in future.

At this point Dr Gibson left the meeting and Dr T G Taylor joined.

When the meeting reconvened Dr Ludlam reported that all the Haemophilia Directors were happy to accept the modified Lille process and that they would support the SNBTS in doing so. However, they would appreciate clarification as to why if the Lille process is so good, they are developing a monoclonal purification process.

Professor Cash replied that this was not been developed by Lille but by CNTS Paris and it is believed that this monoclonally purified Factor VIII product is in clinical trial. He added that to the best of his knowledge