NOTE OF A MEETING HELD AT PFC ON 17 MARCH 1986

Present: BPL - Dr Lane
Dr Snape
Dr Harrison
Dr Smith
Mr Vallet

SNBTS - Dr Perry
Dr Foster
Dr Cuthbertson
Mr McQuillan )
Dr Prowse ) Morning only
Dr Dawes )
Dr Urbaniak )

Plasmapheresis

1. Dr Smith presented a review of data gathered at PFL relating to Dideco, Organon and Haemascience plasma and the behaviour of this plasma in medium scale (200 kg) fractionation trials. Dr Lane provided reports of each study (in confidence) which will be submitted to individual manufacturers in due course. The meeting endorsed the conclusions of the recent meeting at BPL in that there are potential major plasma quality and processing problems associated with filtration of plasma.

2. SNBTS data was summarised in respect of the Aberdeen study, which was designed to provide a computer evaluation, under highly standardised conditions of Dideco, Haemonetics, Recovered and Platelet rich plasma and the performance of this plasma under fractionation conditions.

It was agreed that:

(a) PFC would supply 10 litres from each pool to PFC for evaluation at small scale fractionation.

(b) Donation samples would be stored for future (though undefined) assays.

(c) Significant observed differences between Aberdeen plasma quality measurements (FpA and BTS) and NBTS measurements may be due for non-standardisation of sampling, processing and donation procedures at RTC's.

3. In view of (2) above, it was generally agreed that future studies should be designed to minimise plasma collection, sampling and assay variables to permit a better comparison of plasma quality.

Aberdeen is capable of extending its efforts in this area (to include other machines - particularly Haemascience) and Dr Lane indicated that Manchester BTS would be able to set up similar studies aimed at highly standardised small pools for evaluation in the proposed small scale fractionation model at PFL.

SNBTS would attempt to procure Haemascience machine and HSE machine for placement in Aberdeen. Dr Lane would similarly attempt to procure HSE, Haemascience and Haemonetics machines for plasma at Manchester.

4. It was agreed that a standardised 'core' protocol would be devised to maximise comparability between studies conducted at different centres. Dr Smith, Dr Prowse and Dr Urbaniak agreed to co-operate in the production of such a protocol.

5. Dr Smith confirmed that PFL/BPL had now ceased the large scale evaluation of plasmapheresis pools pending more fundamental studies of predictive plasma quality measurements and small scale modelling.

However PFC confirmed that Aberdeen pools will be processed as large scale batches (250 kg) in order to assess primarily cryoprecipitability of pheresis plasma and thrombogenicity of FIX in both laboratory and dog studies. A decision to process further batches at large scale will depend on the results from the Aberdeen pools. In any event, the SNBTS will direct effort towards collection and processing of small pool batches. Aberdeen batches will be processed to IgG to assess any effects on Cohn fractionation.

6. Dr Smith reported that the design of a small scale model system for F VIII and F IX was at an advanced stage and addressed the downstream behaviour of cryoprecipitate.

PFC felt that duplication of such a model in PFC may require major effort although the possibility of modelling cryoprecipitation was feasible and may complement the BPL work. Dr Foster agreed to investigate the feasibility of such a programme.

It was agreed that plasma collection protocols in NBTS and SNBTS should allow for exchange of small pools between PFL and PFC.

7. Dr Prowse would investigate how best to study the effect of anticoagulant ratio and formulation on small pool behaviour.

VIRUS INACTIVATION STUDIES

1. Dr Cuthbertson outlined the studies performed so far using model viruses such as Vaccinia, Humps, Herpes Simplex etc.

Evidence is emerging which suggests that product freezing and freeze drying has an impact on the efficacy of subsequent virucidal processes such as heating.

It was agreed that Dr Smith would liaise with Dr Cuthbertson with a view to establishing the level of virus activation achieved with BPL BY material. This would involve the transfer of samples between BPL and PFC and the development of a protocol which accurately simulated routine BPL formulation and treatment conditions.

PFC are also carrying out studies of IV IgG and IM IgG process steps.

The need for duplication of such studies at both BPL and PFC was discussed and it was concluded that such studies, which involved standard virological

techniques, formed an important part of continuous process validation and design and QA and therefore it was appropriate that such technology should be adopted and/or expanded at BPL. Dr Harrison indicated that preliminary studies had already been initiated. PFC offered assistance in training and experimental design and both Centres agreed to exchange data and maintain close liaison in such studies.

2. Dr Lane indicated that a collaborative chimpanzee study with Prince had been established in respect of the virucidal effect of thin layer freeze drying from ethanolic solution.

It was hoped that such a study would provide useful information which might explain the safety of IH IgG with respect to NANB hepatitis. PFC indicated that chimpanzee studies were not being considered in Scotland although the results of the BPL study could be calibrated with virus inactivation models.

3. PFC outlined the proposed collaborative HTLV III inactivation studies with Professor Weiss and University of Edinburgh (Dr Peutherer). An outline of the studies was tabled (attached). It was generally agreed that the experiments and their relative priorities was appropriate at the present time. Dr Lane suggested that the effect of alcohol in Cohn fractions and supernatants at different temperatures should be incorporated into the studies as a medium priority since such studies may indicate that transient deviations of temperature during processing may be key inactivation events. Dr Cuthbertson confirmed that such studies could and would be included in the programme of work.

4. It was agreed that HTLV III studies would be confined to Edinburgh for the time being and Dr Perry confirmed that he would ensure that the study timetable would include studies of BPL products and processes so that UK interests as a whole were met in this area. As in 1 above studies of BPL products and processes will require central design in order to ensure that "off site" studies in Edinburgh accurately reflected BPL processes. Dr Cuthberton and Dr Foster will liaise with Dr Smith and Dr Snape in this respect. Immediate BPL priorities are heat treated coagulation factors.

5. Dr Smith outlined clinical trial results of the BY F VIII product so far. While results cannot be considered conclusive at this stage, he indicated that no cases of virus infection have occurred (attributable to BY material) after 12 months experience of BY in virgin haemophiliacs.

6. It was agreed that commonality or at least consistency between PFC and BPL was essential in respect of product release and recall in situations where plasma pools contain infective or suspect donations. Dr Lane agreed to examine the PFC SOP on this subject and indicate any areas where disparity or major policy differences exists. Preliminary examination indicates that BPL may release F VIII and F IX products in situations where recall or quarantine options are implemented at PFC. Such differences can be reconciled with the more severe BPL heating conditions (F VIII).

R J PERRY
24 March 1986