EC 7/94

UK BTS/NIBSC PLASMA FRACTIONS COMMITTEE

MINUTES OF MEETING HELD AT NIBSC ON 9 SEPTEMBER 1993

Present Dr T W Barrowcliffe, NIBSC (Chairman)
Dr T J Snape, BPL Elstree
Dr B Cuthbertson, PFC Edinburgh
Dr R Thorpe
Dr G Kemball-Cook, NIBSC

1. **Apologies**: Dr A R Hubbard, NIBSC
Dr S Knowles, NLBTS, London — Miss Sigurd-A. Slopecki to replace.
Dr K Forman, RBTC, Sheffield
Dr R Lane, BPL, Elstree

2. **Minutes of Previous Meeting of 23 March 1993**:

Were accepted.

3. **Matters Arising 23 March 1993**:

Item 4: Guidelines for plasma for fractionation-revision Vol II.
Dr Snape reported the intention to continue with revisions on an ongoing basis. In addition, the Committee agreed that parts of the Guidelines should form the basis for drafting similar documents for the EPFA.
Chapter 2: (Product Characteristics) was seen as the next area for revision. Drs Cuthbertson and Snape agreed to undertake revision outside the Committee and present the results to the Committee at the next meeting. Antibody to Hepatitis A and Endotoxin alterations have also been recommended.

Item 7: Hepatitis A and Factor VIII. All manufacturers have been invited to submit position papers to the MCA.

4. **Composition of Committee**:

Dr Barrowcliffe introduced the issue of whether the Committee should continue and in what form. The Committee agreed that Dr Barrowcliffe be invited to continue as Chairman; also that the present composition (NIBSC, BPL, PFC plus any RTC input possible) was appropriate. The Committee could continue to invite any specialist contributors to meetings when required. Should Dr Knowles resign another member should be co-opted.

5. **European Matters**:

5.1 Batch Release Documentation: (Ad Hoc Committee notes for guidance).

5.1.1 Both BPL and PFC have or are expressing their opinions directly to Patricia Brunko (Ad Hoc Working Group, Brussels), via MCA and via EPFA, as well as to this Committee.

5.1.2 An annotation has been added at the front of each referring to virological marker testing, using 'antigen tests or PCR....'.

5.1.3 Dr Cuthbertson tabled a document "Comments on Draft Documents on Control Authority Batch Release Testing". A point strongly expressed in it (1.1) was the inappropriateness of quoting PCR testing as a potential requirement in plasma testing. Drs Snape Cuthbertson and Barrowcliffe all agreed, however, as to the desirability of both manufacturers and control authorities testing pools for viral markers by the current methods.

5.1.4 Dr Barrowcliffe expressed the opinion that protocol documents should contain some reference to the kits used for virological testing to ensure they are appropriate. Perhaps BPL and PFC should deposit details of kits with NIBSC, and then use a statement to the effect that such kits were used (PFC document point 1.2).

5.1.5 Sources of plasma (PFC point 1.3) was discussed. Dr Barrowcliffe felt that the information about country of origin was important. Dr Snape raised the issue of reworked batches using many small portions of previous batches. It was agreed that details of all the pools be included. Various typographical errors and alterations were corrected.

5.1.6 The possibility and desirability of manufacturers gaining access to results of the testing done by control authorities was raised: manufacturers would find this most useful from a quality assurance stand point. Dr Barrowcliffe thought this would be most difficult to incorporate into the EC documents, and that NIBSC would prefer to operate by more informal communication.

5.1.7 Concern was expressed by Dr Snape over the Phase 2 batch release procedures, and when they would be required.

Dr Barrowcliffe explained that the division of control testing into Phases 1 and 2 was originally based on consideration of vaccines, and the possible necessity

to perform such scientific tests as thought proper in addition to those stipulated in the EP. Having defined 'EP' and 'non-EP' tests, it was then necessary to define when the additional tests could be required.

BPL's attitude would be that such additional tests must be taken from the list of tests required from the manufacturers (found in the marketing authorisation). It was agreed that the examples list on p5 could not constitute an appropriate 'phase 2' list.

Some tests might be appropriate for one manufacturer or product (depending on the marketing authorisation) but not for another - therefore such a list might encompass many tests which were irrelevant to particular manufacturers.

5.1.8 Dr Snape will copy BPL's comments to MCA, EPFA, EP and this Committee.

5.1.9 The immunoglobulins document was thought by both BPL and PFC to be needlessly exhaustive: Dr Thorpe was in agreement.

5.2 <u>EP Group 6B Papers</u>:

5.2.1 Document D from Dr Calam - report from EP Commission, plus details of 2nd phase of biological standardisation programme (Dr Barrowcliffe is named as Project Leader for Factor 1X).

5.2.2.1 Document E: EP Group 6B 52nd meeting (via Dr Snape). Dr Snape gave notice of the relevant items on the upcoming 6B meeting in September 1993 (albumin, monoclonal antibodies, FVIII assay and standards). Of the other documents circulated (F-H), thrombin had been omitted but is little altered from an earlier circulated version.

5.2.2.2 Anti-CMV IgG: The only correction was that the measure is not an international unit (since there is no IS). The possible requirement for an Anti-CMV International Standard was raised; this could be pursued by Virology Division at NIBSC.

5.2.2.3 Anti-HB: The lower limit for IV products was agreed at not less than 50 Iu/ml.

5.2.2.4 Anti-D: minimum protein content was set at not less than 100 mg/ml. The IV paragraph has been deleted. The question of a draft text for a new assay method would be raised, based on an assay developed at NIBSC.

5.2.2.5 Fibrin Glue: Dr Cuthbertson stated that PFC produce this product at less than 60g/l and will write to Dr Castle in Strasbourg.

6. **Standards**:

6.1 International Standards (Dr Barrowcliffe):

6.1.1 Replacement FVIII IS Plasma was established in 1992 and is now available.

6.1.2 FVIII IS Concentrate will be up for replacement in 1994: a meeting will be organised at NIBSC in the near future to discuss candidate materials, methodology etc, possibly in late November 1993.

6.1.3 2nd IS FII-IX-X Concentrate: a candidate material (84/683) had been calibrated in 1987 together with the current 1st IS. A check calibration study was carried out in 4 laboratories (BPL, NIBSC, PFC, Kabi) and the report has been submitted to WHO, recommending adoption of 84/683 as the 2nd IS with potencies as determined in the original collaborative study.

6.2 European Standards (Dr Barrowcliffe):

6.2.1 FVIII EP Standards already discussed.

6.2.2 EP FIX: Dr Barrowcliffe has had an official request to organise a study with a view to establishing a working standard.

6.3 British Standards: (Dr Kemball-Cook)

6.3.1 10th BS Recalibration: the combined two-stage/chromogenic figure was accepted by the participants and the report has gone to the NIBSC Director for approval.

6.3.2 19th BS Plasma FVIII: this is now approved and being distributed.

6.3.3 3rd BS F II-IX-X: the report is being written and will be forwarded to BPL and PFC within 5-7 days.

6.4 Possible New Standards:

6.4.1 FXI plasma and concentrate standards are under discussion.

7. **Virology**:

7.1 Hepatitis C in plasma donations/criteria for batch recall. Retesting earlier donations by RTC's has revealed occasional positives in donations previously found negative and issued for fractionation. This has caused great problems to fractionators in terms of batch recall.

Dr Snape has agreed to write a draft for the EPFA QA

working group. Dr Cuthbertson agreed that the Guidelines for the BTS should be updated to clarify this situation. Nobody appears to contend that these compromised batches constitute a health hazard, however there is reluctance to authorise release.

BPL and PFC want to continue to receive the updated information from RTC's. There may be a case for treating the various viral markers differently - but this must be supported by definite scientific arguments.

Dr Snape commented that viral safety is assured by several factors only one of which is the result of these tests, thus a coherent position could be taken up in the different possible situations. Key points or criteria for safety of issue might be; sensitivity of tests, number of positive donations, viral inactivation step(s), proven safety record of product.

The text for the guidelines might include a reference to the Extension to the EC Directive. Both BPL and PFC wish to be able to make the decision themselves re release of a product in this situation, based on agreed written guidelines on viral safety, bearing in mind the criteria mentioned above.

Dr Snape agreed to present his draft EPFA document to the Committee.

7.2 Anti-HBs plasma (letter from Dr Cash, Document J to Dr Perry, Director of PFC): on the possibility that a significant number of donors who supply anti-HBs plasma may be disbarred from donation due to being defined as 'high risk' on questionnaire. Dr Cuthbertson will reassess the donor exclusion situation as defined in RTC document (NBTS 110 or equivalent). This might involve the Components Group.

8. **Any Other Business**:

None.

9. **Date of next meeting**:

Early - mid November 1993.