UKBTS/NIBSC

WORKING GROUP ON PLASMA FRACTIONS

Minutes of 5th meeting at NIBSC, South Mimms, Hertfordshire at 10.30am on Monday, 25 April 1988.

Present:

Dr D P Thomas	(Chairman)	NIBSC
Dr D R Bangham	(Secretary)	NIBSC
Dr T W Barrowcliffe		NIBSC
Dr B Cuthbertson		PFC, Edinburgh
Dr K T Forman		RTC, Sheffield
Dr J K Smith		PFL, Oxford
Dr T J Snape		BPL Elstree

Apologies from Dr R Thorpe.

Precirculated papers included:

- Agenda
- Minutes of 4th meeting (March 1988)
- Factor IX concentrates. First revision, March - J Smith

Tabled:

- Specification of virus inactivation procedures needed during manufacture of clotting factor concentrates.
  Draft 21.4.88 B Cuthbertson
- Specification for plasma intended for fractionation.
  Draft 15.2.88 B Cuthbertson

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1 Minutes of 4th meeting were accepted with correction:

Page 2 item 2 para 5 - after 'precisely a concentration limit' add 'for ay'.

2 Meeting of Liaison Group 2 March 1988

2.1 Dr Snape attended in lieu of Dr Thomas.

2.2 Dr Thomas commented briefly on discussions mentioned in the draft minutes.

2.3 Correction to those minutes was noted: 3 para 4 (multicentre time), replace 'NIBSC' with 'Bristol'.

3 Matters arising from minutes

3.1 In response to the proposal that there should be a British Standard for HBsAg, NIBSC has asked whether the preparation would be used as a daily control in all RTCs or to calibrate reagent kits used in the BTS. The number of ampoules registered for the former use would be very considerable. The WG on Microbiology should be consulted.

3.2 The central control of diagnostic kits was highly desirable. NIBSC has been requested to find out to what extent, and how, control was exerted in other countries. WHO Requirements for manufacture of radioimmunoassay kits (31st Report of WHO Expert Committee on Biological Standardization, TRS no 658, Annex 8 1981) covered many aspects, and compliance with them could be invoked when purchasing such kits.

3.3 There is an urgent need for a standard, or a 'positive control' reference serum for HIV, but suitable premises and facilities for ampouling large numbers of ampoules with potentially infectious material have not yet been identified.

3.4 A copy of the WHO Requirements for Blood and Blood Products document amended in the light of the meeting in December 1987 has now been received by Dr Thomas. He did not consider the changes merited circulation of the paper.

3.5 There had been a meeting on 30 March at NIBSC of manufacturers of blood products, from Europe and the USA, to discuss current practice to remove or inactivate viruses from plasma and blood products. Although the discussions were informative, the meeting had not discussed any conclusions. Dr Thomas was assembling an informal record of the points made.

4 Factor IX Concentrates - document 1st version, March, from Dr Smith

Points arising from the discussion included:

4.1 The title should indicate that Factors II and X were also present in the products even though limits for their content may not be specified.

4.2 There should be a statement that specifications for the final product are given in the BP/EP monographs.

4.3 The introduction should say whether the product described was suitable for self medication.

4.4 The limit for endotoxin determined by the EP/BP LAL Test should (probably) be 0.1 iu endotoxin per iu Factor IX.

4.5 It is difficult to specify exactly what in vivo tests for thrombogenicity should be done on typical batches in laboratory animals. There was not general agreement that dogs were the most suitable test animals, and mention of them would be omitted.

4.6 A statement should be made in the general introduction to the BTS/NIBSC Requirements that blood products are made only from blood from unremunerated donors.

4.7 A revised version will be prepared by Dr Smith and circulated to members.

5 Specification for the validation of virus inactivation procedures Draft 21.4.88 B Cuthbertson

5.1 Apart from the change in the first line of 2.1 (replace 'data must' with 'data should') the document was agreed to.

5.2 It will be offered to the WG on Microbiology and to Dr P Minor (virologist, NIBSC) for comment.

6 Specification for plasma intended for fractionation Draft 15.2.88 B Cuthbertson

Points arising from the discussion included:

6.1 The lowest detection limit of assay kits for HBsAg, presently thought to be 0.5 iu HBsAg/ml, will be checked by the WG on Microbiology, in the light of results of the current UK collaborative study.

6.2 The upper acceptable limit in tests for ALT in donations, stated as 1.5 times the accepted upper limit of normal, will be confirmed in the light of the results of the current multicentre trial (by Bristol, Edgware and Manchester).

6.3 In practice, the most frequent, and problematic, circumstance requiring a decision about recall of a plasma is when the donor is reported to have developed an infectious disease. The fractionation Centre must be informed and the decision whether to withdraw the plasma is taken by the responsible staff at the Centre.

6.4 Minor amendments will be made by Dr Cuthbertson and the document then offered to the WG for Blood Components and the WG on Microbiology for comment.

7 Requirements for products of clotting factors

7.1 A pattern of topics in 'requirements' for clotting factor products include:

1. Specification of the quality of bulk plasma - (cf document agenda 6 above)
2. Emphasis on the importance of the 'design' and the intended qualities of the product
3. Reference to the measures to demonstrate virus inactivation or removal (cf document agenda 5 above)
4. Compliance with Good Manufacturing Practice is required
5. Specification of the in-process control tests - and their limits
6. Reference to BP or EP monographs as specifications for the final products
7. Reference to appropriate WHO Requirements or guideline documents

7.2 The general style and content of the documents on different clotting factors (eg for Factor VIII and for Factor IX) are necessarily different from each other.

7.3 Dr Thomas will draft an Introduction, to include general points (including mention of selected donors for special products such as fibrinogen for radionuclide labelling).

7.4 All the agreed documents would be assembled together and passed to the Liaison Committee, after consideration by a meeting of Chairmen of the Working Groups when/if they can meet before the next provisional date (8 September) for the Liaison Committee.

8 The next meeting of the Working Group

8.1 A document on Albumin preparations should cover the general policy for making the two types of product (containing 5% or 20% albumin) made by the BPL and the PFC. Dr Cuthbertson will draft this. Dr T Hubbard (NIBSC) will be co-opted for discussions on albumin.

8.2 A document on Immunoglobulin preparations will be drafted by Dr Snape, and include products intended for im and for iv administration.

8.3 Provisional dates for the next meetings

Wednesday, 29 June at 10.30am at NIBSC
Tuesday, 6 September at 10.30am at NIBSC