NIBSC/BTS PLASMA FRACTIONS COMMITTEE

MINUTES OF MEETING HELD AT NIBSC ON 12th SEPTEMBER 1991

Present:

Mr D Wesley, BPL, Elstree
Dr J K Smith, PFL, Oxford
Dr B Cuthbertson, PFC, Edinburgh
Dr R Perry, PFC, Edinburgh
Dr S Knowles, North London Blood Transfusion Centre
Dr T W Barrowcliffe, NIBSC
Dr R J Thorpe, NIBSC
Dr P Minor, NIBSC
Dr G Kemball-Cook, NIBSC
Dr A R Hubbard, NIBSC

Apologies:

Dr T J Snape, BPL, Elstree
Dr D P Thomas, BPL, Elstree
Dr K Forman, RBTC, Sheffield

1. Minutes

Drs Hubbard and Kemball-Cook agreed to take the minutes.

2. Remit of Committee

This was the first meeting of the committee as outlined in the letter from Dr Wagstaff to Dr Barrowcliffe. The main tasks of the committee are: revision of the NIBSC/BTS Guidelines, Volume 2, and consideration of other relevant items where collaboration of NIBSC and BTS can be of benefit, with particular emphasis on European legislation.

3. Hepatitis C Screening - Implementation and Quality Control

The RTCs have implemented 2nd generation ELISA anti-HCV screening since 1 September 1991, although it is uncertain which tests are being used by which centres.

A. Usage of Unconfirmed Positives

The main area of contention for both transfusion centres and fractionators concerns what to do with plasma donations which are ELISA screen +ve but confirmatory RIBA (recombinant immunoblot) -ve on repeated test. In the UK it appears from studies on large numbers of donors that about 0.7% of plasmas test +ve by ELISA, but only perhaps a maximum of one-fifth of these are confirmed by RIBA (referred to as unconfirmed positives).

A general discussion ensued on the question of using these donations in fractionation. Some key points which emerged were:

1. RTCs may prefer to treat all screen +ves the same, (ie withhold them all) regardless of the results of RIBA tests: it is simpler and probably more cost effective, although donor counselling may be a problem. Different RTCs may hold different views on these issues.

2. Dr Gunson has issued a recommendation that no screen-positive RIBA-negative donation should be released for fractionation until further notice.

3. Fractionators are confident that with current close attention to manufacturing procedures and especially viral inactivation steps, unscreened plasma donations (in stock at the fractionation centres and currently still used) pose no significant health risk despite a presumed HCV load: inclusion of unconfirmed positives which may be infectious would therefore pose no extra problem. However, since the number of units which would be lost is very small; since these units will not be sent for the time being anyway (see above); and since there are strong operational and legal arguments in favour of rejecting these donations for use, the fractionators would concord with the non-use of these plasma units.

Overall, those present at the meeting concluded that a consistent and defensible position was to recommend that these unconfirmed positive donations not be used for fractionation for reasons of both operational and legal significance: the scientific arguments were seen as relatively marginal in the absence of more data on this group of donations.

This recommendation would be communicated to Dr Gunson, and to the Standing Committee on Donors, for further consideration.

B. Anti-HCV Testing of Plasma Pools

It was generally agreed that testing of plasma pools either by fractionators or NIBSC should only be carried out on pools from screened donors, using tests of similar sensitivity to those used for the original screening: this constitutes an appropriate test of GMP but little else.

C. Use of Current Stocks of Unscreened Plasma

Since the fractionators hold large stocks of plasma, there will obviously be a transition period during which some products will be made purely from screened donations, some from unscreened, and some from a mixture. In addition there is a European initiative to switch completely to use of screened plasma by a certain date (possibly end December 1992). It was agreed that the fractionators would investigate the likely transition period for their various

categories of plasma, including rare hyperimmune plasmas, with a view to minimising this period. It was thought useful for both the UK fractionators and the members of the European Plasma Fractionators Association (EPFA) to communicate their views on this topic to the Ad Hoc Working Party in Brussels; Dr Perry agreed to contact Dr van Aken as Chairman of EPFA.

4. EC Guidelines Document

It was agreed that this document requires considerable revision - particularly with reference to the use of placentae from unscreened donors in the manufacture of albumin etc. It was considered that each placenta should be treated as a single donation and subjected to the same screening procedures as a blood donation.

Dr Smith questioned the comment by NIBSC that only new mono-component FIX concentrates should be tested for thrombogenicity in an animal model. It would be preferable if new PCC were also tested in this way. Dr Perry stressed that it was important to state which animal model should be used and questioned whether the tests should be carried out as part of batch release procedure or only as part of a product licence submission.

5. Revision of UK Guidelines (Red Book)

It was intended to carry out a revision of the relevant sections of this document, and most discussion centred around Chapter 3 of Volume 2.

Donor selection - it was pointed out that Transfusion Centres tend to work to BPL specifications for plasma than to the specifications in the Guidelines. Basically they use different specifications for donors for transfusion and for fractionation and sticking rigidly to the Guidelines would result in the wastage of a considerable amount of plasma for fractionation. It was agreed that there should be different donor selection criteria for plasma for fractionation and that this should be consistent through all the RTCs. The Guidelines as they stand are too vague and should be made more specific. Dr Knowles circulated a list of suggestions from NLBTS: PFC and BPL agreed to consider these and come back to the Committee with their own comments. These will be discussed at our next meeting before being forwarded to the Standing Committee on Donors. The ultimate aim would be an agreed set of specifications for all RTCs and fractionators.

Storage Temperature

The practical problems of the transit temperature for plasma were also mentioned. Basically, plasma is carried in trailers provided by BPL but transported by the RTCs. These trailers are designed to keep plasma at -30°C during transit but are sometimes not very reliable. When they fail it is not possible to use a commercial substitute since they do not store at -30°C and it is

important that the storage temperature should not exceed -25°C. In Scotland this is not a problem since the plasma is actually collected by the manufacturers. A more robust trailer would apparently solve the problem in England.

Documentation

Following a letter from Dr Gunson, it was agreed that a member of this Committee should also sit on the Barcode/Label Advisory Committee: Dr Snape at BPL will be asked. The question of long term storage of records was also raised, as was the subject of library samples. Members agreed to bring forward suggested alterations to the next meeting.

Notifications

This was seen to be another area requiring detailed discussion: there are closely related areas of plasma recall by RTCs and product recall by fractionators. BPL and PFC agreed to supply details of their current procedures for discussion at the next meeeting.

Product Characteristics

This will need updating to encompass the recent changes in the UK: it was also suggested that another product category be created to include the minor products (eg At III, FVII etc).

The Committee members agreed to compile their suggested alterations to the Guidelines for consideration at the next meeting: NIBSC will circulate all the suggestions if participants can forward them to TWB at least a week beforehand.

6. Storage of Blood at 20°C: Implications for Plasma Products

The consequences of storing blood at 20°C on plasma components and fractionation were discussed. This storage temperature is already used in The Netherlands and apparently is associated with improved quality of platelets. Dr Smith thought it to be an unattractive proposition in terms of fractionation since it would almost certainly reduce the yield of FVIII and possibly lead to FIX activation. BPL are presently carrying out a small scale study with Cardiff RTC (3 kg) to look at the effects. The fractionation will not be carried through to finished product. Samples for thrombogenicity testing in animals will only be available after a large scale preparation. Apparently the storage temperature of blood (and periods of storage) vary in different RTCs at present. The decrease of FVIII during storage could be reduced by using half-strength citrate as suggested by PFC. Storage at 20°C apparently has no effect on albumin or IgG according to the experience of the Dutch - however BPL will have no data of their own until they carry out a large scale preparation. Studies on the cellular components of blood are being coordinated by Dr W Ouwehand and Dr L Williamson, Cambridge RTC. Studies are also required to investigate the possibility of increased frequency of bacterial infection with storage at

20°C.

7. Items for Future Discussion

Future meetings will continue discussion on the following topics:

Revision of UK Guidelines
Hepatitis C Testing
Revision of EC Guidelines
Effect of Storage of Blood at 20°C

8. Any Other Business

None.

9. Next Meeting

The next meeting is planned for early/mid December and the Chair will circulate members to set a suitable date.