UKBTS/NIBSC
STANDING ADVISORY COMMITTEE ON BLOOD COMPONENTS MEETING

WEST END DONOR CENTRE, LONDON
10 JUNE 1999 AT 11.00 AM

MINUTE

SACBC 99.3 1.1 **PRESENT**

Dr L Williamson (Chair)	**LW**
Mr M Bruce (Secretary)	**MB**
Dr K Forman	**KF**
Mr P Garwood	**PG**
Dr P Metcalfe	**PM**
Dr D Pamphilon	**DP**
Dr CV Prowse	**CVP**

SACBC 99.3 1.2 **APOLOGIES**

Apologies were received from Mrs M Ashford, Dr C Dash and Mr A Slopecki.

SACBC 99.3 1.3 **DECLARATION OF INTERESTS**

Only CVP had a new interest to declare. On behalf of SNBTS, he was entering into a short term contract with Macopharma for the evaluation of their FFP MBT system. CVP to confirm this in writing to MB. **CVP**

SACBC 99.3 1.4 **MINUTES OF THE LAST MEETING**

1.4.1 It was agreed there was duplication of text involving the last sentence of 2.3.12 and 2.3.13. The former to be deleted.

1.4.2 Re 2.3.12/13 and italicised comment added after meeting, it was noted that Cerus now have phase III approval for platelets and plasma (plus phase Ib approval for red cells).

SACBC 99.3 2.0 **MATTERS ARISING, NOT OTHERWISE ON THE AGENDA**

SACBC 99.3 2.1 **RED BOOK AVAILABILITY**

2.1.1 The SACBC discussed the availability of the Red Book in electronic format.

2.1.2 It was agreed that there was a need to improve the availability/accessibility of the Red Book. Intra and Internet were seen as tools that could assist this process, but brought inherent problems of document control.

2.1.3 It was agreed that current document control measures were cumbersome and full compliance was difficult to guarantee.

2.1.4 SACBC considered that document control should be enforced within the UKBTS.

2.1.5 It was proposed that if the Red Book were to be accessible on the Internet, then there should be a clear statement that regular checks of the website should be made to ensure that:

- changes introduced over time have been downloaded;
- that regular checks of the website should be made to ensure that changes have been downloaded.

The website manager would be responsible for ensuring that the 'current' document identities were clearly posted.

It was agreed that Internet documents should have a distinguishing watermark (this could include 'the disclaimer').

2.1.6 The principles outlined in 2.1.5 should also apply to 'Intranet' documents and copies.

2.1.7 LW to take these proposals to the Red Book Executive. **LW**

SACBC 99.3 2.2 **RE-ISSUE OF BLOOD COMPONENTS**

LW updated the SAC. It was agreed that this should be off agenda until I Wilcox and the group has made significant progress. It was noted IW had been encouraged to use the guidelines to develop a protocol for re-issuing blood components under a concessionary release protocol.

SACBC 99.3 3.0 **MATTERS ARISING FROM MINUTES OF THE RED BOOK EXECUTIVE COMMITTEE, 01 APRIL 1999**

SACBC 99.3 3.1 **SACBC COMMENTS ON RESTRUCTURING**

Unfortunately, due to a delayed flight, MB had arrived at the meeting after discussion on these comments had started. SACBC noted the decisions recorded.

SACBC 99.3 3.2 **4th EDITION TIMETABLE**

3.2.1 SACBC expressed concern at the November 1999 deadline recorded in the Executive Committee minutes. MB advised he understood this to be the date when the Executive expected to receive revised manuscripts.

3.2.2 SACBC wished to record that, as a result of leucodepletion, the Blood Components sections would require significant change. Previous experience suggested that several iterations would be needed to achieve a final version.

3.2.3 MB and AS would write to colleagues in SNBTS/NIBTS and NBS/Welsh BTS respectively, indicating that the revision process for the 4th Edition is underway, and inviting comments/suggested changes by 31 July 1999. MB would communicate this to AS. **MB/AS** **MB**

3.2.4 SACBC would send suggested changes to MB by 31 July 1999. MB would attempt to produce a draft revision for the SACBC in September 1999. **ALL** **MB**

3.2.5 LW to raise the concerns about timescale with the Executive to ascertain the milestones on the publication plan and seek assurances **LW**

that all SACs will be held to an agreed set of dates.

SACBC 99.3 3.3 **SAC ON FRACTIONATION**

It was noted that this SAC would continue to meet but on an infrequent basis. The working party on Immunoglobulins would not, at this time, merge with the SAC on Fractionation.

SACBC 99.3 3.4 **APHERESIS WORKING PARTY**

3.4.1 It was noted that the Executive had agreed the NBS Apheresis Technical Group should be reconstituted as a UKBTS Group, although it was not clear whether this had been progressed. LW to follow up. **LW**

3.4.2 SACBC continued to feel that there should be one Apheresis Working Party which reported as appropriate to the SAC on Donor Selection and SACBC. LW to raise at next Executive Committee meeting. **LW**

SACBC 99.3 3.5 **SACBC TECHNICAL SUB-COMMITTEE**

3.5.1 LW advised that the Executive Committee had endorsed a proposal for the above Technical Sub Committee.

~~3.5~~.2 PM/CVP agreed to produce a draft remit for the sub committee before the September 1999 SACBC meeting. **PM/CVP**

3.5.3 It was planned to have a finalised remit for the October 1999 Executive Committee meeting. It was envisaged that the sub committee would start work in the Spring of 2000.

3.5.4 It was agreed that SACBC should nominate the sub committee chair. SAC to submit proposals for chair and members to LW. **ALL**

SACBC 99.3 4.0 **PROPOSALS FOR CHANGES TO BLOOD BAG BASE LABELS**

SACBC 99.3 4.1 The Executive Committee had approved the proposed base label changes. MB/AS would seek legal opinion on the changes. **MB/AS**

SACBC 99.3 4.2 LW advised that she had presented the proposals to the BCSH Blood Transfusion Task Force, who also agreed the proposed changes were appropriate.

SACBC 99.3 4.3 LW advised that the draft 6th Edition of the Council of Europe text gives an option of incorporating information that would normally appear on the label into a Product (Component) Information Sheet. SACBC felt that if used, a copy would need to be provided with each component.

SACBC 99.3 5.0 **REPORT FROM WORKING PARTY ON HAEMOPOEITIC GROWTH FACTORS**

SACBC 99.3 5.1 SACBC discussed L177 (the recirculated, 3 page version) and the following were noted/agreed:

SACBC 99.3 5.2 F Boulton and V James represent SAC on Donor Selection on the above working group. The working group considered that the use of donor granulocyte mobilisation should be subject to a controlled study prior to making recommendations about the use of this approach. SACBC endorsed this proposal.

SACBC 99.3 5.3 Steve Deveraux, Mike Murphy and DP have written to A Robinson

seeking support for the relevant study which would require ethics approval. AR has circulated this for comment, but no feedback has been received.

SACBC 99.3 5.4 SACBC discussed the problems and concerns arising from the need to release these components prior to completion of mandatory testing. It was suggested that these concerns could, in part, be allayed by, eg:

- specifying highly accredited donors (similar to the donor specification for Anti-D boosting, ie RhD positive red cell donors);
- testing the donor where possible (eg G mobilised), the day before granulocyte harvest (in addition to testing the sample taken with the donation).

DP agreed to incorporate these suggestions into a revised donor specification. **DP**

SACBC 99.3 5.5 There was discussion as to whether mobilised granulocytes should be incorporated into manufacturers' 'specials' licenses. AS/MB to consider. **AS/MB**

SACBC 99.3 5.6 SACBC were asked to send DP comments on L177 by 11 June 1999. DP will redraft and recirculate. **ALL**

SACBC 99.3 5.7 It was agreed that the Executive Committee needed to be aware of this activity, but was considered that the proposed study should be completed prior to submitting formal proposals to the Executive for inclusion in the Red Book. **LW**

SACBC 99.3 6.0 **BLEED TIMES**

SACBC 99.3 6.1 SACBC reviewed L182; L206; L207 and M99_ 25 (which was issued by MB after the main agenda papers had been circulated). MB advised SNBTS had discussed this at length and had sought advice from AABB (who had recently changed their specification to 12-15 minutes for FFP and platelet production).

SACBC 99.3 6.2 SACBC noted that there was no literature to support a specified bleed time and noted that SNBTS, NBS London and South East Zone, and NBS Midlands and South West Zone all use a 15 minute cut off for FFP and platelets.

SACBC 99.3 6.3 SACBC agreed that 15 minutes should be the bleed time cut off for component production. LW would make this proposal to the forthcoming Executive Committee meeting and also would reply to E Love. **LW**

SACBC 99.3 7.0 **GAMMA IRRADIATION OF BLOOD COMPONENTS**

SACBC 99.3 7.1 DP made specific comments on refs. # iv.1.bi and # iv.1.ei and LW will communicate these to FDA. SACBC were asked to submit comments on L183 to LW. **LW ALL**

SACBC 99.3 7.2 Regarding component irradiation for premature infants (L208), SACBC noted the SNBTS position but were unable to support this because:

i) of concerns about loss of GMP control resulting from having to irradiate these components outwith an MCA licensed facility.
ii) this group of patients was considered when the current BCSH

guideline was produced but was excluded on the basis of lack of evidence of GVHD risk.

iii) all such patients would be receiving leucodepleted components.

SACBC 99.3 7.3 LW advised that the Blood Transfusion Task Force had commissioned a drafting group to revise the guidelines for neonatal transfusion. DP and A Todd are on this group and will be asked to address the risks for such patients versus GMP/operational concerns. **DP/ A Todd**

SACBC 99.3 7.4 SACBC noted that there has been one case of GVHD in a neonate reported to SHOT. This patient had a major immunodeficiency syndrome and received non-leucodepleted red cells for a top-up transfusion.

SACBC 99.3 8.0 **APHERESIS**

SACBC 99.3 8.1 **COBE SPECTRA: BACTERIAL CULTURE OF COMPONENTS**

8.1.1 At an earlier meeting, SACBC had agreed that prior to 'signing off' COBE Spectra leucodepleted platelets, there should be a study to confirm lack of evidence of bacterial contamination in such components.

8.1.2 MB had circulated a report (M99_24) which reported the results of culturing over 1000 COBE apheresis platelets.

8.1.3 MB agreed to further analyse the data into COBE Spectra and COBE Spectra Turbo, leucodepleted and non-leucodepleted and would report back (if possible for the 30 June 1999 Executive Committee meeting). **MB**

SACBC 99.3 8.2 **BAXTER AMICUS**

8.2.1 MB had circulated a copy of the phase 0 evaluation of the Baxter Amicus leucodepleted plateletpheresis system performed by the team at the Dundee RTC.

8.2.2 SACBC approved progression to phase 1 studies.

8.2.3 It was noted that phase 0 studies were also in progress in Trent and Cardiff blood centres. MB raised concern at this, as a key objective of the generic evaluation protocols was to avoid duplication of effort (especially in phase 0).

8.2.4 It was agreed that co-ordination of such activities via the Apheresis Group and the recently approved Components Technical Sub-Group, both reporting to SACBC, would resolve this problem. LW to raise again with the Executive Committee. **LW**

SACBC 99.3 9.0 **FRESH FROZEN PLASMA**

SACBC 99.3 9.1 **HOLD TIME PRIOR TO PREPARATION**

9.1.1 SACBC discussed L178 and M99_25. LW also referred to the draft 6th edition of the Council of Europe component guidelines (which specifies a maximum hold time prior to preparation of 18 hours versus the current Red Book specification of 8 hours).

9.1.2 SACBC agreed the UK specification should be changed to "processed within 18 hours of venepuncture by a process that ensures 75% of components have ≥ 0.7 IU Factor VIII / ml".

SACBC 99.3 **9.2 DEFINITION OF ACCREDITED DONORS (FOR FFP PREPARATION)**

9.2.1 SACBC noted (M99_23) that the changed definition for 'accredited donors' for FFP preparation incorporated in the recently revised Red Book section on Neonatal Components, had not also been completed for adult plasma components.

9.2.2 MB advised that the wording in this revised definition was open to interpretation. SACBC agreed this definition should be revised to:
"a donor who has been tested at least once in the last 24 months and who has produced negative results for mandatory markers on all occasions."

9.2.3 This change will be incorporated in the next edition of the Red Book. Meanwhile, MB to communicate the change to National QA Managers. **MB**

SACBC 99.3 **9.3 VIRUS INACTIVATION OF FRESH FROZEN PLASMA**

9.3.1 With regard to the DNV risk assessment (extract L195), SACBC noted that MSBT have not taken a view on the continued use of UK plasma for direct clinical use.

9.3.2 SACBC also noted the Council of Europe comment on virus inactivation of FFP (extract, L209), but felt this could be open to interpretation (ie the reference to the availability of virus inactivated products could refer to fractionated products).

9.3.3 SACBC discussed the 'statement' on FFP from a group of UK Haematologists (L210). SACBC were concerned at the content of this document:

- it conflicted with the agreed (but draft) BCSH Task Force position, ie not to recommend 100% VIP;
- the document expresses a desire to have a virus inactivated FFP available in the UK as soon as possible but also expresses doubts about Methylene Blue and concerns about solvent detergent treated components;
- the document raises the possibility of importing plasma for FFP production. However, MB pointed out the potential virological risks of such plasma if used without a virus inactivation process (especially if paid donors were to be used);
- there was no input to the discussions from an experienced virologist;
- personal communication from some of the Haematologists named on the document indicated they had not agreed its' contents;
- it was not clear to SACBC to what extent those involved in the discussions from which the document resulted were fully up to date with the subject matter as developments were ongoing.

9.3.4 SACBC agreed it was essential that an up to date position on FFP, its' country of origin and virus inactivation options was produced and issued to users. It was agreed a newsletter was the best vehicle for doing so. DP agreed to produce a draft section on FFP and would circulate this for comment in the next 3-4 weeks (ie by 10 July 1999). **DP ALL**

9.3.5 SACBC continued to endorse the use of MBT FFP and the on-going

exercise to collect data and evidence on absence of toxicological effects. LW to advise the Executive Committee of this position. **LW**

9.3.6 Regarding the draft specification for MBT FFP (M99_15), SACBC agreed the Factor VIII specification should be 0.5 IU/ml. MB to modify. **MB**

9.3.7 SACBC noted that NBS were in discussion with Cerus concerning the evaluation of S59 for virus inactivation of FFP.

9.3.8 SACBC noted the FDA recalls of SD treated FFP (L214) due to transmissions of parvovirus B19.

SACBC 99.3 **10.0 LEUCOCYTE DEPLETION**

SACBC 99.3 **10.1 SPECIFICATIONS**

10.1.1 SACBC discussed L215-L219 and concluded that it should recommend a leucodepletion specification of 99% of components to have $< 5 \times 10^6$ leucocytes with 95% confidence.

10.1.2 Data from UK services suggested this would not be problematic, although it would probably be most challenging for SNBTS who were leucodepleting almost all whole blood at 20^0 C and had encountered a number of constraints to achieving effective leucodepletion by this approach.

10.1.3 MA/MB will produce a summary of capability data for the next SACBC meeting. **MA/MB**

10.1.4 The specification will be kept under continual review and will be adjusted as appropriate.

SACBC 99.3 **10.2 LABELLING**

10.2.1 SACBC noted that NBS would be incorporating the words 'Leucocyte Depleted' on their component labels. MB advised SNBTS had registered a 'set' of leucodepleted plasma component labels with Mike Clarke.

10.2.2 SACBC noted LW's correspondence with Henry Hambley (L220) and agreed that item 4 of L220 should be kept under review (the time at which 'leucodepleted' would be removed from the label).

10.2.3 MB would advise National Quality Managers of the agreed name to be printed in the label of 'neonatal components'. **MB**

SACBC 99.3 10.3 **HbS DONORS**

10.3.1 SACBC noted the data provided by LW from NBS studies to date (L221).

10.3.2 DP advised that arrangements had been made to collect donations from a number of HbS donors in Bristol. The evaluation of filters with these donors will be discussed at a forthcoming NBS project team meeting.

10.3.3 LW advised that with regard to the 01 April 1999 Executive Committee minute, item 10.5, T Wallington will be convening a group to bring forward recommendations on the management of HbS donors. The options were likely to be:

- remove from panel;
- keep on panel and count each one;
- continue to search for suitable filters;
- use for platelets/plasma only (but note, cannot apherese).

SACBC 99.3 10.4 **PROFICIENCY TESTING**

10.4.1 **NEQAS**
Process at advanced stage, preliminary data (L222) showed excellent correlation between centres. Twelve, monthly exercises will be run in the pilot study.

10.4.2 **PEQAS/REQAS (NBS Scheme)**
This scheme is on-going and uses filtered components. LW advised that SNBTS would be welcome to join. MB noted that data analysis would be performed by NIBSC and agreed to progress SNBTS involvement. **MB**

SACBC 99.3 10.5 **CMV SAFETY**

10.5.1 SACBC discussed L223 and the last 2 pages of L218. It was agreed the best approach was to compile around one year's leucodepletion performance/capability data and present this to SACTTI.

10.5.2 SACBC noted that the text in the Red Book regarding CMV equivalence of seronegativity and leucodepletion would need to be modified to reflect current SACTTI/Executive Committee view. **MB**

SACBC 99.3 11.0 **AOB**

SACBC 99.3 11.1 **FDA PROPOSAL ON PLATELET EVALUATIONS**

CVP had pre-circulated an FDA discussion document on the evaluation of platelet components. There was a 60-day deadline for comments. CVP advised that if all the proposals were accepted then virtually no UK service would be able to comply and, from discussions with US colleagues only one, or at most two US services could. CVP/LW to compile a response. **CVP/LW**

SACBC 99.3 11.2 **PAPERS TABLED**

The following papers were tabled at the meeting:

- L225 Adverse Periocular Reaction After Blood Transfusion;
- L226 Hypotension and Bedside Leucocyte Reduction Filters.

SACBC 99.3 12.0 **FUTURE MEETINGS**

Wednesday 15 September 1999, Edinburgh (venue to be arranged)
Wednesday 15 December 1999, West End Donor Centre, London