UKBTS / NIBSC

STANDING ADVISORY COMMITTEE ON BLOOD COMPONENTS
NEWCASTLE BLOOD CENTRE

11 March 1999, 11.00 am

MINUTE

SACBC 99.1 1.1 PRESENT

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

SACBC 99.1 1.2 APOLOGIES

Apologies were received from Dr C Dash, Dr K Forman, Mr A Slopecki.

SACBC 99.1 1.3 MINUTES OF PREVIOUS MEETINGS

The minutes of the 10 September 1998 meeting and note of the 17 December 1998 meeting were approved as a true record.

SACBC 99.1 1.4 DECLARATION OF INTERESTS

There were no new interests to be declared.

SACBC 99.1 2. **MATTERS ARISING FROM PREVIOUS SACBC MEETINGS, NOT ON THIS AGENDA**

SACBC 99.1 2.1 RED BOOK AMENDMENTS 1998

Final copy of the various amendments were attached for information as L185 - L190. The various documents had been proofed. Final publication/issue dates were not yet known.

SACBC 99.1 2.2 RED BOOK: AVAILABILITY

MB had received an inquiry from a colleague in Denmark regarding the availability of the current edition of the Red Book. On checking, MB noted there was no ISBN reference number. This also applied to subsequent addenda, eg Blood Component Labelling; EDI. LW/MB to raise with Virge James. **LW/MB**

SACBC 99.1 2.3 METHYLENE BLUE FFP

2.3.1 LW referred to the update given in the paper (L193) from AS that was tabled at the meeting. This indicated that MDA were

seeking to confirm the Baxter product conformed to the relevant medical evaluation criteria.

2.3.2 MB has again asked Dr M Kavanagh to confirm the MCA position in writing. MB has had four verbal assurances, LW one, that as the Baxter product has a CE mark, it is 'licensed' as an in-vitro Medical Device and is available for use in the UK (Europe). As the MB Baxter Pathinact system is a medical device, the primary responsibility for this lies with the MDA who are investigating. (MB has also written to MDA without reply).

2.3.3 CVP updated the SAC on the position with MBT FFP elsewhere in Europe.

In Germany, the Paul Ehrlich Institute (PEI) have not yet licensed the Springe technology. However, this was due to concerns about lack of evidence to demonstrate non-toxicity, not about concerns about the efficacy of HCV inactivation process.

It was thought that in Germany, removal of MBT by filtration was likely to be a requirement for approval by PEI. CVP had been attempting to procure information from Dr Harold Mohr at Springe and agreed to follow this up. **CVP**

In Spain, the Grifols plant is routinely producing MBT plasma using the Springe technology.

2.3.4 CVP advised that in Scotland, use of MBT FFP is currently around 2000 units/year (approximately 10% of demand) vs an estimated demand of 4000 units.

2.3.5 SACBC noted the imbalanced UK position re MBT FFP availability and reaffirmed their support for the introduction of this component as recommended by MSBT.

2.3.6 SNBTS now had 8 months experience of routine production of this component and SACBC agreed that, as requested by the Red Book Executive, the Quality Monitoring data from these should be used to support a final specification which the Executive Committee would be invited to approve. MB to draft. **MB**

2.3.7 CVP agreed to produce a summary position paper on MBT FFP to accompany the final specification. **CVP**

2.3.8 LW will write to Angela Robinson to ask her to confirm the MSBT position re MBT FFP. **LW**

2.3.9 MB agreed to contact MCA to ask them to record their position in writing and would also follow-up with MDA. **MB**

2.3.10 LW will ask Virge James to put this item on the forthcoming Red Book Executive meeting. MB will present. **MB**

2.3.11 LW tabled L195 which was an extract from the vCJD Risk Assessment document that addressed the issue of pooled vs un-pooled plasma components. This was clearly of relevance to virus inactivated plasma (VIP). There was difficulty in

comparing risk of nv CJD in plasmas from different sources but, in general, single donor components were to be preferred unless blood infectivity was shown to be very low. LW would take this to the next meeting of the BCSH Blood Transfusion Task Force on 19 March 1999. (The VIP addendum to the BCSH guideline on use of FFP had been held pending the publication of the Risk Assessment). **LW**

2.3.12 Regarding the Baxter/Cerus Corp virus inactivation development programme, CVP advised he had an update on S59 for FFP in Phase IIb trial. CVP to circulate. DP suggested that Cerus were having difficluties gaining FDA approval with regard to Phase III clinical trial. **CVP**

2.3.13 DP indicated that Cerus were having difficulty gaining FDA approval with regard to Phase III clinical trial for S59 treated platelets.

Note added after meeting: *CVP advises that Cerus now have US and european approval for Phase III trials.*

2.3.14 DP put forward an informed view that S59 treated FFP/platelets will not be available for at least 2 years. This was important information, particularly with respect to MBT FFP introduction.

SACBC 99.1 **3. MATTERS ARISING FROM THE RED BOOK EXECUTIVE COMMITTEE MEETING, 14 DECEMBER 1998**

SACBC 99.1 3.1 STRUCTURE OF THE RED BOOK

3.1.1 There was unanimous support for a proposal that an important part of the remit of the SAC members would be to consult widely on proposed changes/developments but that no formal infrastructure to permit this was in place.

3.1.2 LW proposed that there was a need for a technical group of SACBC to work on matters such as sampling protocols, counting systems, use of statistics in quality monitoring etc. This received unanimous support. LW/MB to ask the Executive Committee for approval to define the remit and reporting lines for such a technical working group. **LW/MB**

3.1.3 There was discussion concerning apheresis working groups and the SACBC view was that there should be a single UK group, within the Red Book Structure.

3.1.4 It was noted that some Working Parties may need to report to more than one SAC on different aspects of their activity, eg apheresis may report to the Donor SAC on donor matters and the SACBC on component evaluation matters.

3.1.5 It was noted that there seemed to be two working parties on stem cells, one reporting to the Donor SAC and one reporting to the Tissue Banking SAC.

3.1.6 There was a need for consistency in naming working parties, subgroups etc.

SACBC 99.1 3.2 IMMUNOGLOBULIN WORKING PARTY/PLASMA FOR FRACTIONATION SAC

3.2.1 L173 and L174 were noted. The SAC agreed these were important working groups which needed to keep abreast of developments to ensure smooth re-introduction of UK derived anti-D and other fractionated products (if approved).

3.2.2 There was discussion on whether the Immunoglobulin Working Party and the Plasma for Fractionation Group could merge, at least for the time being and be a combined sub-group of SACBC.

3.2.3 One possibility was for such a merged group to report through SACBC. However, LW was of the opinion that SACBC would be fully occupied dealing with issues arising from leucodepletion and virus inactivation.

3.2.4 LW to produce a written summary of these views for the Red Book Executive meeting. **LW**

SACBC 99.1 3.3 TERMS OF OFFICE

3.3.1 SACBC supported the general principle of fixed term appointments but felt this would cause multiple practical difficulties. A review point after say three years was preferable.

3.3.2 SACBC were concerned that fixed terms of office for SAC members may impair functionality through loss of expertise; inability to use appropriate expertise; lack of suitable personnel.

3.3.3 MB raised the issue of dual SAC membership to create linkages and facilitate parallel developments. These would be problematic if terms of office were fixed.

3.3.4 SACBC felt it was important that any new Chair normally was appointed from within the SAC - this may demand an element of succession planning.

3.3.5 If the proposed fixed terms of office should be introduced, many members of SACBC will be obliged to stand down at the same time.

SACBC 99.1 3.4 LW/MB would take these views to the Executive Committee

SACBC 99.1 4. **LEUCOCYTE DEPLETION**

SACBC 99.1 4.1 CONFIRMATION OF MSBT REQUIREMENTS

4.1.1 LW had asked Angela Robinson to confirm that the deadline of 01 November 1999 represented the date from which all manufactured components will be leucodepleted.

Note added after meeting: *This has now been confirmed by Dr Robinson.*

4.1.3 MB raised the issue of frozen red cells. Many units currently held in frozen storage were not leucocyte depleted. However, these will be washed on thawing. NBA have a concessionary

issue process for such components and will use this approach.

SACBC 99.1 4.2 EVALUATION PROCESS

4.2.1 It was noted that all NBS evaluation reports are being sent to AS. MB/AS to share evaluation reports; this to be extended to Welsh BTS and Northern Ireland BTS. **MB/AS**

4.2.2 The evaluation and validation of leucodepletion systems to be discussed in more detail at the next SACBC meeting. **LW**

SACBC 99.1 4.3 CAPABILITY DATA/NEW SPECIFICATIONS

4.3.1 MA highlighted a few of the processes/changes that will impact on capability data and component specifications. ie:

- changes to sampling protocols;
- differences in whole blood collection volumes;
- red cell loss over filtration;
- accuracy and consistency of sampling for white cell counts;
- problems/differences in counting equipment (Newcastle analyser non-linear on upper limit platelet counts).

4.3.2 NBS are implementing process improvements to try and optimise red cell yield, eg new Optipress backplates; 'dry' buffy coats.

4.3.3 MA to collate as much capability data as possible on leucodepleted components. MB to provide MA with SNBTS data. **MA MB**

4.3.4 It was noted that the target date for the next Red Book edition was April 2000. This was a significant undertaking for SACBC.

4.3.5 It was agreed that percentage haemolysis at expiry should be measured during phase 0 and phase 1 studies on leucodepleted red cell components.

Swirling should be performed during platelet studies and eventually considered as a quality parameter. **MB**

SACBC 99.1 4.4 LABELLING REQUIREMENTS

4.4.1 The SAC noted the correspondence between Drs Hambley and Williamson (L173/L174) and discussed the paper (m99_06) produced by MB.

4.4.2 The SAC agreed:

- the ultimate objective (ie some time after 100% leucodepletion had been implemented) would be to remove the statement 'LEUCOCYTE DEPLETED' from the label;
- during the transition and for a period of time thereafter, red cell and platelet components that had been subjected to a leucodepletion process would be labelled 'LEUCOCYTE DEPLETED';
- it would be inappropriate to specifically label those components where the white cell count had been tested

and found acceptable, eg 'CONTAINS < 5 x 10^6 / Leucocytes unit.

- for platelets for IUT, each component would be counted. Any which failed the specification ie > 5 x 10^6 / Leucocytes unit would be discarded or issued under concession.

4.4.3 There was considerable debate about labelling of plasma components as leucocyte depleted.

MB felt strongly this was the most secure mechanism for achieving an effective swap out of non-leucodepleted plasma components. NBS colleagues had planned to make the swap out on the basis of date of manufacture (ie date by which all plasma components were leucodepleted).

MA highlighted a PULSE labelling problem that would require plasma components to be labelled 'LEUCOCYTE DEPLETED'. MA to follow up. **MA**

MA to discuss this issue with NIBTS/Welsh BTS prior to next weeks NBA Leucodepletion Project Implementation Board. **MA**

4.4.4 There was tacit acceptance of the need to label plasma components as 'LEUCOCYTE DEPLETED'. This then prompted significant discussion on the labelling requirements for the newly revised, 'in press' section on components for use in neonates and children under 1 year.

4.4.5 DP (L194, tabled at meeting) requested that the component name be contracted to facilitate printing, ie from 'Red Cells in Additive Solution: Suitable for use in iut, Neonates and Infants Under 1 year' to 'Red Cells in Additive Solution: Suitable for Neonates and Infants'.

4.4.6 It was agreed that MB would contact the other National QA Managers to advise them of this labelling change. **MB**

4.4.7 The SAC noted that the practical problems arising from the length of the name had not been recognised during the development process. To avoid this in future, PG agreed to produce a flow-chart setting out various links and interdependencies with, eg users; other SACs; the Executive; MCA; MDA etc. **PG**

4.4.8 The revised section on components for neonates etc (L190) had deliberately removed 'LEUCOCYTE DEPLETED' from the label as this was part of the component specification. This was discussed at length and, for the time being, it was agreed not to change the labelling requirements for these components, ie not to re-introduce 'LEUCOCYTE DEPLETED'.

4.4.9 LW agreed to summarise the situation and make a proposal for consideration by the Red Book Executive. **LW**

4.4.10 LW tabled L196, from Liz Love requesting guidance with respect to labelling requirements for platelets (re what constitutes an adult dose and whether this could be stated on

the label).

SACBC agreed that this matter was best dealt with through local education of users. LW to write to Liz Love. **LW**

SACBC 99.1 4.5 HbS DATA

4.5.1 LW summarised the results available to date. Whilst the majority of donations from HbS donors had blocked the filters, there was also concern that there may be a higher than expected failure rate. LW will send an update to SACBC members. **LW**

4.5.2 SACBC agreed it was important to identify such donors. Thereafter, donor management options included:

- removal from panel;
- chose a filter type that can be used (Pall best results at present, NPBI still to be tested);
- 100% testing.

This has the potential to be particularly problematic because of the obvious ethical issues. There also will be problems arising from the contribution some HbS donors make to rare cell panels. LW to summarise for the Executive and to suggest that Frank Boulton be asked to take this issue forward with the SAC on Donors. **LW/MB**

SACBC 99.1 4.6 NEQAS

4.6.1 LW summarised the current position. Work with NEQAS has been on-going. Problems have been identified as arising from the 'fixed' nature of white cell samples which fall outside the counting 'gate'. LW will provide collated data. **LW**

4.6.2 Results of QC testing platelet samples had not yet been reviewed.

Note added after meeting: *NBS Science and Quality Group (NBS SQG) had reviewed the total data available. This is satisfactory and the NBS Leucodepletion Project Implementation Board (PIB) will enter into a contract with NEQAS. The SQG and PIB also endorsed the continuation of the in-house exercises.*

4.6.3 LW advised that peculiar dot plots were being obtained with some Baxter filters (some fail on 'flow' but pass in Imgen and Nageotte). This was being discussed by the NBS Science and Quality sub-group.

4.6.4 CVP asked if there would be additional benefits in using in-house filtered components to reflect the actual position. It was agreed this should be discussed at a future meeting. **LW**

SACBC 99.1 4.7 COBE TRIMA REPORT

4.7.1 The SAC discussed and approved this report (L191).

4.7.2 The following clarification was given in response to questions

raised:

- if approved by SACBC, the next steps would be to progress through phase 1 (100 donations) and phase 2 (1000 donations);
- any intention of splitting to provide a double dose would be preceded by a platelet count of the harvested component.

4.7.3 It was acknowledged that there was a need to consider establishing an evaluation for collections other than platelets.

4.7.4 LW to formally communicate SACBC approval to MB and COBE. **LW**

SACBC 99.1 **5. NEW PROPOSALS FOR COMPONENT BASE LABELS**

SACBC 99.1 5.1 MB introduced paper m99_07 and explained that development of ISBT 128 labelling for the UK would require close collaboration between SACIT and SACBC.

5.2 SACBC agreed to review the mapping of current ABC Codabar barcodes and names to the ISBT 128 format once this was to hand.

5.3 SACBC noted the change in ISBT 128 labelling to a quadrant design and agreed that the following could be removed from the label:

- the statement 'do not vent';
- the additive/anticoagulant formulation.

5.4 SACBC recommended the 'CAUTIONARY' note on the CT label to be changed as follows:
From:

CAUTION

- *Always check patient/component compatibility*
- *Do not use if there are signs of deterioration or damage*
- *Use a standard transfusion set*
- *Risk of adverse reaction/infection*
- *Please contact your blood bank/BTC for further information*

To:

INSTRUCTION **MB**

- **Always check patient/component identity**
- **Risk of adverse reaction/infection - inspect for signs of deterioration or damage**

5.5 SACIT to be asked to advise whether the following can be printed beside the expiry date: **'DO NOT USE AFTER'.** **MB**

5.6 SACBC asked to be informed of the implementation timetable (Project Initiation Document is being finalised) and proposed that the opportunity should be taken to discuss labelling changes with users (eg NBA and SNBTS Users Groups; SHOT; BCSH). **MB**

	5.7	It was noted that implementing ISBT 128 may provide the ideal opportunity to remove 'LEUCOCYTE DEPLETED' from the label.	
	5.8	LW/MB to summarise for the Executive.	**LW/MB**
	5.9	AS/MB to explore the legal implications of these proposed label changes	**AS/MB**
SACBC 99.1	6.	**RE-ISSUE OF BLOOD COMPONENTS**	
SACBC 99.1	6.1	SACBC discussed L179 - 181 and L 192. Whilst understanding the thrust of the proposals, SACBC felt it would be helpful to have an indication of the extent to which this approach would significantly increase the availability of blood and how many hospitals would be able to provide a full audit trail. LW to ask Ian Wilcox for information.	**LW**
SACBC 99.1	6.2	SACBC recognised that under exceptional circumstances blood components are currently taken back into stock from hospitals under concession. It was thought developing the protocol for use in this application, ie for concessionary issues would be useful. LW to communicate this to Ian Wilcox.	**LW**
SACBC 99.1	7.	**ISSUE OF UNTESTED GRANULOCYTES**	
SACBC 99.1	7.1	DP introduced this topic which was set out in L194 (tabled at meeting). It was agreed that at present this should be covered by a concessionary issue, authorised by appropriate medical staff and documented accordingly.	
SACBC 99.1	7.2	SACBC considered that this issue represented one of risk management ie the relative risk of infection associated with the use of this component vs the risk to the patient of not receiving the component on time (critical clinical condition and deterioration of component). SACBC could address the shelf life of the component but six hours would seem to be the limit.	
SACBC 99.1	8.	**CMV TESTING OF SKIN DONORS** LW tabled L197, correspondence from Ruth Warwick asking for a view from SACBC on whether skin donors for use in burns cases should be screened for CMV. LW to suggest that an opinion be sought from SACTTI.	**LW**

SACBC 99.1 9. **CARRIED FORWARD TO NEXT MEETING**

The following items will be carried forward to the 10 June 1999 meeting: (I know we touched very briefly on a few of these but must have been asleep if there was anything significant to record).

1.1 (Ref 6.2) Approved L/D Systems, evaluation status
1.2 (Ref 6.3) Capability Data/New Specifications
1.3 (Ref 6.5) Temperature Requirements During Processing
1.4 (Ref 6.8) Batch pre-acceptance of filters
1.5 (Ref 6.9) Contingency for 'out of specification' incidents
1.6 (Ref 8.0; L177) Working Party on Haemopoietic Growth Factors
1.7 (Ref 9.0; L178) Preparation of FFP
1.8 (Ref 11.0; L182) Bleed Times
1.9 (Ref 12.0; L183) Gamma Irradiation of Blood Components

SACBC 99.1 10. **FUTURE MEETINGS**

Thursday 10 June 1999, West End Donor Centre, London
Wednesday 15 September 1999, Edinburgh
Wednesday 15 December 1999, West End Donor Centre, London