2001

JOINT MEETING OF THE UKBTS/NIBSC STANDING ADVISORY COMMITTEE ON BLOOD COMPONENTS AND TRANSFUSION TRANSMITTED INFECTIONS UNIVERSITY OF MANCHESTER, 26 NOVEMBER 2001

1. PRESENT

Lorna Williamson	Willie Murphy	Marcela Contreras
Liz Love	Geoff Geddis	Angela Robinson
Chris Prowse	Keiran Morris	Patricia Hewitt
Martin Bruce	John Barbara	Neil Beckman
Graeme Rowe	Kate Soldan	Carl McDonald
Sheila MacLennan	Katie Forman	Peter Garwood
Brian McClelland	George Galea	Roger Eglin
Michelle Ashford	Rebecca Cardigan	Chris Hodson

2. Questions/Comments on Kate Soldan's Presentation
Bacterial Risks in Platelets and Red Cells

C V Prowse — From the data presented were there any transmissions involving red cells and platelets from the same donation and does the data presented include Scotland?

K Soldan — No, and no i.e. there is a non-fatal bacterial transmission to be added from Scotland.

L Love — Asked K Soldan whether the SHOT data presently being assembled show a sustained increase in bacterial transmissions.

K Soldan — No, nor is there evidence that universal component leucodepletion has generated an increase or a decrease in transmissions.

N Beckman — With regard to the post transfusion infections that had not been traced back to the donor, NB asked if any information was recorded regarding the pack type, pack manufacturer, processing method, etc. It was noted this was not being done at present but merited further consideration.

There was a general discussion about the different position regarding Yerseinia and the relative incidence of TTI cases in various parts of the world but no authoritative figures were available.

J Barbara — Advised that screening for bacteria would detect some and leucocyte depletion will remove bacteria but not toxins.

P Garwood — Asked if anyone had explored the distribution of anaerobic versus aerobic bacteria in TTI's.

C McDonald — Advised all of their cases had been aerobic with the exception of one case involving Clostridium.

G Rowe — Noted that apheresis platelets seemed to carry only 50% of the risk associated with pooled platelets (pools are derived from 4 donors, therefore 4 times less risk would be expected from a single donor component).

3. Questions/Comments on Carl McDonald's Presentation
Effects of Arm Cleansing/ Divert Pouches

Carl's presentation set out the data which supported the potential risk reductions that could be achieved by introducing improved VP site preparation, diversion of the first Xmls of the donation and bacterial screening.

With regard to the first of these strategies, NBS had found the Mediflex alcohol/iodine process operationally difficult to implement. CMcD advised that Mediflex had developed single step an alcohol/chlorhexidine device which compared well with the alcohol iodine system. Unfortunately, this latter system contained too much alcohol therefore took 90 seconds to dry.
Mediflex were working with CMcD and his team in an attempt to produce an effective VP site preparation device that would fit in with the practical constraints of blood collection (i.e. single step, 30 seconds clean, 30 seconds drying time – preliminary studies were promising).

M Ashford — Asked whether the studies looked at operational issues as well as scientific aspects. CMcD confirmed science only.

L Williamson — Asked whether the single stage alcohol device would replace the alcohol/iodine system used in apheresis if it proves of equivalent performance. CMcD answered in the affirmative.

J Barbara — Expressed concern that NBS implementation of the system had been substantially delayed because of concerns raised by blood collection staff (the length of time taken for the procedure which would have a disruptive effect on blood collection). Also expressed concern that NBS Donor Services had been unable to send a representative to input to this joint SACTTI/SACBC meeting because of a previously arranged directorate conference.

M Contreras — Asked CMcD to confirm that in the arm preparation effectiveness studies, no donations were tested i.e. especially from those donors showing significant growth post arm cleaning. CMcD confirmed this was the case, and noted the method used was incompatible with normal donation technique.

M Bruce — Asked CMcD to advise whether the same methodology was used for validation and monitoring studies. CMcD advised that validation studies used swabs which were subsequently used to inoculate plates. Contact plates were used in monitoring exercises. The strategy was to use a more sensitive approach in validation studies.

B McClelland — Raised the issue of palpation of the vein by the venepuncturist post cleaning. This provoked discussion in which it was acknowledged that some donors have very difficult veins; that NBS SOPs and training are explicit re the need for "no touch" VP technique; that arm preparation is one (albeit very important) of a number of measures that can be taken to reduce the risiks of transmitting bacterial infections.

S Maclennan — Asked whether all NBS apheresis teams were using the two stage alcohol/iodine method. CMcD responded that the majority were but not all were doing so. This exchange led to a realisation that K Soldan needs such information to optimise her analysis of the data i.e. of a bacterial transmission has taken place, what was the arm preparation procedure? Was the first 30ml of donation "diverted"? etc.

A Robinson — Expressed concern that 24 months after CMcD had illustrated the superior performance of the Mediflex alcohol/iodine arm preparation procedure it still had not been implemented by all the NBS apheresis teams.
With regard to palpation of the vein, AR re-emphasised that NBS training and SOPs were very strict on a "no touch" technique. A Robinson expressed her full agreement with the earlier comments made by J Barbara about the non attendance of NBS Blood Collection

Staff at this meeting.

L Love — Asked K Soldan to apply the projected reduction in risk arising from various approaches to estimate the number of transmissions saved.

M Bruce — Regarding diversion, Carl McDonald's data had shown that diversion into pouch 2 still produced bacterial growth. Therefore, there was a need to specify a minimum volume to give confidence that diversion will be effective. This was agreed, to be considered in the afternoon session.

W Murphy — Expressed surprise at the high rate of bacterial contamination reported in the diversion study (1.5%) and wondered whether the study reflected actual practice.

G Geddis — Asked how long after collection the diversion samples were taken. CMcD advised cultures were set up within 4 hours of donation. It was agreed this also needed to be discussed in the afternoon session.

W Murphy — Made the observation that the strategies being employed to reduce bacterial risks appear to be 66% effective but we do not fully understand why.

G Geddis — Suggested it would have been more informative to have linked the diversion studies to actual donations (CMcD had anonymised the donations).

N Beckman — Re-iterated his concern that our faith in the safety of "closed systems" is too great – bag faults may play a role.

J Barbara — Expressed the view that environmental contamination (i.e. such as bag faults) is unlikely to play a major role.

B McClelland — Suggested we should challenge the assertion that bacteria cannot penetrate "closed systems". It was agreed this would be revisited in the afternoon session.

4. Questions/Comments On Roger Eglin's/Chris Hodson's Presentation
Testing – The Current Options Available and Their Implications for Platelet Availability

With regard to R Eglin's presentation, the key points were to determine when to test (i.e. how long after donation) and how to test. It was agreed these issues would be discussed in the afternoon session. It was noted that R Eglin concluded that, at present, Bactalert offered the only realistic automated testing solution and that leucodepletion had made no real difference to the incidence of bacterial transmissions.

Chris Hodson described how Bactalert is being used in Holland. A 5ml platelet sample is taken within 2 hours of component manufacture and incubated for 7 days (aerobic and anaerobic). All components are quarantined for 24 hours pending availability of NAT results. Thereafter, platelets are issued depending on the current Bactalert test status. If the test becomes positive after the platelets have been issued, they are recalled immediately, other components are recalled the next working day (this policy was agreed by hospitals prior to implementation). Approximately 1% of platelets test Bactalert positive.

J Barbara — Asked C Hodson how many recalls were made – information not available.

G Geddis — Presently piloting Bactalert with day 2 sampling and read right through to day 5. 50 – 70% of production being tested (i.e. many untested), have had 16 or 17 recalls to date with 1 or 2 red cell units positive.

K Forman — Emphasised the importance of notifying hospitals if they have received a platelet

component that was subsequently found to be Bactalert positive.

M Contreras — Asked C Hodson whether the Dutch culture recalled red blood cell packs and, if so, how many were positive – information not available.

L Williamson — Asked R Elgin to confirm that the Pall Gas Chromatography approach could be used as a point of issue second check. RE confirmed this was correct.

5. Questions/Comments on Presentations on S59 Photo-inactivation of Platelets from:

J Barbara	***Efficacy in bacterial inactivation and other microbial benefits, including parasites, syphilis and known and unknown viruses.***
R Cardigan	***Laboratory Data on Functionality of S59 Platelets.***
Chris Prowse	***Toxicity.***
L Williamson	***Clinical Studies and Effect on TA-GvHD.***
M Ashford	***GMP Aspects.***

J Barbara — J Barbara was very confident that the S59 system will inactivate parasites, but noted some concerns on inactivation of non-enveloped viruses such as hepatitis A.

L Williamson — Proposed that the joint meeting should make a strong recommendation to the JNPAC with regard to systematic implementation of effective VP site cleaning and diversion of the first Xmls of donation ("X" to be determined).

P Hewitt — Cautioned that implementation of these measures should be developed against a backdrop of ensuring there is no detriment to existing measures that have been put in place to ensure component safety.

A Robinson — Recommended that if palpation of the "prepared" VP site was judged necessary then procedures should stipulate this must take place above or below the prepared area.

M Bruce — Proposed that the recommendations concerning VP site preparation (and its validation), monitoring the effectiveness of VP site preparation and diversion should be sufficiently detailed to permit UK standardisation/comparability of data.

B McClelland — With regard to screening tests for bacteria, BMcC strongly supported the further exploration of this option as this introduces no changes to the components Cf. pathogen inactivation which clearly does.

J Barbara — Advised that screening would be a useful approach for detecting bacteria derived from bacteraemic donors e.g. Yersinia entercolitica.
J Barbara proposed that K Soldan should provide an analysis of the benefits of adopting the various risk reduction strategies (singly and in various combinations) i.e. improved VP site preparation, diversion, screening and pathogen inactivation. ***K Soldan to provide this analysis to L Williamson.***

With regard to Pathogen Inactivation (specifically S59), J Barbara felt the cost/benefit analysis would be more complex as there were benefits not directly related to the reduction in bacterial risks.

P Garwood — Proposed there was a need to consider these risk reduction measures in a wider context, i.e. testing systems for bacterial contamination are available now. Should we divert resources to do this now? If we do, what do we stop doing? (e.g. monitoring the effectiveness of VP site preparation).
PG also questioned whether we should pathogen inactivate and test for bacteria and whether, if we did implement both risk reduction measures, whether we would

subsequently withdraw testing but continue with pathogen inactivation.

B McClelland — Recommended the development of standardised sampling procedures.

Various — A detailed discussion took place on the specification for monitoring the efficiency of VP site preparation. There were two main points of view i.e.:

- Specify a % reduction in bacterial colonies post preparation of VP site
- Specify say 90% of arms monitored having less than 10 colony forming units per plate

It was acknowledged that VP site preparation was a measure intended to reduce the potential for bacterial contamination - it was impossible to eliminate this risk.
Also it was accepted that the implementation of diversion would significantly reduce any residual bacterial risks (i.e. derived from bacteria on skin at the VP site).

It was noted that the NBS plan was to monitor the performance of every member of staff who prepares VP sites four times per year. Failure to perform satisfactorily will result in specified corrective action e.g. retraining. It was also the NBS intention to "validate" the efficiency of each batch of preparation devices before they are QC approved for use.

There was a discussion about the need for component recall if the arm preparation monitoring exercise failed to meet specified limits. CMcD felt this would be "re-prepared" after taking the post preparation contact plate. Nevertheless, there remained a possibility of poor technique failing to achieve sufficient "re-cleaning". The Working Group to consider this possibility in their deliberations.

6. *RECOMMENDATIONS*

6.1 *Arm cleansing*

It was agreed that all aspects of arm cleansing formed a critical step in bacterial prevention, and that this should be performed to an improved and agreed standard as rapidly as possible. The Mediflex system provided a good example of what could be achieved. SACTTI would appoint a Working Group to develop specific details of recommendations for arm preparation; sampling techniques; numbers of donors to be tested; numbers and frequency of staff to be tested etc. target date for recommendations April 2002.

6.2 *Diversion*

Regarding diversion, it was agreed that there was a need to consider the minimum and maximum volume to be removed pre donation. It was considered that the minimum volume should be 20ml, although it was noted that 30ml would provide an increased margin of risk reduction. However, it was noted that there was a need to comply with the requirement to remove a maximum of 13% of the donor's circulating blood volume per donation.

It was agreed that these matters also would be considered and included in the recommendations to be made by the SACTTI Working Group – timescale also April 2002.

It was noted that implementation of improved VP site preparation (and associated monitoring) and diversion of the first 20 – 30mls of the donation will result in a 70 – 75% reduction in the risk of transmitting bacterial infection with blood transfusion (and probably, in the risk of actual transmissions).

6.3 ***Bacterial screening***

It was further agreed that the SACTTI Working Group would be asked to review:

- ***The Bactalert data from assessments that have been performed in Colindale, Belfast and Glasgow with a view to recommending the optimal protocol for UK Blood Services ie considering factors such as minimum length of time from VP (or production) to sampling, incubation temp (aerobic ± anaerobic), action on positives re platelet and other components.***

- ***The potential impact of S epidemidis strain that becomes positive between days 5 and 8 (any relevance to sampling/ test protocol?)***

Target date for recommendations April 2002.

6.4 ***Pathogen Inactivation***

The way forward is to be discussed at the meeting with manufacturer in Manchester on 31st January 2002 and taken up by SAC.BC and Service operational groups for any operational assessment (expected licensure date for S-59 is April/May 2002 for EU).

EOR/NBS to assess risk reduction benefits of platelet pathogen inactivation (Baxter are doing their own Health Economic analysis and will present this at the 31st Jan meeting).

IT, illumination bulb lifetime and service and GMP aspects need to be addressed (MA). Buffy Coat and Apheresis procedures differ somewhat.

Other factors include:

- ***Are there any particular concerns for neonates (e.g. toxicology)?***
- ***What QC measures are required for the S-59 removal device?***
- ***What is the component specification (volume, platelet, %plasma, red cell limits, etc.) for component entry to the process and what are the apheresis machine options?***
- ***Are there any data on TTV/SEN-v inactivation and extension of storage to 7d?***
- ***Are there sufficient data on neoantigen absence?***

Post- meeting note from Chris Prowse: Irish regulators have passed toxicology assessment on S59 system -January 2002.

6.5 ***Haemovigilance***

It was agreed that the UK Blood Services would be asked to ensure that relevant changes in procedure (e.g. improved arm cleansing) are appropriately recorded and notified to Kate Soldan and thereby to the SHOT database.