EC 26/99

UK BTS/NIBSC STANDING ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED INFECTIONS (SACTTI)

CONFIDENTIAL

Minutes of the meeting held at
North London Centre, (Zonal Meeting Room, DBR)
on Wednesday 5th May 1999 at 11.00 am

Present:	Dr. C. Bharucha (CB) - Chairman	Dr. B McClelland (BMcL)
	Dr. P. Hewitt (PEH) - (Secretary)	Dr. P. Minor (PMi)
	Professor I. Franklin (IF)	Dr. P Mortimer (PMo)
	Dr. B. Dow (BD)	
Observer		Dr. J. O'Riordan (JO'R)

In attendance for part of meeting Dr L Williamson-Chairman SAC BC

1. Apologies

Dr. J. Barbara, Dr. Angela Robinson, Dr. Terry Snape, Professor R.S. Tedder.

CB welcomed Dr. Joan O'Riordan (Irish Blood Transfusion Service Board) as an observer. Lorna Williamson (LW) was invited, (at the request of AR) to attend for discussion on the DNV risk assessment.

2. Declaration of Interests

No new interests were declared. All members have now supplied an annual written declaration of interests.

3. Minutes of the previous meeting held on 9th March 1999.

The minutes were accepted as accurate.

4. Matters arising from 9th March 1999

4.1. Proficiency panels for HCV PCR

PMi noted that a report has been sent to participating labs. The results were presented to members. The exercise had included 2 preparations, of type 1 and type 3 in dilutions, and sent to 5 participating laboratories. The results were deemed satisfactory. It

is planned to repeat the exercise 6 monthly and using different genotypes.

A copy of the report is circulated with the minutes **(21/99)**

4.2. Leucodepletion and CMV screening.

CB has responded to Dr. Lorna Williamson and Dr. Derwood Pamphilon that more robust data is required before reaching any conclusion about equivalence of leucodepleted components and CMV negative components.

BMcL mentioned a recent paper from a Japanese group, published in "Transfusion". This is a flawed study, but it has been published. There was no evidence of benefit of filtration in prevention of CMV disease in this study.

Action: A copy of the paper to be distributed with the minutes. (22/99)

4.3. Plasma/ serum archives

A report is awaited from JAB.

4.4. Malaria antibody testing (MAT)

BD reported on this item. The NBS now has a list of approved batches of the MAT kit. The North London Centre has issued an in-house control sample to other Centres and SNBTS which is working well. SNBTS has not implemented NAT for donor screening, although testing is being carried out for NIBTS. There are apparent supply difficulties and further kits are awaited from Australia. Welsh BTS has not implemented routine MAT screening for donations because of supply difficulties.

5. HTLV (19/99)

A paper by PMo was previously circulated. PMo discussed the previous studies in the US and UK looking at transmissions to recipients, which is the best way of quantifying current risk. The most obvious group to study is multi-transfused recipients, but there are difficulties in carrying out such studies and a previous initiative by PHLS had been halted.

CB reminded those present that SACTTI has previously strongly recommended the introduction of HTLV screening for UK blood donations. With this in mind, JO'R had been invited to present the experience of the Irish BTSB.

JO'R reported that routine screening of blood donations in Ireland commenced in November 1996. A total of 380,000 donations have been screened with a repeat reactive rate of 0.05% using Abbott Prism HTLV-1 and -2. There have been 2 confirmed positives (1 in 190,000), 1 each of HTLV-1 and HTLV-2. The HTLV-1 infected donor had a partner who was also infected and who had an identified risk of blood transfusion in the US for cardiac surgery many years ago. The HTLV-2 infected donor was confirmed by PCR, although indeterminate on Western blot. Archive blood samples are also PCR positive. There is no identified risk apart from maternal transfusion at the birth of the index case. A lookback for the HTLV-1 infected donor has identified one recipient who has tested negative. A lookback for the HTLV-2 infected donor has been initiated. JO'R pointed out that the HTLV-2 prevalence in HIV infected iv drug users in Ireland is 14.6%, compared with a rate of 2.3% in a cohort of IVDUs with a lower (19%) co-infection rate with HIV. PMo was asked whether there were any prevalence studies in UK ivdus, and there are none at present.

BMcL commented that regular discussions take place at MSBT, which have also supported the introduction of screening of UK blood donations, but that this recommendation was not supported by NHSE. It is likely that this issue cannot move forward unless further data is forthcoming. The complicating factor of leucodepletion will also impact on this issue. Although there is no scientific evidence, there is a strong suggestion that the risk of infection would be reduced by the use of leucodepleted blood components. It was agreed that a further serological study in the UK, combined with the data from Ireland, would be needed to present to MSBT. PMo pointed out that cost effectiveness was a major factor in the NHSE decision, but matters have now moved on. Large amounts of money are being spent on PCR testing for HCV and the risk of HTLV transmission through blood transfusion is likely to be greater than the risk of acquiring HCV from a window period donation. It was noted that there is now a good test available from Murex, which has high specificity and sensitivity. It was agreed that JO'R would supply the current prevalence rates in various European countries, which fall between 1 in 40,000 and 1 in 50,000. The 1991 North London study reached a prevalence of 1 in 19,000 in unselected donors, but PMi reminded the group of the data on selected South Thames donors. PEH commented that this data is currently being prepared for publication, but that the prevalence was approximately 10 times higher than in the unselected North London donors. PMi reminded members that the situation had not changed since the decision of SACTTI 2 years ago to support HTLV screening of blood donations.

LW joined the meeting at this point.

It was agreed that the question of equivalence of leucocyte depletion and HTLV screening would be raised. There is currently no data to support the view that the two interventions are equivalent.

The points raised in PMo's paper were then discussed.

5.1. Agreed that SACTTI still believes screening to be worthwhile. The costs are much less than for HCV PCR testing and leucodepletion.

5.2. Studies are underway in the NBS looking at the effect of leucodepletion on removal of T-cells and on an HTLV infected T-cell line. There are no recorded transmissions of HTLV from plasma, FFP, or cryoprecipitate in reported studies. For cellular components, there were higher transmissions from platelets and fresh red cells than from stored red cells. Leucodepletion is likely to reduce the risk of infection, but the infective dose is not known and it is impossible to state whether leucodepletion will completely remove infectivity.

5.3. It was agreed that, at least in the initial stage, each donation shouldbe tested. The previous recommendation was for screening of all donations for 2 years, during which time data could be accumulated and then reviewed. There was no reason to change this view.

5.4. Serological testing appears sensitive and specific but there is not enough information on PCR tests to recommend pooled testing. It is uncertain whether pooling for PCR testing would be valid for a cell associated virus.

5.5 PMo proposed that a group would need to be constituted to design a protocol for a prevalence study. It was suggested that CB, IF, AR and PMo would be members of that group and together identify specific pilot studies. It was also vital that LW reported back to SACTTI on the leucodepletion studies being carried out in the NBS. Studies on multi-transfused recipients should ideally take place before screening is introduced (and after introduction of leucodepletion) but JO'R outlined the problems she had experienced in dealing with HTLV-1 both in BMT survivors and in lookback recipients.

Action: J'OR to supply prevalence rates in various European countries. (19a/99)
CB to constitute a group to discuss this issue further. CB to brief BMcL and AR before the next MSBT meeting.

6. Det Norske Veritas report (DNV report) (20/99)

CB introduced the final report on *Assessmmt of the risk of exposure to vCJD infectivity in blood and blood products* and reminded those present that DNV had been commissioned by SEAC and the objectives were stated to be to assess which components and blood products are risk

factors, to identify those groups of patients which are at high risk from blood and blood products and to consider the benefits and disbenefits of introducing a range of measures aimed at reducing the risks. DNV have sugested a number of possible measures and the views of SACTTI are pertinent t any future discussions relating to these. CB reminded the meeting of the need to consider the DNV report and the NBA position statement, which is used as a basis for decisions in England and Northern Ireland. IF commented that no instance of nvCJD has occurred in a donor in SNBTS (and given the change in source of plasma supply it would be unlikely that there would be a plasma product recall in the future) therefore no position statement exists for the SNBTS.

It was noted that the position statement was of relevance to patients treated with plasma products manufactured from a pool which includes plasma from a nvCJD donor. The position of recipients (of blood components) who might themselves become donors needs to be clarified. Both NBA and SNBTS have taken legal advice. The NBA advice has been passed to DoH, who are also taking advice. It seems clear that there is a duty to inform individuals who themselves volunteer to become donors and further advice from DoH is required.

Two of the measures which were reccommende have been implemented following announcements from DoH:

- leucodepletion
- elimination of UK plasma products

IF left the meeting at this point

LW pointed out that there is insufficient data on survival of transfused patients, but BMcL pointed out that firm data exists on the age of transfused patients and on the high mortality of individuals transfused more than 6 units of blood in 24 hours. The data on the role of B cells in nvCJD is now questioned, but formed a basis for DNV's report. LW pointed out that there are very few evidence based benefits of leucodepletion, and potentially some disbenefits (e.g. renal transplant recipients given pre-transplant transfusion). There is a need for a national body with the remit to oversee all matters relating to blood transfusion in its entirety; NICE would clearly have a role.

It is necessary for the SACTTI to have a view on the other points raised for consideration. The other risk reduction measures were discussed point by point:

6.1. Reduction in use of blood components: There is a need for collection of data for feedback to clinicians. Improving access to, and knowledge of, relevant data, trials etc to assure clinically effective transfusion should be a priority.

Action: BMcL to produce sample data for CB

6.2. Preventing blood transfusion recipients from donating blood: The data on the number of donations which would be lost is available from recent surveys done across the UK. . In addition to the adverse impact on blood supplies,there are other disbenefits e.g. a disincentive to family members, and what to do over those who do not know they have had a transfusion. Studies have shown that many patients who have been transfused during surgery were unaware of this.

Action: BMcL and LW to collate existing data

6.3. Maximising the use of whole blood:
BMcL pointed out that there is some published data from Edinburgh and SNBTS has developed a policy. There is a need to evaluate the benefits and drawbacks of the use of whole blood for specific indications. This proposal implies that donor exposure would be reduced, but there is no conclusive evidence that this would be the case and this would require formal evaluation.

6.4. Maximise the use of autologous transfusion:
This includes all forms of autologous transfusion and it was agreed that making appropriate use of autologous transfusion in clinical situations where it is likely to be of benefit, could well be included in point number 1.

6.5. Use of imported pooled plasma (FFP)
This is relevant to the question of imported SD FFP, but single unit imported FFP was not considered in the report. It is not currently known what proportion of FFP recipients receive FFP alone. FFP could be sourced from outside the UK whereas this does not apply to red cells and platelets. It was agreed that there is a need to avoid pooling, but imported single dose FFP should be considered further.

6.6. The use of high purity factor VIII is now irrelevant as no UK plasma is being used.

6.7. Prophylactic treatment against vCJD: This point is worth investigating further.

The NBS position statement should be reviewed in the light of the DNV report. PEH reminded the Group that further ethical advice has been requested from Professor Ian Kennedy, relating to notification of blood component recipients transfused with units originating from donors who developed nvCJD. A reply is awaited.

Action: PEH to include the letter to Professor Ian Kennedy with the minutes. (23/99)
CB to write to AR with reminder of the need to review position statement and review advice relating to recipients of blood components who might themselves become blood donors.

7. Draft programme for SACTTI Special Meeting

It was agreed that representatives of the Irish BTSB and of PHLS laboratories currently supplying reference testing to the NBS should be invited.

Action: Comments from all members on the agenda to CB by 19th May.

8. Any other business

8.1. CB would like a subgroup to consider the nvCJD issues: to keep a watching brief on tests, confirmation, donor issues etc and reporting to the main group at, say, every third meeting. It was proposed that BMcL would head this group, with wide representation. It was suggested that PMi, members of the NBS CJD R&D Group etc should be invited.

Action: BMcL to give thought to the membership of the subgroup

8.2. IF had asked CB for clarification of the imperative to use PCR as a release criterion for cellular components. It was agreed that this action appear to be driven by the Paul Erlich Institute, and is being followed by action in other European countries. The need for PCR testing for regulated products has an impact on cellular components and on donors. Whilst not wishing to be out of step with the rest of Europe, the drive to PCR testing as a release criterion for cellular components would appear to make the NHSE decision over HTLV screening even more perverse. It was agreed that plans should continue in line with other European countries.

9. Date of next meeting

Tuesday 6th July 1999 at Deansbrook Road Centre, Edgware.