Venue: Room LG 17, DH Wellington House, 133-155 Waterloo Road, London SE1 8UG

Date: Monday 22 January 2001

Time: Coffee: 10.00am Meeting: 10.30am

AGENDA

1. Apologies
2. Minutes of meeting of MSBT, held 26 June 2000
3. Matters arising:

   Information on tissue recipients from CJD Surveillance Unit – Dr McGovern/Dr Doyle/Dr Wyatt

   Guidance on surgical instruments – **MSBT 22/(4) - information paper**

   Combi test for HIV antibody and antigen – Dr Robinson

4. Variant CJD:

   i. Fresh frozen plasma **MSBT 22/2**

   i. Donor Transfusion History Survey **MSBT 22/3**

   ii. Tonsil biopsy in tissue transplantation **MSBT 22/5**

   iii. Actions to minimise the risk that vCJD could be transmitted by transfusion **MSBT 22/4**

5. HTLV Testing **MSBT 22/1**
6. NAT testing – progress report Dr Robinson **MSBT 22/6**
7. EC Directive - Dr McGovern/Dr Robinson
8. Update on HCV Litigation – Mr Lister/Dr Robinson
9. Any other Business

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF BLOOD AND TISSUES FOR TRANSPLANTATION

MINUTES OF MEETING: MONDAY 22 JANUARY 2001
ROOM LG16/17 WELLINGTON HOUSE

Chairman: Dr Pat Troop (Paras 1-14)
Dr Mike McGovern (Paras 15 onwards)

Members:

Dr Dash
Dr Gorst
Dr McClelland
Dr Mortimer
Dr Perry
Dr Robinson
Dr Warren
Professor Zuckerman

Observers:

Dr Peter Doyle	-	DH
Dr Peter Bennett	-	DH
Dr John Stephenson	-	DH
Dr Lincoln Tsang	-	MCA
Mr Stephen Lee	-	MDA
Dr Aileen Keel	-	Scottish Executive
Dr Tim Wyatt	-	DHSS Northern Ireland
Dr Lorna Williamson	-	National Blood Service
Dr Gail Williams	-	Welsh Blood Service

Secretariat: Charles Lister.

APOLOGIES FOR ABSENCE

1. Apologies were received from Dr Cant, Professor McMaster, Mr Forsythe and Dr Nicholas.

MINUTES OF THE MEETING OF 26 JUNE

2. The minutes were agreed subject to the following amendments:

- para 7 – deletion of the words "though they had a test for B19 DNA" in line 4.
- para 20 - deletion of the last sentence.

3. Professor Zuckerman stressed the importance of accuracy in MSBT minutes.

MATTERS ARISING

(i) Potential donors who have received implicated blood/TMER

4. It was noted that the recently established CJD Incidents Panel was developing a framework for managing clinical incidents involving possible transmission to patients of CJD and variant CJD. The Panel's remit encompassed surgical instruments, blood and blood products and tissues.

5. Dr Doyle said that the Data Protection Act issues arising from the proposal to harmonise the NBA and UK Transplant Service databases remained unresolved.

(ii) Combi test for HIV antibody and antigen – MSBT 22/7

6. Members considered a short paper prepared by the Standing Advisory Committee on Transfusion Transmitted Infection (SACCTI). Dr Robinson said that ELISAs that detect anti-HIV 1 plus 2 and HIV Ag in a single assay format had been found to reduce the window period by around 48 hours. NBS felt comfortable using a Combi test. There were several on the market, and these were being evaluated by the Blood Services' Kit Evaluation Groups.

7. Dr Robinson said that NAT testing for HIV RNA did not provide much reduction in the window period, and NBS had no plans to introduce it. SNBTS were, however, considering using the test.

Fresh Frozen Plasma – MSBT 22/2

8. Members were invited to consider two papers

- Paper 1 (by DH): an analysis of the potential risk of vCJD transmission via FFP and how that risk might be reduced by sourcing the product from the US;

- Paper 2 (by NBS): an analysis of measures available to reduce the risk of viral transmission via FFP using UK-sourced plasma and the options available if a decision is taken to switch to US plasma.

The Chairman reminded members that it had been agreed, at the special meeting in February 2000, that the real risks of viral transmission of FFP using non-UK plasma had to be weighed against the theoretical risk of vCJD transmission. Members were therefore asked to focus on the balance of risk rather than questions of cost, which was a secondary issue and for Ministers to decide.

(i) Paper 1

8. Dr Bennett introduced Paper 1. Given the level of uncertainty in this area, particularly around the prevalence of people incubating infection, it had only been possible to estimate the degree of risk by examining different scenarios for the primary vCJD outbreak. The best estimate was that a primary outbreak of 10,000 (as an illustrative figure) could lead to around 85 new infections a year from UK-sourced

FFP. This was not a large figure, but not negligible either. The model also showed that the number of new infections remained the same at levels of infectivity between 1 and 0.01 ID_{50} per ml (Table 2 of Paper 1).

9. The Chairman invited members to say whether they were confident with the assumptions made in the risk assessment.

10. Members asked whether the predicted 85 new infections per year were at the peak of the epidemic or whether it averaged out. Dr Bennett said that SEAC had advised that, in the case of the lympho-reticular system, people should be regarded as infected throughout the incubation period and that the level of infectivity would plateau at a very early stage. The risk assessment therefore used that model. The assumption was that if 10,000 people were currently incubating vCJD, they all had the potential to transmit infectivity.

11. Dr Nicholson reported that the latest information from the Institute of Animal Health's (IAH) sheep experiment was that no other sheep were showing signs of infectivity. IAH planned to set up an experiment using leucodepleted blood. However, this would be difficult given the fragile nature of sheep blood.
Final results from the IAH study were not expected until 2002/03.

11. Dr Nicholson also informed Members that at a conference before Christmas, Paul Brown had reported that, in an experiment using hamsters and hamster-adapted scrapie, blood from only a very small number of animals had been capable of transmitting infection.

12. One possible conclusion was that, although infectivity could be transmitted in animal experiments, this was rare suggesting that the level of infectivity must be quite low. However, some members were sceptical about the reliance that could be placed on laboratory models. The point was also made that it was hard to interpret the lack of further evidence from the sheep study without knowing whether other donor: recipient pairs had reached the same stage as the pair where transmission had been successful.

13. During discussion, Members agreed that it was unclear how much the results of the sheep study would influence assumptions on infectivity, especially as it was necessary to go down to very low levels in the model (below 0.01 ID_{50} per ml) before the predicted number of new infections fell below 85 per annum. In any case, these results were unlikely to be available for some time.

14. Members therefore agreed that the risk assessment model reflected the best evidence currently available. It was also agreed that a vCJD risk assessment was needed on the plasma component of platelets and red cells.

(ii) Paper 2

15. Dr Williamson set out the options identified by NBS for US-sourced FFP. She also drew attention to the high incidence of viral markers in the US, which were possibly between 4 and 9 times higher than in the UK. This placed a great deal of pressure on the testing strategy and would make NBS very dependent on the

supplier to carry out genome testing properly. A virus inactivation step would therefore be required as an additional precaution. At present Methylene Blue (MB) was the only method available for single units.

16. NBS had considered:

- American Red Cross (ARC) plasma: single unit plasma from voluntary donors. This was not leucopepleted and used first time donors. MB treatment would be needed but would not be possible for NBS to undertake this in house. One option would be to contract the MB treatment step to Grifols.

  Most ARC plasma was sent for fractionation. Much also went to Vitex for production of pooled FFP and back to ARC for distribution. This accounted for 20% of US FFP. ARC had told NBS that they would have to go back to their Board to see if their Terms of Reference allowed them to supply to the UK;

- ABRA: apheresed single unit plasma from paid donors. Availability of ABRA plasma was getting tigher;

- Vitex: pooled voluntary donor plasma. Vitex had submitted a product licence application to MCA. Current technology for viral inactivation of pooled products did not deal with non-lipid coated viruses such as B19

17. Dr Williamson asked MSBT whether Vitex would be an acceptable alternative if supplies for single unit plasma were limited or unavailable. Members views were also sought on prioritising supplies of single unit FFP if supplies were limited, eg for neonates/children.

18. Professor Zuckerman said that, on a precautionary basis, he would be willing to support a switch to single unit FFP from voluntary donors combined with initiatives to educate clinicians to reduce FFP use. However, he was opposed to using paid donor plasma because of the increased viral risk, particularly from hepatitis B.

19. Some Members expressed concern about increased risk of parvovirus B19, which could be devastating for some patients (eg those with bone marrow problems). However, it was unclear how this correlated to use of FFP.

20. Dr Perry drew attention to the lack of security of supply of US plasma and pointed out that collections had dropped by 15% the previous year. There was also a risk that other European countries (eg France) could end up competing in the same market. Members expressed concern about reliance on monopoly suppliers and loss of self sufficiency.

21. Dr Perry raised the question of cryoprecipitate, made from UK plasma and mostly prescribed as a replacement for fibrinogen. SNBTS/BPL were working on a

virus inactivated fractionated fibrinogen concentrate which would probably allow cessation of cryoprecipitate production. They were attempting to expedite a license for this product with MCA but had reached impasse on the issue of clinical trials. MCA had asked for evidence of efficacy but would not accept evidence from bio equivalence studies. Members expressed concern that a product was being held up that would allow virally safe treatment for acutely ill patients using US plasma.

22. Members agreed that:

(i) there were sufficient grounds on precautionary basis to look at the feasibility of a switch to US plasma;

(ii) if there was to be a switch to US sourced FFP:

(a) Members had a clear preference for using single unit voluntary donated, MB treated plasma. If supplies were limited, this should be used for neonates and children;

(b) Members would need to have confidence in the processes for viral inactivation;

(c) Members would not favour using pooled solvent detergent treated FFP unless a 2nd viral inactivation step could be incorporated to deal with non lipid viruses;

(iii) there was a need for a wider scoping exercise addressing safety, supply (need for sustained alternative provision) and logistics;

(iv) the issue should be brought back to MSBT for a special meeting in April.

Action

- Secretariat to provide NBS with written instructions to investigate feasibility of ensuring sustained supplies of US plasma.
- Secretariat to take up issue of cryoprecipitate with MCA.

Actions to Minimise the Risk that vCJD could be Transmitted by Transfusion – MSBT 22/4

23. Dr McClelland introduced a paper produced by SNBTS. The purpose was to invite MSBT to look at the broader issues on vCJD risk reduction and to clarify where responsibility lay for these areas, accepting that it might not be with MSBT.

24. Aside from issues already on MSBT's agenda, the following areas were discussed:

- plateletpherisis: It was agree that this was for MSBT and that a feasibility assessment was needed on the impact on infectivity of sourcing all platelets by apherisis;

- EPO: It was agreed that this should be raised at the forthcoming Better Blood Transfusion conference. This was also suggested as a possible issue for NICE. Some Members thought that it might already be on NICE's agenda;

- platelet substitutes: Dr McClelland said that research on platelets alternatives seemed to have ground to a halt. He suggested that there might be a case for reviewing the evidence to see if it might be possible to kick start the projects again. However, Members acknowledged that it was not biologically easy to demonstrate efficacy.

- use of aprotinin/gelatin infusions for blood volume replacement - Members agreed that this was an issue for MCA

- Population based project on use of transfusion. This was already part of current NBS blood safety research and included identifying recipients and monitoring survival. The MRC Biostats Unit were involved and SNBTS hoped to join forces.

- selective transfusion policy. It was agreed that this was a possible item for the new National Transfusion Committee

- financial disincentives to BBT practice (eg patients receiving transfusions who could be on EPO but option ruled out on grounds of cost). Members agreed that this should be raised at the forthcoming Better Blood Transfusion conference and put on the agenda for the National Transfusion Committee.

Better Blood Transfusion

25. Dr Mortimer asked who would be responsible for Better Blood Transfusion in future. Dr Robinson said that she was looking towards the Chair of the new National Blood Transfusion Committee who would be either a CMO or Ministerial appointment. The Committee would have links to Hospital Transfusion Committees through Regional Transfusion Committees.

26. Dr Mortimer also expressed concern at the perverse incentives preventing blood safety, eg the fact that autologous transfusion was not as well developed in the UK as in other countries.

27. Dr Robinson said that consideration needed to be given to the issue of informed consent to blood transfusion and educating patients in the risks. It was agreed that patient representatives should be invited to the Better Blood Transfusion conference.

Survey of Transfusion Recipients – MSBT 22/3

28. Dr Robinson introduced a paper giving the results of a NBS survey of blood donors to identify those who have received blood transfusions. The survey, which related to red cells not blood products, showed that between 7.7%-14.5% of the donor base were transfusion recipients. Excluding these donors would reduce collections by between 8.2% and 16%. At least 20% of donors did not know if they had been transfused. Dr Robinson said that such an exclusion would have a dramatic impact. If introduced immediately, blood stocks would be exhausted within 10 weeks. To avoid this, NBS would need to increase recruitment rates by 39% - a huge task and not to be underestimated. Although France had claimed to have lost only 5% of donations through excluding transfusion recipients, France had large number of regular donors. NBS retention, by contrast, was poor.

29. Dr Robinson also drew attention to the considerable impact of such an exclusion on apherisis donors. Donations of bone marrow, stem cells and tissues would also be reduced. It would be necessary to phase in such a measure. France had taken 12 months (inc counselling and advice). NBS would need at least 6 months to build up stocks. NBS were recruiting more donors but the use of red cells had increased by 15% over past 5 years. Although more was being spent on advertising to recruit donors, NBS were faced with diminishing returns.

2 years

30. Dr Bennett said that he had completed very preliminary work on vCJD risk reduction arising from excluding transfusion recipients. Although, it was vital to avoid a self sustaining epidemic from all sources (eg blood, surgery etc), it was difficult at this stage to see this measure having a huge impact. However, a full risk assessment could not be completed for 4-6 weeks.

31. Members noted that, if transfusion recipients were excluded from giving blood, consideration would also need to be given to whether they could donate organs and tissues.

Action:

It was agreed that this issue would be brought back to MSBT in April. MSBT should have EOR's risk assessment and a NBS implementation plan. MSBT would also need to address impact of this measure on reducing risk from recycling of viruses.

HTLV Testing – MSBT 22/1

32. Dr Robinson introduced a paper by SACCTI. MSBT had last looked at this issue in 1996. Ministers had decided not to introduce the test on cost:benefit grounds but wanted it kept under review. SACCTI had looked at the issue again and concluded that there was a significantly greater prevalence of HTLV infection markers in certain ethnic groups than was the case in 1996. SACCTI also noted that the issue of whether leucodepletion had obviated the need to test for HTLV had not been resolved.

33. SACCTI had endorsed their original recommendation that screening for HTLV antibody should be introduced within the UK. They also recommended that a risk assessment on the impact of leucodepletion on HTLV should be undertaken

34. Dr Robinson informed Members that the majority of other countries screened for HTLV, placing the UK a little out of sync. One way forward might be to begin by screening all donors, then new donors only. SACCTI had recommended that the UK Blood Services conduct a feasibility study of HTLV screening, recognising that there are ongoing significant changes affecting blood safety that have yet to be fully implemented, eg NAT testing for HCV RNA.

35. Members agreed that testing for HTLV should be introduced as a matter of urgency.

Action: NBS to undertake a feasibility study, with recommendations for the introduction of HTLV screening, to bring back to MSBT in April. Secretariat to refer to Ministers.

NAT Testing

36. Dr Robinson reported that two NBS laboratories were up and running making it possible for NBS to introduce phased release of NAT testing. Phasing would begin with London and the South East and Leeds followed by Birmingham. Members agreed that phased release of NAT testing should go ahead.

37. Dr Robinson informed Members that Scotland were considering introducing NAT testing for HIV within 6 months. She thought that Germany and Holland might have similar plans. This was not on the NBS agenda, and Dr Robinson expressed concerned that this put them out of sync. This issue would be brought back to MSBT for the June meeting.

Action: NBS to produce a paper for MSBT on 11 June.

Draft EC Blood Directive

38. Dr Robinson updated Members on the draft Directive which had now been published. She noted the concern that the draft still contained detailed technical annexes regulating, among other things, the selection of donors and the screening and storage of blood. The annexes would be updated by committees established by the European Commission, which raised concerns about how these would impact on the work of MSBT.

Update on HCV Litigation

39. Mr Lister informed the Committee that the case had now concluded and that a Judgement was expected by the end of February or early March.

Date of next Meeting

40. The next meeting would be on Thursday 19 April.

BLO 8/4

MSBT: 22 JANAURY 2001

ACTION POINTS

FFP – 22/1

vCJD Risk Assessment:

Agreed: model reflects best evidence available now, we not likely to have more evidence (eg on sheep studies) for some time and this would be unlikely to significantly affect the model.

Need for vCJD risk assessment on plasma component of platelets and red cells.

Viral Risks

Options for US plasma:

- ARC (voluntary single unit – not leucopepleted - uses first time donors. Need for MB treatment – suggest contract to Grifols. Most goes to Vitex for pooling and back to ARC for distribution – 20% of US FFP. ARC have to go back to Board to see if TOR allow them to supply to UK)
- ABRA (paid single unit – but availability getting tighter)
- Vitex (pooled voluntary donor –submitted licence application to MCA)

MSBT asked whether Vitex would be acceptable alternative if supplies for single unit plasma limited/unavailable. If limited, single unit could be prioritised for neonates/children.

Prof Zuckerman – concerned about paid donors. Wd go for single unit from voluntary donors combined with BBT initiatives. Opposed to using paid donor plasma because of increased viral risk (high levels of Hep B).

Concern about parvovirus B19 – can be devastating for some (eg with bone marrow problems) – how does this correlate to use of FFP?

Concern about lack of security of supply of US plasma – collections dropped by 15% last year. (Bob Perry suggests looking to other sources, Europe or Australia (but goes to CSL – no obvious opportunities for surplus plasma)). Also risk that other European countries (eg France) may end up competing in same market. Some members worried about reliance on monopoly suppliers and loss of self sufficiency. But if screening test in two years or so, single contract for US plasma might see us through.