ANNEXC

EXTRACT FROM MINUTES OF MSBT MEETING : 25 MARCH 1997

7. CJD : Blood and blood products

7.1 The Chairman pointed out that the UK was free to decide on donor exclusion criteria and other matters relating to the safety of blood, but was bound by EU decisions as regards blood products. The issue of CJD was topical because the MSBT meeting coincided with a closed WHO meeting on the subject, and there was press interest in research being carried out by Paul Brown which was due to be reported at that meeting. Dr Stephen Dealler was suggesting we were about to face an explosion of CJD infection transmitted through blood/blood products. MSBT needed to consider if they wanted to modify their advice as regards blood, and also to advise SEAC of their position.

7.2 Dr Robinson said that Dr Barbara, Dr Will and Dr Flanagan were representing the UK at the WHO meeting. The impression the press had gained was that plasma fractions had transmitted CJD in humanised mice. Dr Dealler felt he had a duty to warn the public if their safety was at risk, and was wanting to discuss with the BTS various suggestions for stopping inappropriate use of plasma.

7.3 Initial UK reports from the WHO meeting were that there were two sets of experiments. One set of experiments involved spiking human blood with highly infectious hamster derived prion. The other set of experiments had involved blood from mice which had been subjected to passage of human CJD by intracranial inoculation. The blood of the mice had become infectious after 8 weeks, and CJD had developed after 16 weeks. Various components from both these experiments had been tested and each had shown some level of transmission of CJD by the intracranial route only. Paul Brown's conclusion was that more information about epidemiology was needed; there was no evidence of blood transmission in humans so far, although the theoretical risks had been considered for several years.

7.4 The UK experts considered that there was a need for further work related to critical inoculation routes, such as intravenous injection. It was very unreliable to extrapolate from mice to the human situation. Dr Robinson thought there was little new development. No haemophiliacs world-wide had been reported as developing CJD. However, the media had gathered that CJD might be transmissible by plasma and plasma products.

7.5 The Chairman recalled that previous experimental work had shown that buffy coats transmitted CJD.

7.6 Dr Rotblat said that CPMP had been aware of the WHO meeting, but not of the full content of Paul Brown's paper. At a CPMP meeting the previous week the general feeling had been that CJD was not transmitted by blood products, but the focus of CPMP had been on whether to recall batches of blood products because

donors were later identified as being at an increased risk of CJD. There was agreement at the Council of Europe on exclusion criteria for donors, except as regards dura mater recipients.

7.7 Problems had arisen over the interpretation of the previous CPMP line on product recall. Where 2 donors had subsequently been identified as being in risk groups for CJD, an immunoglobulin product had been withdrawn in the US and France had followed suit. (The product had not been on the UK market.) The latest CPMP meeting had therefore endorsed a recommendation from their Bio-Technology Working Party intended to clarify the position. It still maintained that there was no evidence of transmission of CJD by blood products, but there was a theoretical risk and insufficient data to rule this out completely. CPMP had now made it clear that while plasma pools where a donor was subsequently found to have CJD were not to be recalled by the Member State concerned, if a product was withdrawn in the US or in any Member State, that withdrawn product should not subsequently be exported to an EU Member State, whether from the US or another Member State. (FDA practice was to withdraw in the US products where a donor or relative of a donor was subsequently found to have CJD.)

7.8 The US policy could lead to shortage of a product. The Chairman mentioned a case where Canada had withdrawn a product and asked the UK for a replacement product. However they chose not to buy the UK product when they realised the UK did not have the same rules as they had for withdrawal.

7.9 Dr Snape noted that within the UK there was not the same rigorous system of advice to fractionators, including the transfusion service, which would enable us to guarantee that a product was free of CJD.

7.10 Members were concerned as to how to respond to questions from the press and others about such matters as the blood service's policy on CJD and blood. The Chairman said that existing blood service guidelines deferred relatives of CJD sufferers, and individuals who had been treated with human pituitary growth hormone or human gonadotrophin of pituitary origin from giving blood. He asked if members remained content with this, and with not excluding also recipients of dura mater, as some of Europe did. This was because of the difficulty of identifying dura recipients among would be blood donors, as they might well not be aware that dura mater had been used.

7.11 Dr Perry was content with the present position on blood products, and thought the parallel position on blood was to make no change. The Chairman supported this view. If MSBT decided to change its advice on blood, we would need to look again at blood products, and whether to take a more stringent position than CPMP.

7.12 Dr Rotblat thought that the Commission's DGV were planning a meeting which would consider the implications for blood. As Mrs Silvester was unable to attend, it would be helpful if an alternative UK official, eg Dr Rejman, could be invited, but

it was noted that the Commission would decide who should be invited to the meeting.

7.13 Answering a question from the Chairman, Dr Rotblat confirmed she was not aware of any gene amplification techniques which were relevant as a test for CJD.

7.14 Dr Perry questioned whether a recipient should be told if (s)he had received blood from a donor who had subsequently developed CJD.

7.15 Dr Robinson asked about the proposals considered by SEAC for further experiments as to whether particular components can transmit CD. Dr Toy said that the joint MRC/DH research advisory group thought there was very low risk of transmission of TSE infection through blood or blood products, although this might need to revisited in relation to new variant CJD. The group had not been particularly impressed by the Minor/Williamson proposals. However the joint DH/MAFF funding group meeting on 7 April would prioritise research proposals, and then advertise for bids to carry them out.

7.16 The Chairman noted that MSBT, SEAC and the Research Advisory Group all had an interest in CJD and blood.. In view of the public sensitivity it was important there should be no difference between MSBT's and SEAC's lines. MSBT should therefore set out its position and convey this to SEAC indicating that they would be interested in any comments SEAC might have. The research group, covering both animals and humans, would be prioritising research proposals, and blood would need to be high up on their list. (In passing it was noted that following EC intervention abattoirs now had to filter off and destroy blood, as it was suggested this might be a potential risk of infection.)

7.17 Dr Wyatt asked if blood from new variant CJD patients was being used in any current experiments. Dr Toy said this was being done in America, using blood from UK patients, injected into squirrel monkeys.

7.18 A number of members asked for advice, and to see question and answer material, on how to respond to questions about this issue, including about what measures were being taken to find out if infection was transmitted by blood/blood products. It was agreed that the Secretariat would send them material supplied by their research colleagues which gave details of the role and membership of the DH/MRC Research Advisory Group, and research currently being funded, which were already public knowledge. However, firm information about new research could not be given until after the 7 April meeting.

7.19 Dr Robinson reported on progress with the research follow up study of CJD patients who had been blood donors being undertaken by Dr Will. Approval had been obtained from the Lothian Ethics Committee, on the strict understanding that the work would be anonymised and that no attempt would be made to trace recipients or

tell them they had received CJD-implicated donations. Dr Will had a control group of patients who were CJD-free but had a history of donating blood or receiving transfusions. The study would be "blinded" with only the CJD Surveillance Unit knowing which patients had received implicated donations. Hospital and NBS staff would not know which were the control cases. Hospital involvement would only go as far as haematologists, whose co-operation would be sought on a one to one basis.

7.20 The names of donors, controls and recipients to be followed up were being given by Dr Will to the English or Scottish BTS. So far England had received 100 names and addresses. 47 index CJD cases had been identified among people who had given blood after 1980 where recipient records were likely to be available, so the study seemed viable. England also had details of some transfusion recipients; more names for both groups were to follow. The Chairman said recipients would be followed up by flagging their names in the NHS Central Registries, so any deaths would be notified.

7.21 Dr Robinson felt there was particular urgency to identify recipients of blood from donors with new variant CJD. There were three new variant CJD patients known to have given donations.

7.22 Dr Robinson had taken advice and believed that in the present state of knowledge it was legally and ethically acceptable not to inform recipients of donations from donors who subsequently developed CJD. This would need to be reviewed if the position changed, eg if diagnostic tests or treatment became available. The likelihood of transmission was low and also since the study was blinded those responsible for the care of the recipient would not know whether he had received blood from a control or an implicated donor. The Chairman felt that the conditions imposed by the ethics committee could be cited in defence of this line.

7.23 Members asked about MSBT's response to questions about what was being done about CJD blood transfusion donors, and whether we would be following up new variant CJD cases. The Chairman suggested at present the reply should be that this was being considered - as no actual studies were yet in progress. To the second part we could say we were planning to undertake follow up.

7.24 Dr Warren asked what we would do if it should became known that there was pre-clinical infectivity. The Chairman thought MSBT should hold to its existing position on deferral of those who might pose a risk. Dr Warren also raised the question of deferring recipients of blood donations from CJD patients. It was suggested that this would involve breaking the conditions set by the Ethics Committee.

7.25 On the question of dura mater, the Chairman commented that while the UK would prefer to defer dura mater recipients, MSBT had taken the view that this would be very difficult to implement, since dura mater (which came from cadavers) was used for various surgical procedures, not only neuro-surgical work. Members recognised the difficulty of the issue, which MSBT had considered carefully in the past. The

issue was a practical one of finding a reliable way of identifying patients who had received dura mater grafts for non-neurosurgical procedures. Dr Robinson said that donors who had had neuro-surgery would be deferred from donation in any case.

7.26 Dura mater had come under the Medicines Act. The Chairman said that one licence for an earlier dura mater product (as a medicine) had been withdrawn. Members were however not sure that licensing could guarantee the product was safe. It was uncertain which EU-based controls were now in place. Mrs Dhell agreed to provide material on whether dura mater was now covered by the Medical Device Directives.

7.27 Dr Rotblat felt that some other Member States had decided on the deferral in dura mater cases without recognising the difficulty of identifying them. It seemed fairly clear that deferral would shortly be agreed by Europe despite these practical problems.

7.28 Dr McClelland saw a need for a system of recording and auditing, as in the case of other tissues, particularly as dura mater was arguably the most dangerous tissue. The Chairman agreed, saying that dura mater was high on the EU list of tissues at risk of transmission of TSEs.

7.29 Dr Snape thought the question would need to be addressed, and robust defence given, when other Members States and North America were operating a dura exclusion. It was hard to defend the UK acting differently. The Chairman noted that, unlike some other countries, the UK was reluctant to agree to measures which sounded good in theory, but where there was no obvious means of implementation. If the EC or WHO could develop practical criteria to identify dura recipients, these would be worth considering. Dr Rotblat said the UK had asked how other European countries had achieved implementation, but had received no sound answer and so had defended the UK position.

7.30 Dr Robinson, asked if it had been shown that dura mater transmitted CJD only if used intracranially, as that would make exclusion easier. Some members thought that was the case. Dr Robinson, and the Department of Health, agreed to check if there was any relevant evidence. Dr Toy and Dr Rotblat warned that even if records did not show any such cases that was not conclusive, Dr Rotblat suggesting that the use of dura mater was not always included in hospital records. The Chairman said that Dr Will's records included all operations.

7.31 Dr Wyatt asked how much dura was used. Mrs Dhell undertook to find out.

7.32 After extensive discussion members the Chairman asked if MSBT wished to change its position on blood donation, while agreeing with the CPMP position on blood products. Members did not propose any change. The Chairman noted that MSBT would now set out its position to SEAC to ensure there was no difference in

their stance. The Secretariat would provide information to members as promised, including about the research in progress. MSBT would return to the topic at its next meeting.