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SACTTI 03/31

DRAFT MINUTE

MEETING OF SACTTI WORKING GROUP ON vCJD
Held on 13th December, 2002 by Video Conference

VENUES SNBTS Diagnostic Scotland , Liberton Campus, Edinburgh EH17 7QT

The Library, National Blood Service, Oxford Centre, John Radcliffe Hospital, Headington, Oxford OX3 9DU

ATTENDENCE
At Edinburgh: Dr Bruce Cuthbertson, Dr Moira Bruce, Dr Phil Yates, Dr Marc Turner (Chair)
At Oxford: Dr Pat Hewitt, Dr Roger Eglin, Dr Frank Boulton, Dr Tim Wallington

1. **Apologies**

Dr Philip Minor, Dr David Anstee, Dr Mike Murphy, Dr John Stephenson, Dr Elizabeth Love, Professor James Ironside, Dr Richard Knight, Dr Brian McClelland, Dr Peter Bennett, Dr Charles Lister

2. **Minutes of Meeting held on 12th June 2002**

Were accepted as correct. There were no matters arising.

3. **Current Epidemiology: Progress on work on appendices and tonsils**

This item was not discussed in the absence of Professor Ironside or Dr Knight and will be brought forward to the next meeting.

4. **Position with regard to importation of blood components**

It is understood that imported methylene blue treated fresh frozen plasma will be available for neonates and children born since 1996 in SNBTS from the beginning of the second quarter of 2003 and in the remainder of UK from the third quarter of 2003. It is unclear whether importation of other blood components for this group is under consideration by MSBT or has been evaluated by EOR. MLT to enquire with regard to this via the Chair of SACTTI.

5. **Review of changes in donor selection criteria: potential exclusion of blood component recipients**

Two documents are available to the working group, the NBS donor transfusion history survey (market research paper; RP0030) and an SNBTS research document on health histories of blood donors and the general public. It is understood that consideration as to whether blood component recipients should themselves be deferred as blood donors is currently resting with MSBT though no decision has yet been made. An EoR assessment has

been carried out but this is not currently available to the group. MLT to request access to the document for the Working Group through the chair of SACCTI. It is not clear whether a similar evaluation has been made for bone and tissue.

6. **Patient exposure to blood and plasma products from donors who later develop vCJD. Information and management.**

12 patients with variant CJD have been blood donors, representing 10% of reported variant CJD cases almost twice the rate of donation compared with the general population. 32 blood component recipients have been identified. None of these appear on the CJD SU database. Approximately half are deceased. There was discussion over the time between receipt of the potentially infected blood component and death in those recipients who are deceased, and the time since recipient of the potentially infected blood donation to current date for those recipients who are still alive. This information may help to clarify how many blood recipients are actually within in the time frame where they might be expected to develop clinical evidence of variant CJD if they have been infected. There was also interest in the time between the blood donation and the development of clinical disease in the variant CJD affected donors themselves. PH agreed to do some further work on these issues and report the information back to the group. There was discussion over whether the recipients may have received post mortem neuropathological examination. This is unknown from surveillance of the death certificates but in general is thought to be unlikely. It was discussed whether routine post mortem surveillance should be undertaken in the same way that the haemophiliacs have agreed to undergo routine post mortem as surveillance strategy. This is clearly not possible in blood transfusion recipients unless they themselves have been informed of their exposure.

There was discussion over the position with regard to informing the component and plasma product recipients of their exposure. The advice from the Department of Health and Lothian Research Ethics Committee (on establishment of the TMER study) were to the effect that the recipient should not be informed. This advice has not formally been superseded. However, BPL needed to inform Haemophilia Directors in England that three batches of Factor VIII were still in date and needed to be withdrawn. The Haemophiliacs concerned were offered the opportunity of information at the time. A survey of the traceability of other plasma products including intravenous immunoglobulin and albumin in one of the London centres suggests that over 50% of these would not be traceable. In view of this, the advice not to inform recipients who have received "low risk products" on the DNV risk assessment and Clinical Incidents Panel it was decided not to take this further at the time. MLT to ask the chair of SACTTI for access to the updated DNV risk assessment.

With regard to the recipients of blood components, NBS has established a reference service whereby concerned individuals can ring to enquire whether they are on the list of exposed recipients but have not proactively contacted patients.

In Scotland one donor has been identified who contributed to plasma products in 1987 – 1989 including Factor VIII, Factor IX (DEFIX) albumin and intramuscular immunoglobulin. An additional donor gave two blood components. On interim advice from the CJD incidents

panel, Haemophila Directors and the doctors looking after the two patients who had received blood components were informed in November 2001, though the doctors involved did not inform the patients at that time because there was no clear guidance from the Clinical Incidents Panel as to what they should be told. Advice in this regard, has to our knowledge, not been forthcoming.

There was discussion over whether this position may change if a compound or compounds capable of effecting the clinical or incubation phase of variant CJD therefore at a potential benefit to patients at risk of iatrogenic CJD transmission became available. It was agreed that in general this would need careful reconsideration by the CJD Therapy Committee and the CJD Incidents Panel.

The Working Group expressed concern that definitive guidance was still not available from the CJD Incidents Panel, and that this was leading to differences in the way donors and patients were being managed in Scotland and England.

The Working Group was greatly concerned that the TMER study remains underfunded and that as a consequence its focus has been narrowed to only variant CJD patients. The Working Group felt it critical that the UK Blood Transfusion Services and Departments of Health put the funding of this essential surveillance on a sound longterm footing. The recent paper from Professor Collinge and colleagues highlights the possibility that variant CJD may present in an atypical fashion and the Working Group encourages re-establishment of the original aims of the TMER which was to include surveillance for all forms of CJD.

Three blood transfusion recipients have developed vCJD and between them were exposed to 117 blood components of which 111 have been traced to identified donors. Again there are differences in the way these donors are being handled in England and Scotland. In England the donors have not been notified nor deferred from donation. In Scotland they have been deferred from donation but have not been notified. There was much discussion over the correct policy. The general consensus was that it is unlikely that a secondary recipient would have developed the disease and died whilst the original donor was still alive and healthy. It was considered that this could be possible given that it is known that the efficiency of transmission increases and incubation period shortens with serial passage in animal models and also that codon 129 heterozygous donor may well have a longer incubation period then a methionine homozygous recipient. It was considered that if the donors were to be permanently deferred on these grounds they would have to be informed, which is likely to have a very negative impact. Further consideration of this difficult issue is clearly warranted to balance the potential public health interests against the welfare of the blood donors involved.

It was suggested that the donors could be notified to the CJD Incidents Panel who have the responsibility for trying to resolve these issues.

The committee did express concern that there appears to be a discrepancy in policy across the UK and it was felt that this needed to be flagged to SACCTI, JPAC and the relevant Medical Directors.

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7. Assay Developments

- **Progress on experiments for detection of infectivity and PrP^{SC} in blood**

MB reviewed progress on a number of assays including conformation dependent immunoassay, Western blot and capillary immunoelectropheresis in which sensitivity is now beginning to approach that of bioassays. There was discussion over the possibility that a small amount of PrP may be in the PrP^{SC} form in normal individuals. A major concern of the group was that there is still no established process for evaluating the sensitivity and specificity of these assays. MLT indicated that the WHO Working Group on TSE had established a blood group in April 2002 but there appeared to be little progress from this group. MLT agreed to write to Dr Phil Minor and Dr Anna Padilla expressing concern over continued lack of progression.

- **Horizon screen on test**

The consensus of the group was that it was more likely that surrogate assay may become available and be implementable within the next few years. There was concern that the criteria for implementation of any putative assays had not yet been established. It was unclear where this action may rest either with the TAF, MSBT, the WHO Working Group or with this group. MLT agreed to write to the Chair of SACCTI expressing concern that a appropriate sub group be established to take this forward.

- **NBS test assessment facility**

It was noted with some concern that this initiative had not been funded and it was felt by several members of the group part of the reason was a perceived competition for prion research funds and in fact this was an operational rather than a research proposal. The Working Group felt that if or when a putative diagnostic donor screening assay became available it would be essential to evaluate the impact of this in a large cohort as soon as possible and that this could not be assembled rapidly.

The group asked to signal through the chair of SACCTI to JPAC their concern over the lack of progress in this area.

8. Therapeutic Developments

MB commented on a recent conference on TSE Diagnostics in Paris and there was a large number of compounds which are known to interfere with PrP^{SC}/TSE infectivity in vitro systems, some of which have been tested by animal models. The use the use of pentosan and of monoclonal antibodies look most promising, reports on both of these approaches have been submitted for publication recently.

It was agreed that further exploration was required of agents which may be possible to add to the blood components to reduce the level of infectivity. MLT/MB to review.

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9. Tissue Service – testing cardaveric donors

PY summarised recent SAC TB / SACTTI meeting in Manchester. MLT indicated he felt the most easily practicable approach to screening cardaveric tissue donors involve brain, optic nerve or tonsillar biopsy. Further work clearly needs to be done on both the sensitivity and the applicability of these approaches. MLT to discuss with James Ironside and PY to discuss with SACTB.

10. Parental exposure to animal products: Department of Health letter for information

MLT will forward to George Galea as chair of SAC TB.

11. Revised position statement

This was reviewed and it was agreed that there was no pressing need to revise again at present, though issues surrounding notification of blood and plasma product recipients may be considered for inclusion at the next Working Group meeting. It was agreed that a position with regard to the potential implication of any putative therapeutic approaches should be prepared where possible prior to publication to the relevant papers.

12. AOCB

The Working Group had been requested by the chair of SACTTI to take a view on the recent sheep transfusion studies. These were reviewed by MB and in effect show that in experimental BSE and naturally scrapie infected sheep from which blood transfusions were taken both during the clinical and the incubation phases of disease, up to 20% of secondary recipients developed disease. The Working Group took the view that this work was proof of principle that the animal models of blood transfusion could transmit infection and was therefore of considerable concern even though in itself it did not prove that variant CJD would be transmissible in the same manner. MLT indicated that discussions had taken place between colleagues in UK BTSs and IAH with regard to a programme of work looking at infusion of a variety of blood components both leucodepleted and non leucodepleted, titration of infectivity in original donors and recipients and secondary transfusion from the blood transfusion recipients themselves. This proposal is currently under discussion with the Department of Health.

13. Date of next meeting

Friday, 4th April, 2003 at 1400-1700 by video conference possibly at three sites i.e. London, Manchester and Edinburgh.

Encl. 1. Accepted minute of meeting held 12 June 2002.
2. Department of Health letter re Parenteral exposure to animal products in reply to MLT's letter of 25 March, 2002.
3. vCJD references January 2003