EC 24/96

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

**Minutes of meeting (2/96) held at Deansbrook Road, North London Transfusion Centre, on 16th April 1996 at 11.00 a m**

1.0 **Present:**

| | | |
|---|---|---|
| Dr P Flanagan | (Chairman) | Dr P Minor |
| Dr L Williamson | (Secretary) | Dr P Mortimer |
| Dr J Barbara | | Dr A Robinson |
| Dr E Follett | | Dr T Snape |
| Dr J Gillon | | Professor R Tedder |
| Dr P Hewitt | | Dr R Warwick (for item 7) |

1.1 **Apologies:** Prof J Cash

**Action**

2.0 **Declarations of Interests**

In accordance with the previously agreed format, Dr Flanagan circulated instructions for members to declare commercial interests. **These should be completed and returned to the Secretary, who will maintain a library file.** **All**

3.0 **Minutes of Meeting held 31st January 1996**

These were accepted as a true record with the following amendments:

*Item 1.6* **Estimation of Seronegative Transmission Risk**
In the section beginning 'The residual risk would depend on' insert 3) Population incidence.
Under the same item, SCIA should read SCIEH (Scottish Centre for Infection and Environmental Health).

*Item 7 (ii)* Section h), ALT(at the bottom of page 6). HBG virus should read Hepatitis G virus.

4.0 **Matters Arising**

1.6 **Residual Transmission Risk**
Dr Snape will make available data from the European Community on seroconversions/risk analysis. **Dr Snape**

7.0 Dr Barbara reported that he had not yet received confirmation of the Scottish Office requirement to store archive samples for five years from Professor Cash, as agreed at the last meeting. **Prof Cash**

4 (i) **Anti-HBc Study**
(Paper 28/96 tabled by Dr Hewitt at the meeting refers)
In reply to the points raised at the last meeting, Dr Williamson raised



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the following points:

a) The size of the study had been based on assumptions regarding likely number of donors proving HBV DNA positive and likely number of patients alive and able to be tested. The following new relevant information was available:

Of 173 donors tested, three had proved positive for HBV DNA (results to be confirmed). Two had isolated anti-HBc, while the third appeared to have extremely low level anti-HBs, although this required confirmation by a different assay. To date, 40% of recipients are known to be deceased. A greater number of donors (70) than anticipated had been found to be anti-HBc positive without any anti-HBs. Consideration was still being given to the use of data from the NLTC study to control for the possible protective effect of anti-HBs, but no HBV transmissions have yet been seen in that study.

b) Anti-HBs levels on donors to be reinstated had been re-done with AusAb on Abbott Commander and good correlation with IMX had been seen.

c) Correlation between IMX and Ortho anti-HBc was less than had been seen in the previous study. However, look-back would be performed on all IMX positive donors.

d) As highlighted in Dr Hewitt's report, additional resources will be needed, particularly in South Thames, if the study is to be completed by October. Additional funding has been requested for this from Abbott Diagnostics.

4 (ii) **National HCV Look Back Update**

Approximately 550 LBF3 forms have now been returned. Of the remainder, it appeared that approximately 50% of recipients would be deceased. The major limiting factor to completion of the look-back was proving to be Medical Records Departments. Dr Robinson had suggested to MSBT that Trust Chief Executives be contacted to facilitate this. In general resources for counselling and hepatology referral were adequate.

As before, between 25 and 30% of recipients were testing negative. Dr Gillon reported that in Scotland consistently non-transmitting donors were in general PCR negative. In reply to a question from Professor Tedder, it was recognised that the percentage of donors and patients in England who had had genomic detection performed was variable across the country, but there was potential for good analysis of these data in certain parts of the country.



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Regarding the look-back on indeterminate donors, Dr Robinson confirmed that the result obtained on the index sample should be used to determine whether or not look-back is performed.

4 (iii) **Malarial Antibody Testing**

Dr Barbara reported that the test kits were undergoing final modification and were waiting confirmation from Dr Chiodini. The manuscript had now been accepted, subject to minor modifications, by Vox Sanguinis, but this was not a condition of the Transfusion Services agreeing to implement the test.

4 (iv) **Red Book Revision** (Paper 18/96 refers)

This had now been submitted to Dr Wagstaff . The draft has been circulated to members of the Red Book Executive for comment, along with submissions from other SACs. *Note added after meeting - Dr Flanagan confirmed that the revision is now approved and publication of the next edition of the Red book is awaited.*

4 (v) **Virally Inactivated Plasma**

Dr Robinson reported that the FDA may licence Octaplas in the summer, and that a licence application was with the Medicines Control Agency. It was predicted that the American Red Cross would move to SDFFP once the FDA licence was granted. Methylene blue plasma would not be available, even for trial purposes, until the end of 1997 as the methodology was proving very difficult to validate. Dr Flanagan felt that it was important that SACTTI reach a consensus view on SDFFP prior to any launch in the UK. It was agreed that this would be a major topic for discussion at the SACTTI meeting on 1st July 1996. With a view to this the following papers would be produced by the end of May:

- Virological Considerations (Professor Tedder/Dr Follett)
- The Fractionaters' View Point (Dr Snape)
- Clinical Aspects (Dr Williamson)
- Model for Residual Risk of Blood Components (Dr Barbara)

**Those listed, plus Dr Flanagan to contact Dr Duguid**

Dr Jennifer Duguid would also be asked to produce an update on the status of methylene blue plasma.

5.0 **HIV-Subtype O** (Paper 19/96 refers)

A meeting had been held on 22nd February to define UK Transfusion Services' policy in relation to HIV1 subtype O. In view of the very limited availability of samples, it had been agreed that the UK Transfusion Services were not in a position to conduct an independent evaluation of currently proved test kits to detect subtype O. Suitability would, therefore, have to be assessed on the basis of information provided to Scottish and English evaluation committees.



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Professor Tedder had been offered the use of certain positive samples from colleagues in mainland Europe.

It was agreed:

(i) That the recommendations reached at the meeting on 22.02.96 be accepted.

(ii) Professor Tedder and Dr Mortimer would further consider the best use of HIV1 subtype O positive samples. **Prof Tedder, Dr Mortimer**

In reply to a question from Dr Robinson, Dr Flanagan reported that algorithms for use within the NBS were being developed by Alan Slopecki to cover the situation where kits were being modified to detect particular viral variants.

6.0 **HTLV Special Meeting** (Papers 20/96 and 21/96 refer)

The format proposed by Dr Flanagan was accepted. Dr Follett wondered whether it would be useful to gather information from diagnostic laboratories testing positive samples, but there were limitations in using such information to calculate overall prevalence, as discovery of an index case usually resulted in testing of the rest of the family. It was felt that disease prevalence would be adequately covered by Dr Graham Taylor at the meeting in May.

In reply to a question from Dr Barbara, detection of HTLV-II vs HTLV-I would be included in a paper from Dr Mortimer previously considered at MSBT.

7.0 **Microbiological Advice on Tissue Banking**
(Paper 22/96 refers, Dr Ruth Warwick in attendance)

Dr Warwick reported that she had been asked to chair a Red Book SAC on Tissue Banking, which had grown out of an ad hoc group with representation from Edinburgh, Cambridge and North London. The SAC was in recognition of the increasing tissue banking activity undertaken within the UK Transfusion Services, but it was recognised that other Tissue Banks, which were members of the British Association of Tissue Banking, were also undertaking this activity. Corneal banking was being undertaken by UKTTS. Two members of SACTTI were involved in the SAC in Tissue Banking; Dr Barbara in the main group, and Dr Hewitt on a sub-group considering donor selection. Donors were either surgical or cadaveric and appropriate testing strategies would have to be developed for each of these groups. Current problems included the fact that virology test kits were not validated for cadaveric samples, and that international standards varied as to the fate of tissues which were virologically initially reactive but negative on confirmatory testing. Transfusion prior to the death of cadaveric donors could lead to haemodilution, and also could be a risk factor for viral transmission to tissue recipients. A number of ways of handling virological and bacteriological issues in relation to tissue banking were discussed. The options considered were

- to develop a sub-committee of SACTTI
- to have more intensive cross-representation between the two SAC(s)
- or to conduct a separate one-day meeting to consider all the issues together.



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It was agreed to hold a special one day meeting early in 1997 to consider these problems. Proposals and an agenda would be produced by Dr Hewitt. The minutes of the last SAC meeting on Tissue Banking, which had been sent to Dr Flanagan, will be circulated to all SACTTI members.

**Dr Hewitt and Dr Flanagan**

8.0 **Definition of Designated Laboratories for Confirmatory Testing**

This was raised by Dr Robinson in view of the mention of designated laboratories in the Red Book revision. Dr Barbara reported that this had already been considered by the SACTTI Technical Sub-Committee. It had been agreed that some reference work could be done `in-house`, if the reference areas were physically and managerially independent from the screening laboratory. Other important areas were consistency of algorithms and the managerial control of reference work, whether done in-house or externally. The word `designated` had previously been used to mean allocated by the referring Centre rather than implying any approval by a central authority. It was recognised that the MCA Inspectorate were increasingly expecting documentation and contracts, including agreed investigatory algorithms for the handling of positive donor samples.

A fruitful discussion followed on the question of whether Transfusion Services should undertake their own confirmatory work. Points raised included:

i) Until now Reference Laboratories and Transfusion Centres had obtained considerable mutual benefit in dealing with new problems (Professor Tedder).

ii) There was considerable value in Reference Laboratories also seeing a considerable range of pathological samples from clinical sources (Dr Mortimer).

iii) The role of SACTTI is to set professional standards for the UK Transfusion Services. The issue of confirmatory testing is sufficiently important that it should come back to the full SACTTI Committee, rather than being considered by the Technical Sub-Committee (Dr Flanagan).

It was agreed that the setting of common standards for both internal and external laboratories was essential, followed by an appropriate contract. It was agreed that Dr Follett, Dr Mortimer and Professor Tedder would produce a discussion document on this subject by the end of May, for discussion at the July SACTTI meeting. The meeting wished to formally minute its appreciation of the contributions of Dr Follett, Dr Mortimer and Professor Tedder to reference testing over the years.

**Dr Follett, Dr Mortimer and Dr Tedder**



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9.0 *NEW ITEM*

**Implications of a Possible Creutzfeldt-Jakob Disease Variant for the UK Transfusion Services**

(Papers 26/96 and 27/96 refer)

An ad hoc meeting had been held at the Royal College of Physicians of Edinburgh on the 9th April 1996 to review the possible implications of the recently reported cases of variant CJD for the Transfusion Services. This was in recognition of a change in perception of CJD as potentially infectious until otherwise proven. It was recognised that one difficulty is that there is limited information available from animal experiments in relation to the ability of prion transmission by transfusion. In particular the absence of information of transmission of BSE by blood between cattle was a cause for concern. PM questioned the value of such data given the evidence of species difference and effects of passage. Concrete information was difficult to come by.

It was agreed that the first priority at this stage was to improve the level of knowledge so that appropriate decisions could then be made regarding donor selection, handling of blood components etc. The following actions were agreed:

i) Dr Robinson will ask MSBT for approval to do look-back on recipients of blood donations from donors who had subsequently developed CJD. **Dr Robinson**

ii) Dr Minor will produce a summary of available data, both from the scientific literature and other information which is in the public domain but which has not been subjected to peer review. **Dr Minor**

iii) Professor Tedder will make discreet enquiries to the Spongiform Encephalopathy Advisory Committee (SEAC) for further information with which to brief SACTTI. **Prof Tedder**

iv) In view of the possible transmission via buffy coats, Dr Gillon will produce a paper on the potential role of leucocyte depletion of cellular blood components in providing protection from the putative CJD agent. **Dr Gillon**

v) Any corrections to Dr Flanagan's notes of the meeting of 9th April should be sent to him by the end of April 1996. **All**

9.1 **Use of Controls** (Paper 23/96 refers)

Dr Alan Kitchen (NBS Brentwood) had sought advice on the use of go/no go standards in both microplate and bead assay formats. This was becoming an issue since microplate automation was being upgraded and would become more similar to bead technology. At the present time manufacturers insisted on one set of controls per plate, thus defining a batch, but for Abbott systems one batch was as many as ten trays. Dr Snape pointed out that statistical process control could be used to ensure that control/cut-off ratios remain constant across a series of plates. It was agreed that the important issue was to define a batch of tests. The issue was therefore referred back to the Technical Sub-Committee for further consideration .



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It was agreed that no change to the current approach should be made until information on the reliability of process monitoring by control OD was available.

**Agenda items 9.2, 10, 11 and 12 were deferred**

13.0 **Investigation of Possible Transfusion-associated Hepatitis** (Paper 25/96 refers)

***Please note that the letter from Dr Alexander to Dr Caffrey containing patient details should not have been circulated with the agenda. Will members please remove and shred this letter.***

The issue was how far lapsed donors should be contacted and investigated in the context of management of patients found to have viral markers which may have arisen from previous transfusion. It was agreed that the precise ascertainment of source of infection was of no benefit to the management of the patient. The meeting, therefore, broadly supported the concerns and conclusions set out in Dr Hewitt's letter to Dr Caffrey. The only point of issue is whether there remained any duty of care to lapsed donors to contact them in the event of a possible transmission. It was agreed that Dr Hewitt and Dr Gillon would seek the relevant legal opinions on this matter within the NBS and SNBTS respectively.

Dr Hewitt, Dr Gillon

14.0 **Any Other Business**

None.

15.0 **Date of Next Meetings**

Meeting to consider HTLV 1 screening - 14th May 1996, 11 a.m. at Leeds Transfusion Centre.

Future meetings:

1st July 1996 (Ordinary meeting)
16th October 1996 (Special meeting on HBV and HGV)
4th November 1996 (Ordinary meeting)

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