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

CONFIDENTIAL

Minutes of the meeting held at
North London Centre, (Training Suite, Deansbrook Road Centre)
on Tuesday 7th March 2000 at 10.30 am

Present: Dr. C. Bharucha (CB) - Chairman
Dr. P. Hewitt (PEH) - (Secretary)
Dr. J. A. Barbara (JAB)
Dr. B. Dow (BD)
Dr. Brian McClelland (BMcL)
Dr. Philip Minor (PMi)
Dr. Angela Robinson (AR)
Professor R.S. Tedder (RST)

1. Apologies

Professor Ian Franklin (IF), Dr. T. Snape (TS), Dr. Philip Mortimer (PMo).

2. Declaration of Interests

No new declaration of interests were made. All members are reminded that the annual written declaration of interests is now due.

3. Minutes of the meeting of 16th November 1999

The minutes were accepted as accurate.

4. Matters arising

4.1. HTLV (2/00)

CB summarised the meeting held on 16th November 1999.

A letter from the North London Centre has recently been submitted for publication in the BMJ, emphasising that HTLV infected blood donors detected in the North London study would not have been detected by selection alone. JAB reported that the South London study on HTLV testing in selected donors has been prepared for publication as a letter. There is also now data available from the Birmingham Centre, showing that 1 in 800 Afro-Caribbean donors are anti-HTLV positive (compared with 1 in 250 for South London). It has been suggested that the 2 letters would produced greater impact if submitted at the same time, so the South London paper will be held for a short period to allow the Birmingham data to be assembled. There has also been a recent publication of HTLV associated disease in England and Wales (Tosswill et al, British Medical Journal, 4 March 2000). This is an observational study. Copies were tabled at the meeting.

BD presented Scottish work, testing minipools for the presence of anti-HTLV. Minipools (of 95 samples) are anonymised and then

tested; 1,253 minipools (representing 100 - 119,000 donations) have now been tested. There were no initial reactives using the Murex G80/81 assay, controlled with known HTLV positive samples diluted 1 in 100. A "grey zone" was defined and 19 samples initially fell within the grey zone, but only 2 repeatedly so. This work gives encouragement to the use of minipools for other testing (e.g. for anti-HBc). SNBTS is planning to test a further cohort of donor pools and CPHL (PMo and Jenny Toswill) are also planning (or are currently carrying out) some pooling studies.

AR pointed out that MSBT may wish to review the position with regard to HTLV testing, since it has previously advised the CMO that HTLV testing should be introduced. It was suggested that there was the possibility of producing a paper for MSBT including the option to use minipools for multiple assays. An unknown factor is the position vis a vis leucodepletion. Leucodepletion has not reduced the need for CMV testing, and there is no scientific data to support leucodepletion as equivalent to either CMV screening or HTLV screening.

It was agreed that a paper should be prepared for MSBT, outlining the need for, and feasibility of, HTLV testing. Added value could then be to introduce anti-HBc screening on the same basis, and to provide options for other organisms. This paper should be aimed for

the MSBT meeting in early July and should include some of PMo's data from some years ago, suitably updated.

Action: JAB/RST/BD/PMo to produce a paper.

AR to establish the status of anti-HBc and anti-HTLV screening in the European Union.

* - have I asked, Jussi - M Has (in Vinje's large paper I think.

4.2. ***T. cruzi***

Dr. Peter Chiodini has replied to CB outlining the proposed management of donors with repeat reactive screening tests, including confirmation at the Hospital for Tropical Diseases, using an alternative EIA and IFAT, and clinical referral of confirmed cases. Peter Chiodini envisaged that confirmed positive cases would need clinical follow-up, possibly annually. It should be borne in mind that there may be a need to explore an additional referral centre (e.g. Liverpool).

PMi expressed concern over the apparent introduction of a new screening test, based on the experience with malaria ELISA. JAB explained that a number of assays were evaluated and that two separate assays have been judged very suitable for blood donor screening (Organon Chagatek and the Cell lab assay). RST pointed out that the Kit Tendering Group should be asked to ensure that

both kits are in use throughout the NBA, to avoid a monopoly situation. This will require that the Hospital for Tropical Diseases (as the Reference Lab) should be asked to carry both ELISAs as part of the confirmatory package. It was clarified that the *T. cruzi* screening test is being introduced to reduce donor loss, in particular with the change in donor selection which is now proposed which would increase donor loss and will exclude some donors now on the established donor panel. The SAC on Donor Selection has not yet finalised the agreed donor selection criteria, but it is likely that this will include donors born in (or whose mother or grandmother was born in) South America.

Action: JAB to write to Dr. Peter Chiodini regarding the use of a second ELISA in the confirmatory package, depending upon the screening ELISA used.

4.3. CJD (4/00; 4a/00; 4b/00)

The SACTTI sub-committee met in November 1999. The Group met again in February, now under the Chair of Professor David Anstee.

PMi outlined two projects in which he is involved. The first is a Department of Health project including Professor Bob Will and Dr.

Liz Miller (CPHL). Samples from CJD cases and controls (patients with suspected CJD who have a discharge diagnosis of "not CJD") are obtained and are being stored at the CJDSU. It is not yet known what analyte would be required when a test is developed (e.g. cells, serum, urine, CSF etc). There is a second project, which involves a WHO Group with responsibility for production of an international reference preparation for diagnostic tests (blood, urine, CSF) etc.

AR reported that SEAC and MSBT both held emergency meetings two weeks ago, following advance notice of publication in the Lancet of research by an EU funded group including the Institute of Animal Health. In the study, 55 mice were inoculated intracerebrally with a BSE strain. Blood samples were obtained from the mice at death, and the plasma inoculated intracerebrally into 40 mice of whom 4 developed CJD. It was pointed out that the BSE strain used in this research is more relevant to vCJD than that used in Paul Brown's work (NIH). There were grave misgivings about the publication however, since the methodology has not been seen. There are many unknowns including the protocol for fractionation of the plasma, the possibility of cellular contamination of the plasma, etc. It was pointed out that the study soon to be published gives no information about the pre clinical phase of CJD, since samples were taken from the mice at death. The emergency meetings were held to consider the possible implication for FFP/cryo from UK sources.

Various alternative options arise, e.g. the use of non UK FFP/cryo; the use of paid donor FFP/cryo; methylene blue/SD FFP etc. At the next MSBT meeting the members expect a further discussion on this subject. CB has requested Professor Anstee to prepare a response from SACTTI CJD Subgroup to the anticipated publication in the Lancet.

Any considerations of alternative sources of FFP would require that the prevalence of markers for microbial infection in such donors are known. Although imported paid donor plasma is being used in both the NBA and the SNBTS, this information is not currently available in either country. BMcL has data relating to the prevalence of markers per donation, but not per donor. Grave concern was expressed that this information is not available; decisions relating to alternative sources of FFP cannot be taken without this knowledge. It was resolved that this issue must be raised at MSBT and that the data must be discussed. As TS was not present at this meeting, and should have forewarning of a question to be raised at MSBT, AR and CB would investigate further.

Action: AR/CB to request the data from TS (BPL), with a view to this being presented to MSBT.

JAB pointed out that the error rate within American testing labs is far greater than in UK Blood Services, due to a lack of automation, information transfer etc. BMcL agreed and referred to a case report showing the erroneous issue of HBV infected platelets due to misreading of a fax report of results! RST wished to put on record his concern, highlighting that any concerns about the donor base used for imported plasma for fractionated products were negated by the various measures applied to the fractionated plasma, but the use of such imported plasma for FFP/cryo was a completely different situation where the additional manufacturing steps which gave assurance to fractionated products would not be applicable. This concern was noted.

Agenda items

Agenda items were taken out of order, so that those items requiring RST's presence could be discussed.

6. TMER update

PEH described the current situation with respect to the TMER. Ethical approval has been withdrawn by the Lothian LERC, who feel that there are issues which need to be addressed by the Department of Health. This particularly relates to the need to identify the fate of donations from vCJD

donors, which results in the identity of such recipients being known. DoH has convened an "Expert Group in the Management of Clinical Incidents relating to CJD" and a subgroup will be considering issues relating to notification and information to patients exposed to "risk" of CJD in a variety of clinical settings, including neurosurgical and ophthalmological operations, tonsillectomy, appendectomy, and blood transfusion. PEH reported that a first meeting would take place on the 10th April (but she will be on leave) and a further meeting on the 10th May.

In relation to the discussions on CJD, AR reported on the EU meeting of Transfusion Experts, considering the proposals for a draft directive on the safety of blood. It has been proposed to include a travel questionnaire to donors, which will initially be administered to 1% of donors in each EU country. This will relate specifically to the practicality and advisability of excluding donors with a known period of stay or residence in the UK.

4.5. Reinstatement of donors who have false positive screening results (36/99 and 36a/99)

The letter from IF was discussed. It was agreed that the use of alternative assays for clearance of donors, as currently applied, was satisfactory. Concern was expressed over the last sentence in paragraph 3 of IF's letter "certainly in SNBTS we are most unhappy about the notion about "alternative clearance" for use in this way". It

was felt that this referred to the potential practice of referring a sample from one Centre to another in order to find a negative screening test result. It was agreed that this was not the intention of the alternative assay protocol and that it should not be used in this way. In the absence of IF, further clarification of his concerns was not possible.

Currently, 2 negative reference laboratory results are required, with an interval of 6 months, before the donor can be returned to the panel using the alternative assay. Dr. Andrew Herborn has proposed that the interval between 2 negative reference test results could be reduced from 6 months to 12 weeks, without compromising the safety of the blood supply. All those present agreed that 12 weeks was a sufficient time interval for any developing infection to be reflected in increased reactivity on a reference test package. Therefore, the requirement for 6 months should be reduced to a minimum period of 12 weeks.

Action: CB to take to the Red Book Executive.

4.4. Anti-HBc

This will now be considered along with the paper on HTLV.

4.6. MAT update

Dr. Peter Chiodini has received the reworked EIA incorporating recombinant antigens and is due to start looking at these on his panel of samples. A test is being developed by a second company, also using recombinant antigens. A third company had started to develop an assay, but has not pursued this. Peter Chiodini has written to confirm his views on residency: that 3 months at any time of life would be a safe and sensible time period. The SAC on Donor Selection will take this forward.

Action: CB to write to Dr. Peter Chiodini to ask for a likely timetable for the results of his evaluation.

4.7. CMV (e-mailed correspondence tabled for information only)

It was noted that the information relating to possible CMV transmission by leucodepleted platelets was inadequate. It was dangerous to assume that the CMV positive leucodepleted platelet pool was responsible; there could equally be an error or test failure in the CMV antibody testing of the other blood components given to the recipient.

RST wondered whether a study should be performed to look at the occurrence of CMV viraemia in plasma, which would be missed by CMV antibody screening or leucodepletion.

Action: RST and JAB to discuss further.

4.8. "Combo" HIV assays

The Reference Coordination Group of the NBA (with Scottish and Welsh observers and representatives from PHLS) will take forward the question of confirmatory testing for repeat reactive combo assays. RST felt that a neutralisation test on the original assay was a pre-requisite, using an antibody confirmatory algorithm and an antigen confirmatory algorithm with neutralisation and RT-PCR.

Action: JAB to take back to the Reference Coordination Group and then report to SACTTI.

5. Correspondence about a donor whose husband is an HBV carrier.

CB tabled this item to discuss the principle of deviation from standard policy. It was agreed that this was not a matter for SACTTI to sanction. Once SACTTI had agreed the criteria included in the Red Book, any decision to deviate from this standard policy would be for individual medical

directors of the blood services. It was agreed that in this case, no exception should be made.

7. Any other business

7.1. NAT

RST reported that there will be discussions about harmonisation of tests, terminology etc between NBS and SNBTS with an aim of further discussion at the May SACTTI meeting.

Action: RST and BD.

AR noted that MSBT would be requiring an update on NAT for HCV PCR at the next meeting. She would be reporting that significant progress had been made; that problems with the assay are being addressed and that roll out in a country the size of England is a demanding exercise. The second phase, concentrating on testing for component release, is now underway and commonality between SNBTS and NBA is being pursued. RST noted that the project would have benefited from stronger scientific input and support at an earlier stage, and that an unexpected problem in the transfer of testing from manual to automatic techniques had significantly impacted upon the project.

7.2. Red Book matters

Minutes of the Red Book Executive meeting of 5 October 1999 and Update of the Red Book Organisation (EC14/00) were tabled.

8. Date of next meeting

This has previously been arranged for 2nd May 00, but the new Chairman for SACTTI may not be available on that date. CB is unable to attend, having already arranged holiday for that time. It was agreed that no change to the date could be made until the identity of the new Chairman and the availability of that person for the 2nd May, had been established. If the new Chairman is unable to attend on the 2nd May then a change of date will be necessary.

All present agreed that CB should be thanked for her considerable input into SACTTI over a difficult period; she had succeeded in steering the SAC over a difficult period and through a number of major issues. All wished her well for the future.

Date of next meeting: 2nd May 00 unless notified otherwise.