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

Minutes of the meeting held at Deansbrook Road, North London Transfusion Centre, on 31st January , 1996 at 11.00 a m

Present:	Dr P Flanagan	(Chairman)	Dr T Snape
	Dr L Williamson	(Secretary)	Professor R Tedder
	Dr E Follett		Dr J Gillon
	Dr A Robinson		Dr J Barbara
	Dr P Hewitt		Professor J Cash
	Dr P Mortimer		

Apologies: Dr P Minor

ACTION

1. GRO-A

Professor Cash proposed that in view of GRO-As recent illness, the best wishes of the group be conveyed to him. This was unanimously supported. — Dr Flanagan

2. **Minutes of Last Meeting 18th October 1995:**

These were accepted as a true record.

3. **Matters Arising:**

1.6 **Estimation of Seronegative Transmission Risk for HCV, HBV**
(Paper 16/95, tabled at the meeting refers)

The importance of consistency among all UK transfusion services when quoting residual risk of each infection was recognised, given the sensitivity of the data. The residual risk would depend on:-

1. Inter-donation interval - at present there were apparently major variations in this between centres, which the new IT system may be able to clarify.
2. True population prevalence.

Kate Soldan is acquiring information on seroconversions and is working with PHLS/CDSC statisticians on a model to calculate residual risk. It IS important that Scotland and England uses common methodology. To this end, SCIA, via Dr J Gillon, would be working closely with CDSC.

Dr Snape informed the meeting that these data would shortly be required by European fractionators.

The role of laboratory error in allowing release of positive material should not be forgotten. (Ref: Lackritz et al, NEJ Med, 1995, 333, 1721-5)

1.7 **Cambridge Anti-HBc Study**
(Paper 17/95, previously circulated, refers)

In the paper circulated, some of the Cambridge and S Thames figures were reversed - a revised version is attached. Dr Williamson

Dr Williamson gave an update on the current status of this study. Donor testing was complete, and the lookback phase, spanning the last 5 years, had just begun. Points to consider were:-

1. The study size was at the limit for statistical power.

2. Donors would be tested for HBV DNA by Professor Tedder's modified method, providing 1-2 logs extra sensitivity, but this would still be less sensitive than patient testing as a means of assessing transmissibility.

3. The possible protective effect of anti-HBs in control donors, although most patients would receive very little plasma. The NLTC study would provide additional data on infection rates from donors with no markers of HBV.

4. The protective level of anti-HBs, allowing reinstatement, was being performed on IMX. This would be further validated using AusAb.

Professor Cash wondered how acceptable the information would be to MSBT without Scottish data, and whether inclusion of a Scottish centre would strengthen the statistical power. Edinburgh had pre-transfusion samples going back several years, which might help exclude other sources of HBV acquisition in hospital cases. The meeting agreed that this would be the only opportunity to carry out such a study, and it was therefore important to be sure that it was large enough to draw valid conclusions.

Further discussions with a statistician would be valuable. Dr Williamson

Professor Tedder pointed out that further data on HBV transmissibility might be derived from statistical analysis of PTH cases at NLTC from 'anti-HBc only' donors. Prof Tedder/ Dr Hewitt/ Dr Barbara

5.0 **Audit of Donor Counselling Procedures** (Paper 1/96 refers)

Dr Flanagan had written to the Medical Directors of all UK Transfusion Services. An audit would be co-ordinated by Dr Alison Townley, Leeds Blood Centre, on behalf of the NBA and should be completed within 3 months. A separate audit was being undertaken in Scotland co-ordinated by Dr George Galea. The audit should permit standards to be identified in this area, possibly with eventual incorporation into the Red Book. Centres varied as to whether donor counselling was the responsibility of the Donor Care or Microbiology consultant.

8.0 **National HCV Lookback Programme** (Paper 2/96 refers)

Dr Robinson presented figures (see attached) of the current status of HCV lookback in England. It was recognised that the low percentage of patients testing positive (approximately 25%) could be due to a number of reasons e.g. the donor was HCV negative at the time of donation, blood from the donor was not given to the identified patient, and, finally, true non-transmission. It had already been observed that certain donors consistently failed to transmit.

MSBT had expressed concern at the slowness of progress. The following rate limiting steps were identified:

1. Identifying the implicated components - now virtually completed.
2. Lack of or delay in finding blood bank records.
3. Difficulty in finding or extracting information from medical case records.
4. Counselling time.
5. Delay in receiving appointment with hepatologist.

MSBT had suggested a number of possible solutions, including the use of control of infection nurses to peruse case records, the use of trained counsellors, and use of BTS staff to visit hospitals where there were problems.

Dr Robinson will be asking Zonal Clinical Directors in England to specify the reasons for local delays so that appropriate help can be provided where needed. — Dr Robinson

Funding from the Department of Health will reach Centres soon.

It had been agreed by MSBT that lookback should also be performed on selected indeterminate donors. It was recognised that not all donors and recipients will be identified. Professor Tedder pointed out that in England there was no funding to investigate donors using genomic detection, but Dr Follett did not think this offered significant advantage over positivity in two ELISAs. Dr Robinson will shortly be asking Centres to begin the lookback on indeterminate donors. — Dr Robinson

13.0 **HIV Subtype O** (Paper 3/96 refers)

Dr Flanagan had received information from most manufacturers regarding their HIV kit's ability to detect subtype O, and has convened a meeting in February to define standards and assess information submitted by manufacturers against these. There were potential difficulties:-

1. In defining and obtaining true subtype O samples for validation.
2. In obtaining objective performance data from manufacturers.

It was agreed that Dr Flanagan and Dr Mortimer would discuss how to obtain objective information from European institutions. — Dr Flanagan, Dr Mortimer

4. **Declaration of Interests** (Papers 4/96 and 5/96 refer)

The Red Book Executive had requested that all Standing Advisory Committees devise a mechanism for declaration of members' interests. Dr Flanagan reported that all replies he had received from SACTTI members had been positive, and it remained to decide which of the two proposed systems to adopt. Professor Tedder had had previous experience of the CSM System, which allowed members with conflict of interests to expression opinions but not to vote on relevant issues. He felt that the definitions in the proposed Red Book model were rather vague. It was recognised that most Transfusion Microbiologists had some involvement with at least one commercial company.
Dr Barbara felt that it would be a pity if declaration of a specific interest debarrred a member from debating relevant issues. Dr Flanagan clarified that the intention in proposing the CSM System was to use their definitions rather than to accept the entire package. Professor Cash wondered whether an annual review was sufficient, and that perhaps the Chairman should invite members to declare new interests at the beginning of each meeting. This could relate specifically to items on the agenda. It was also important that all Red Book Committees operate the same system.

It was agreed that:

1. Members should register interests on an annual basis.
2. The Chairman would request at each meeting members' interests in relation to specific agenda items.
3. The system itself would be reviewed in one year.
4. The system would begin to operate at the next SACTTI meeting.

Dr Flanagan will report back to the next meeting of the Red Book Executive. — Dr Flanagan

5. **HTLV Antibody Testing** (Paper 6/96 refers)

Dr Flanagan wondered whether in the light of the recent BMJ Editorial SACTTI should declare its position with regard to HTLV antibody testing. Dr Robinson reported that this had been debated at the last MSBT meeting, where a paper from
Dr Brian McClelland and Dr Philip Mortimer had been presented. MSBT was now asking SACTTI for their professional opinion on this matter. It was agreed that a special one day meeting would be held to review available data, for which specific tasks would be allocated in advance. A special meeting was justified since firstly there was more information now in the public domain, and secondly since `first pass` testing was now approved, at least in principle. The logistic aspects of screening would include testing only selected donors, or blood components for selected recipients, the implications for IT, confirmatory testing and counselling, and the specificity in relation to loss of donations, which was seen to be extremely important. It was recognised that the pros and cons of HTLV screening would have to be seen in isolation, and not compared with the potential value of any other microbiological assay. The following was agreed:

1. A sub-group would be formed to define the questions to be answered, and possible sources of information. — Dr Flanagan
2. Dr McClelland's paper would be circulated. — Dr Flanagan
3. Data from the South Thames study, following the recent donor recruitment campaign, would be made available. — Prof Tedder

It was felt that to achieve a useful review, it would be unlikely that the information would be available for the next MSBT Meeting and that this information would be conveyed back to Dr Metters. Dr Flanagan

A one day meeting was agreed for 14th May, at 11 a.m.

6. **Malarial Antibody Testing** (Paper 7/96 refers)

A major outstanding issue surrounding this test was its specificity and how it would subsequently be evaluated for acceptance by UK Transfusion Services. Dr Chiodini would be meeting with Launch Diagnostics shortly to confirm that the assay was now suitable for its intended purpose. The method for evaluation was discussed. The NBS Kit Evaluation System only had mandatory tests within its terms of reference, but it was felt that the Chairman, Dr Barbara, could, if he so wished, include evaluation of kits for non-mandatory tests. It was recognised that Transfusion Centres would be in a position only to evaluate specificity and not sensitivity. This was, however, an extremely important issue, since this test was not being implemented in order to improve transfusion safety, but in order to make more usable blood units available for transfusion. It was recognised that both the Scottish and English Services would need to agree an acceptable level of specificity, both for initial introduction and for each subsequent batch. Batch acceptance protocols are already in place in both Services. The importance of a consistent approach by NBA and SNBTS was recognised. Further information was required to ensure that modifications had not reduced the sensitivity of the assay. Dr Barbara would obtain information from Dr Chiodini in writing to confirm this. Specificity evaluations would then be undertaken by national evaluation mechanisms. This data would then be assessed on a joint basis. It was emphasised that the test would be optional and need only be used by centres if it was felt to be of value. Dr Flanagan Dr Barbara

7. **Revision of UKBTS/NIBSC Guidelines (Red Book)**

(i) **Annexe 3** (Paper 8/96 refers)

Dr Flanagan had received very helpful comments from SACTTI members. These had been included only for areas in which SACTTI had previously taken a view. There was considerable discussion on the acceptability or otherwise of retrospective testing of archive samples to allow re-entry of donors via the current re-entry algorithm. This was presently being implemented at NLTC, but Dr Follett and colleagues had expressed concern over the time period for which retrospective testing would be acceptable. It was recognised that:

(a) Allowing retrospective testing of archive samples was on occasions extremely useful, particularly in relation to plasma donors;
(b) It would also have a use in allowing current donors to continue donating where there has been a change of assay.
(c) It was undesirable to have local interpretation of Red Book Guidelines, which should be as specific as possible.

It was therefore agreed that Annexe 3 would be further revised to allow such retrospective testing, but that this would specify a gap of at least 6 months but not greater than 12 months between archive sample and index donation. Dr Flanagan

In response to a question from Dr Snape, Dr Flanagan reminded the meeting that the need to archive samples had never been formally defined in the Red Book. In practice all Centres store archive samples but for varying periods. BPL plasma specification currently requires a 6 month archive, as specified by CPMP. The SACTTI Sub-Committee was currently discussing this issue and their report was awaited.

Professor Cash reported that the Scottish Office mandated storage of archive samples for 5 years, and he would copy their written instruction on this to Dr Barbara. — Prof Cash

Dr Williamson requested that the meeting review her suggestion that the Red Book specify that repeat testing on initially reactive samples be done on the same kit as the initial test. At the present time at least one Centre (Cardiff) re-tested some samples by an alternative kit without confirmatory testing. It was agreed that this item was too important to allow such local variations, and that the Red Book should specify that repeat testing of initially reactive samples be done with the same test as initial screening.

Dr Flanagan would inform Dr Tony Napier of this decision. — Dr Flanagan

(ii) Annexe 4 Revision (Papers 9/96 and 10/96 refer)

Dr Douglas Lee had requested review of the testing protocol for accredited donors of immunising red cells for anti-D production. After general discussion, the following was agreed:

a) The need for anti-HBs testing would be removed since anti-HBs positivity without other markers was seen only after vaccination.

b) The test for anti-HBc must be negative irrespective of the level of any co-existing anti-HBs.

c) Donors should be tested for HCV RNA in a reference laboratory.

d) For HIV, now that more data are available it would be unheard of to have a donor who was truly infectious but still seronegative at the end of the quarantining period. Since genomic testing for HIV was difficult and not widely available, the need for HIV PCR testing at the point of release was removed.

e) All the above tests would be performed both at the point of donation, and at release. Because donors were usually on a regular programme of donations, many tests would cover both eventualities.

f) There was no need to test donors for parvovirus B19 since the recipients would not be immunosuppressed.

g) At 5.2 reword to say 'Consider testing for new markers as they become available'.

h) ALT. The need to test for this monthly should be retained since there is currently no widely available test for HBG virus and because there may yet be further hepatotropic viruses identified in the future.

Dr Flanagan will write to Dr Lee informing him of these decisions. — Dr Flanagan

Items 8, 9, 10 and 11 were deferred to the next meeting.

12. **Virally Inactivated Plasma**

Dr Williamson reported that the Medicines Control Agency had just given permission for the Octaplas trial to re-start. Octapharma had also submitted a product licence application, which may be granted during 1996. The UK would then be in the unusual position of having a licensed virally inactivated FFP sourced from European plasma available to clinicians alongside UK untreated FFP. It was recognised that neither SACTTI nor MSBT had reached final decisions on the way forward for FFP.
Dr Flanagan reported that, although many Transfusion Centres were attempting to source as much FFP as possible from apheresis, this may have to be cut back because of financial constraints. Professor Cash thought that although the operational considerations around quarantining plasma were considerable, that SNBTS considered them not to be insurmountable. It was agreed that Dr Williamson would keep SACTTI informed regarding the position of Octaplas. — Dr Williamson

13. **Format of Future Meetings**

It was agreed that the format should be four standard and two special meetings per year. At the next meeting there should be updates on syphilis, HGV and B19, SNBTS having reviewed the last two fairly recently.

14. **Any Other Business**

None.

15. **Dates for Future Meetings**

16th April 1996	Ordinary meeting
14th May 1996	HTLV1 screening
1st July 1996	Ordinary meeting
6th October 1996	Special meeting on HBV and HGV
4th November 1996	Ordinary meeting

Venues for these meetings would be notified by Dr Flanagan. — Dr Flanagan

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February 1996