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

Minutes of the inaugural meeting of the above committee held at West Midland RTC, Birmingham on Monday 11th October 1993.

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| **Present:** | Dr. W. Wagstaff | (Chair) | Dr. E. Follett |
| | Dr. F. Ala | | Dr. P. Minor |
| | Dr. J. Barbara | (Secretary) | Dr. R. Mitchell |
| | Dr. H. Gunson | | Dr. P. Mortimer |
| | Dr. P. Flanagan | | Dr. L. Williams |
| **Apologies:** | Prof. J. Cash | | |
| | Prof. R. Tedder | | |

**Action**

1. The minutes of the seventeenth meeting of the ACTTD were approved subject to the following amendments.

   1.1. page 2, item 3. Drs. Perry and Lane's attendance at ACVSB was not as representatives of the BTS.

   1.2. page 3, item 7, para 2 should read: 'the Liverpool RTC had extended its anti-HBc assessment, restricted to previously untested new donors, and a study protocol had been received.

2. Matters arising were taken with agenda items, the order of which was revised to accommodate presenting members who had to leave early to attend meetings elsewhere.

3. **Terms of Reference (Draft)**
   Dr. Wagstaff welcomed members to the newly constituted ACTTI and presented the following:

   Draft Terms of Reference for the Committee, pending the outcome of a meeting between Dr. Gunson, Mr. Adey and Dr. Metters on 25th October 1993.

   - To advise the UKBTS/NIBSC Liaison organization, the NBA and SNBTS on all matters concerned with the possible transmission of infection by the transfusion of blood, its components and, via donor plasma, fractionated plasma products. This advice should also cover the possible transmission of infection by other banked tissues processed by and held at Transfusion Centres.
   - To commission, conduct and co-ordinate trials of new technology involved in the screening of donors for infectious agents transmissible by transfusion, consistent with the work of the national research committees.

It was noted that ACTTI could have recourse to the minutes of MSBT meetings so that responsibility for microbiological screening policy decisions made by MSBT could be clearly defined.

4. **Declarations of Interest**

Dr Wagstaff thanked members for responding to his letter requesting individual declarations of commercial interest. He felt confident that all members could be completely relied upon to provide unbiased and wholly appropriate opinions. In relation to the above, Professor Tedder's letter expressing concern that Biokit UK might question his impartiality regarding opinions on diagnostic kits was duly noted.

Dr Wagstaff pointed out that members' letters declaring interests would be lodged with the Chairman and would be available for appropriate scrutiny. He suggested that members should withdraw from the decision making process where a direct interest was involved and this was unanimously agreed.

5. **Generic donor readmission protocol**

The final draft from Professor Tedder incorporating minor modifications had been accepted by ACVSB and was tabled by Dr. Mitchell. Immediate implementation was agreed. **Distribution of these minutes to RTDs together with a copy of the donor reinstatement action chart (attached) will constitute formal promulgation of the policy, superseding the July 1987 EAGA minute on readmission for anti-HIV false-positive donors.**

The Red Book Guidelines will require appropriate amendment. **Dr. Wagstaff**

6. **Significance of NS5 antigen in anti-HCV kits**

This question had again arisen following letters from Dr. Douglas Lee and Dr. Angela Dike. The following points were made by various members:

- It had been stated in the minutes of the 17th ACTTD meeting of 14th July 1993 (page 4, item 9): "Theoretically, however, especially in the early stages of assay development for relatively new virus screening systems, a wider range of antigens might increase the range of viral detectability".
- If assays are available which contain NS5 and for which specificity is not compromised or is at a level acceptable to the user, use of such assays may be seen to offer a bonus in terms of potentially enhanced anti-HCV detection range.
- Currently, however, the committee did not feel it was justified to make inclusion of NS5 antigen a mandatory requirement for kit acceptability.
- Abbott Laboratories are offering both 'NS5 containing' *and* 'NS5 lacking' anti-HCV kits.

At this point Dr. Wagstaff (who will be retiring from the committee) relinquished the chair to Dr. Fereydoun Ala and accepted the committee's thanks for his contribution to the work of ACTTD.

**Action**

7. **Study of the use of 2 different ELISAs to define antibody reactivity**

Dr. Williams tabled a progress report and tables of results. She will investigate the possibility of obtaining PCR testing on the 61 anti-HCV indeterminates in the study (either for single, or pooled samples). **Dr. Williams**

Two points ancillary to the study were noted:

- in routine screening the same test should be used for retesting initially reactive samples.
- the study supports the concept that an alternative assay can usefully be used for release of samples reacting falsely positive, within the context of a defined donor-readmission policy (see item 5).

Dr. Flanagan asked how a falsely-positive donor could be readmitted if a Reference Laboratory chose not to perform a blotting test because they did not obtain a reactive result on their ELISA testing of a referred sample. It was generally felt that a blotting test would be needed on at least one occasion to demonstrate absence of anti-HCV lines before readmission was permissible.

Dr. Mortimer and Professor Tedder were asked to liaise to provide advice on a minimal confirmatory package that addressed this question without unnecessary referrals of sample and undue Reference Laboratory testing expenditure. **Dr. Mortimer** **Prof. Tedder**

Dr. Mortimer asked that it be acknowledged in relation to the readmission protocol that an anti-HCV 'indeterminate' donor who did not reattend would not receive notification of his or her HCV 'indeterminate' status.

Dr. Follett felt that the positive:negative ratios in both of the 'alternative' tests needed to be compared when considering readmission. Also, each batch of kit reagents should be checked for sensitivity because of the potential for batch-to-batch variation.

8. **Birmingham RTC follow-up of anti-HCV positive donors**

Dr. Ala will summarise for the committee the results of this study of anti-HCV confirmed positive donors which has involved counselling, history-taking for 'life-style' and other epidemiological aspects, liver biopsy and PCR. **Dr. Ala**

9. **Can RTCs perform their own anti-HCV reference testing?**

Dr. Angela Dike had asked this question (to which Dr. Wagstaff has subsequently replied on behalf of the committee).

No concrete regulations exist regarding the definition of referral sites for microbiological screening tests and the option remains for individual RTCs to provide a defined reference function within their microbiology laboratory.

However, if this option is chosen, a strict separation of function and responsibility should be maintained with an appropriate degree of independence afforded to the person responsible for provision of reference information. There may also be a further option to refer 'difficult' samples for more extensive reference testing.

Disadvantages include:

- potential compromise of the integrity of the two separate functions when contained within one laboratory.
- limited access to a full range of samples with subsequent limitation of experience. This access is a particular strength of established Reference Centres who would continue to require receipt of a broad spectrum of samples so that their extensive range of experience could be maintained.
- economy of scale favours the established Reference Centres who would therefore have economical access to a wider range of tests, equipment and techniques.

Dr. Follett also noted that 'independent' reference work would require measures to demonstrate the quality of the procedures involved.

The question of PHL having to charge for reference work from 1st April 1993 then arose. Dr. Mortimer was uncertain of the exact mechanism for the financial transaction involved. Therefore, Dr. Ala will write to Dr. Diana Woolford (with a copy to Dr. Morag Timbury) to seek clarification on this point. **Dr. Ala**

10. **Screening blood donors for anti-HBc**

10.1. Dr. Gunson reported that the newly constituted MSBT Department of Health Advisory Committee had reached an eventually unanimous decision at their first meeting on 4th October 1993 that anti-HBc need not be mandated as a routine test for blood donors. This decision has been notified to all RTDs/Chief Executives in England and Wales in a letter from Dr. Gunson sent on 8th October 1993. The option for restricting screening to new donors once the donor panel had been tested was then raised by Dr. Barbara; however MSBT had not considered this option as it had not been tabled by ACTTD. Dr Barbara accepted Dr. Flanagan's observation that such a scheme would require reliable identification of established donors who had not undergone anti-HBc testing.
Dr Barbara expressed his disappointment at the decision and itemised his reservations concerning the points raised by MSBT, as follows:

- the suggested level of false-positivity of anti-HBc assays (10 fold) does not seem to be borne out by the recent multicentre study where some of the more specific ELISAs (even in the absence of reducing agent), showed a repeat reactive rate of ~0.7% compared with a 'confirmed' positive rate of 0.55% nor by an earlier multicentre centre (Anderson *et al.*, 1992, Transfusion Medicine

2, 301) where the repeat reactive rate was 0.9%, only 1.4 fold more than the confirmed positive rate of 0.63%. In any case, the specificity of anti-HBc screening would certainly compare favourably with anti-HCV screening, especially when the latter was first introduced.

- the consensus of reactive results by different anti-HBc assays at the Scottish Reference Laboratory in the recent trial correlated completely with a test using reducing agents (IMX) - a far more encouraging picture than with HCV confirmation where a far more 'considerable number of donors' (i.e. those with single antibody reactivities on blot tests) cannot be provided with 'definitive health information'.
- A go-no-go standard for anti-HBs need not be a 'major problem' despite differences in anti-HBs kit epitope recognition since an appropriate safety factor can be built into the cut-off value.
- The difficulty of estimating residual PTH-B transmission rates is to a large extent an indictment of the lack of central UK collation of such cases and highlights the necessity for the urgent introduction of such collation. The same situation pertained for PT-NANBH but this did not prevent the introduction of anti-HCV screening. Furthermore, the level of any excess mortality caused by PT-NANBH 20 years after transfusion is by no means clear cut, as demonstrated by Dr. Seeff's recent study in the USA. There are sufficient law suits relating to 'anti-HBc-only' transmissions in the UK to warrant concern.
- The cost of anti-HBc screening is far less than for anti-HCV screening. In the face of the extent of investment in the latter the *lack* of the further outlay for anti-HBc might seem hard to justify.
- Anti-HBs positive plasma need not be excluded from pooled plasma. Indeed, anti-HBc screening would positively enhance the provision of anti-HBs specific immune plasma.

Dr. Mortimer felt that more evidence was needed for the cost-effectiveness of anti-HBc screening for 'window-period' ddetection of HBV infection. However, Dr. Barbara reiterated that the key role of anti-HBc screening was to identify donors at the 'tail-end' of carriage, with subliminal levels of HBsAg. Dr. Barbara expressed his surprise that anti-HBc screening has now been decided to be unnecessary when earlier even anti-HBs positive (and immune) donors were considered to be sufficiently potentially 'unsafe' as to warrant the initiation of 'life-style marker' studies.

Considerable discussion followed and it was agreed to present the results of further studies to MSBT in the future.

10.2. In the light of the anti-HBc screening decision, the various analyses prepared by Dr. Follett, Mr. Barr and Dr. Barbara would be kept 'on hold' pending future developments. However, anti-HBc 'life-style marker'

studies already in progress would continue and Dr. Follett would coordinate the finalisation of the paper on the recent multicentre anti-HBc trial, with Mr. Barr and Dr. Barbara, as quickly as possible. **Dr. Follett**

11. **Combined anti-HTLV/anti-HIV assay**

The NBA had now approved Dr. Flanagan's assessment of the combined anti-HTLV/anti-HIV kit although formal permission from MCA was still awaited. Dr. Flanagan tabled a report of his results to date.

On 7th October a parallel evaluation of the combined assay and the routine anti-HIV 1/2 assay will start at Leeds for several weeks to assess comparative specificities. Specificity will be monitored during the course of the assessment in case of washer problems or batch variation of kits. In 2 previous evaluations at Leeds, the repeat-reactive rates were 0.25% and 0.28%. For the latest 2,500 samples tested, the initial-reactive rate was 1.1% (?washer associated) and the repeat-reactive rate was 0.38%.

The assessment will last 6 months and will not be extended without further consultation with Dr. Gunson and the ACTTI. The extra cost per test (16p) will be funded by the Region. The study will provide epidemiological data and experience with a mutiple combined assay. If the assay proves satisfactory, despite potential specificity deficiencies, it might offer a streamlined approach if anti-HTLV screening were ever considered necessary. However, the increased cost, and the potential danger of 'drifting' into HTLV screening without a defined need to do so, were noted.

12. **Bacteriological safety of transfusion**

Dr. Mitchell tabled a proposed form for reporting a proven bacteriological transfusion reaction to a central UK BTS register, the working of which has yet to be decided. This form would complement a hospital report form detailing any incidents for investigation. Dr. Mitchell will approach BCSH via Napier to obtain input from hospitals so that this form can be drafted. **Dr. Mitchell**
[At this point Dr. Mitchell left the meeting to fulfill a prior appointment].

Dr. Gunson will finalise the editing of the draft guidelines for investigating potential cases of post-transfusion bacterial transmission. The crucial question remains that of definition of when a transfusion reaction warrants the considerable effort involved in bacteriological investigation. **Dr. Gunson**

13. **Monitoring sample addition in screening assays**

Dr. Gunson reported that Manchester BTS (like NLBTC) now feel that a failure in sample addition was responsible for their anti-HCV false-negative test result. Several other Abbott users reported the likelihood of similar incidents. Dr. Mortimer will arrange with Dr. Barbara the drafting of a letter to kit manufacturers to ask how they control coating of the solid phase of their assays and the monitoring of sample addition (carried over from previous minutes). **Dr. Mortimer**

**Action**

14. **Any other business**

14.1. Recommendations of hepatitis advisory group: HSG 93 40
Dr. Gunson wished to bring this publication to the attention of RTDs with regard to hepatitis B vaccination of appropriate staff in transfusion centres, so that centres could define their own policies.

14.2. Longer term agenda items
Dr Ala discussed potential areas for future ACTTI consideration and asked members for their ideas. Suggestions included:

14.2.1. Cost-effectiveness analysis with respect to alternative pragmatic approaches to testing strategies: e.g. preparation of a discussion document to identify the issues involved in testing pools of samples, rather than individual sera; examination of contexts in which new donor testing rather than whole panel testing might be appropriate.

14.2.2. The value of syphilis testing.

14.2.3. Central Registers for collation of reports of suitably investigated cases of post-transfusion infection.

14.2.4. Lyme disease as a potential hazard of transfusion.

14.2.5. The relevance of *Yersinia enterocolitica* as a UK transfusion risk.

14.2.6. Results on further studies related to anti-HBc screening and anti-HBc as a potential life-style marker.

14.3. Frequency and venue for future meetings
It was thought appropriate to hold meetings at 3 monthly intervals. The venue could vary; because of its convenient access to several committee members, Dr. Contreras has offered NLBTC (Colindale) as a venue and Dr. Gunson could organise facilities at NBA headquarters, Watford.

15. **Date of the next meeting**
Dr. Ala will send members a list of possible dates. **Dr. Ala**

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