UK ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED DISEASES

Minutes of the fifteenth meeting of the above committee held at Gateway House, Manchester, on Tuesday 16 February 1993.

Present: Dr. H. Gunson (Chair)
Dr. J. Barbara
Prof. J. Cash
Dr. J. Craske
Dr. E. Follett
Mr. W. Hughes (for Mr. A. Barr)
Dr. R. Mitchell
Dr. R. Perry
Dr. Mortimer

1. Apologies for absence were received from Mr. A. Barr, Dr. M. Contreras, Dr. R. Lane, Dr. P. Minor, Prof. R. Tedder, Dr. W. Wagstaff.

2. The minutes of the fourteenth meeting were approved.

3. **Matters arising:**
   3.1. Dr. Gunson confirmed that he would continue to chair the meetings for the time being, with the secretarial assistance of Drs. Contreras and Barbara.

   3.2. Specific items relating to anti-HBc would be considered, as they arose, under 'agenda items'.

4. **Agenda items**
   4.1. *ACVSB meeting of 9th February 1993; verbal report, Drs. Gunson and Mitchell.*
   ACVSB asked ACTTD to consider the results of the anti-HBc trials to date so that it could provide recommendations in time for the next ACVSB meeting in May 1993. ACVSB assumed that a uniform national approach to anti-HBc screening policy would be adopted. Dr Lloyd's intention to commence screening on 1st April 1993 was referred to the NBA Chairman.

   4.2. *Reports of anti-HBc trials (distributed in advance).*
   4.2.1. **SNBTS.** All samples considered likely to contain anti-HBc were reactive by the whole range of anti-HBc detection systems tested. The IMX system was the most specific and looked promising in a confirmatory context. However, it was not designed for large scale screening. It was noted that different tests for anti-HBs did not uniformly recognise antibodies to the different epitopes of HBsAg.

Action

4.2.2. **Liverpool.** Concern was expressed regarding modification of manufacturers' test procedures. Dr. Barbara put forward his and Dr. Contreras' view that validation of any assay (standard or modified) and achievement of requisite performance with working standards were the prime concerns. The committee agreed that it was the responsibility of individual Centres to satisfy the MCA as to the integrity of information transfer with modified assays but this might prove particularly difficult with Terasaki based systems.

4.2.3. **Cambridge.** It was noted that the anti-HBc repeatable-reactive rate for Ortho ELISA performed on repeatably reactive sera screened by Abbott Corzyme was remarkably similar in Glasgow (31/10,000) when compared with Cambridge (28/9,000).
However, it was felt that more information would have been obtained if all sera repeatably reactive on the primary anti-HBc ELISA had been tested for anti-HBs.

4.2.4. **NLBTC.** It was noted that a range of ELISAs had been compared for end-point sensitivity on samples of varying provenance. Prof. Cash raised the question of assessing specificity, a factor of considerable practical significance - see item 5.

5. **Comparison of the specificity of different assays**
With the committee's endorsement, Prof. Cash suggested that a definitive study of the specificity of available anti-HBc kits be undertaken as follows:

5.1. 10 ml aliquots of serum from 2,000 blood donations (taken as an extra sample at donation) will be obtained from blood donors at Glasgow. **Dr Mitchell**

5.2. Manufacturers of anti-HBc kits will be offered the chance to provide 2,000 tests from two different batches of their reagents (total, 4,000 tests), free of charge and with appropriate training, for assessment prior to advising the Department of Health as to the range of available kits, should screening be recommended. **Dr Gunson**

5.3. The Procurement Department (DoH, Russell Square; Carol McDonald or Mr. Garden) will be asked for a list of producers of anti-HBc kits with appropriate persons to contact. **Dr Barbara**

Action

5.4. In the first place, 5 UK Transfusion Centres will be approached to ask if they will agree to test aliquots of the 2,000 donor samples for anti-HBc with **two** batches, of each of two manufacturers' kits (a total of 8,000 tests). The suggested breakdown was: **Dr Gunson**

GLASGOW:	Dr Mitchell	Ortho ELISA
		Organon ELISA
*EDINBURGH:	Dr McClelland	Murex ELISA
		Sorin ELISA
NEWCASTLE:	Dr Lloyd	Abbott ELISA
		Pasteur ELISA
LIVERPOOL:	Dr Martlew	Corecell HA (standard method)
		Mercia ELISA
COLINDALE:	Dr Contreras	Biokit ELISA
		Lab-Systems ELISA
		Corecell HA (modified)

If further assays come to light, Sheffield (Dr. Wagstaff) and Leeds (Dr. Robinson) will also be approached.
In the interim, Dr. Gunson will contact Dr. Martlew, to request cessation of her extended trial on 31st March 1993, and Dr. Lloyd, to request that he does not initiate routine screening on 1st April 1993.
**Subsequent to the meeting, Professor Cash contacted the Chairman to say that perhaps Cambridge RTC should be approached in place of Edinburgh. Dt. Gunson agreed that this should be done in view of their previous work in anti-HBc trials. Dr. Lorna Williamson has agreed to participate in the trial using the Murex and Sorin tests.*

5.5. Coordination of detailed protocols will await the outcome of above approaches. Dr. Gunson will fax a draft protocol to committee members for their comments. **Dr Gunson**

5.6. Dr. Mitchell will arrange aliquoting and transportation of samples involving only one freeze-thaw cycle during storage (including those at Glasgow, for consistency). Each participating Centre will receive 2 ml of each of the 2,000 serum samples in labelled NUNC tubes. It was recognised that freeze-thawing may reduce the false-positive rate compared with testing fresh samples, but this is unavoidable. **Dr Mitchell**

5.7. Dr. Follett agreed to test repeatably reactive sera by: **Dr Follett**
The other immunoassays (recording 'percentage inhibition')
Corecell HA titration
Overnight Murex HBsAg assay
Abbott IMX anti-HBc assay
Anti-HBs quantitation
PCR for HBV DNA**
***Dr. Craske is currently comparing PCR techniques for the detection of HBV DNA and will liaise with Dr. Follett.*

Action

5.8. Dr. Mortimer will investigate provision of an anti-HBs 'go-no-go' sample of appropriate titre (calibrated against NIBSC/ International standards) for trial purposes and possibly for routine anti-HBc screening if this is implemented. Cut-off 'tolerance' (to cover the spread of anti-HBs assay detection ranges) will need to be decided. **Dr Mortimer**

5.9 Prof. Tedder's written comment concerning the relatively high titre of 'infectious' anti-HBc-only blood was noted. Dr. Gunson will ask RTDs if they have documentation relating to anti-HBc percentage inhibition values for donations implicated in transmission of PTH-B, for central collation. Ideally, a panel of samples from the actual donations involved should be assembled for assessment of assays' suitability. This will be investigated further. **Dr Gunson**

6.0. It was recognised that biologically significant specificity of anti-HBc ELISAs could be improved by raising kit cut-offs, but this would be a matter for manufacturers to address.

6.1. Consideration of definition of strategies for anti-HBc confirmation will be deferred to the next ACTTD meeting.

6. **Likely date for implementation of routine anti-HBc screening.**
The committee agreed that a recommendation be made to ACVSB that screening should be implemented. The need to complete trials and to allow time for preparation at Centres would suggest implementation in the autumn of 1993. The committee's views would be presented to ACVSB at their next meeting, likely to take place in May 1993.

7. **Anti-HAV in plasma fractions: BPL meeting.**
No firm conclusions had been reached at the BPL meeting. A detailed report of the meeting will be available in due course.

8. **Inactivated FFP**
The committee noted that the MCA had not approved the application by Octopharma for a Clinical Trials Exemption Certificate (CTX) for their product. Furthermore, there have been administrative delays with the Lille product and no CTX application relating to this product has yet been lodged with the MCA.

9. **Guidelines for investigation of transfusion-transmitted bacterial infection.**
This item was carried over pending a meeting between Dr. Gunson and Dr. Barbara.

10. **Any other business**
Dr. Perry will approach ACVSB to raise the issue of pre-existing plasma stocks in relation to implementation of anti-HBc screening. **Dr Perry**

Action

11. **Place, date and time of next meeting.**
North London Blood Transfusion Centre, Colindale
Tuesday 20th April 1993 at 10.30 am

JB/mm/26 Feb 93
Micro/meetings/ACTTD

NATIONAL BLOOD AUTHORITY

U.K. ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED DISEASES

TTD 10/93

Multi-Centre anti-HBc Trial

Examination of the results of the following batches has been undertaken:

1. Two batches of:

   Murex (short incubation) — Sheffield
   Murex (long incubation)
   Ortho } Glasgow
   Organon }
   Behring } Edinburgh
   Kodak }
   Mercia — Liverpool
   Corecell (standard test, Liverpool)
   Corecell (modified, Terasaki plat iverpool)

2. One batch of:

   Abbott (2nd generation, pre-production)
   Radim (tested with second batch of samples only)

Seventy-four antisera gave repeatably positive results with one or both of the above batches.

Only 4 were repeatably positive with all the above antisera!

Just something to give you some thought. Full results will be available for the meeting.

H.H. GUNSON
Medical Director, NBA

19/04/93