FILE

ACVSB 5/11

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ADVISORY COMMITTEE ON THE VIROLOGICAL SAFETY OF BLOOD
MINUTES OF THE 5TH MEETING HELD ON 17 JANUARY 1990

PRESENT

Dr J Metters (Chairman)

Members:
Dr H H Gunson
Dr P Minor
Dr P Mitchell
Dr P Mortimer
Dr R J Perry
Dr R Tedder
Dr E G Tuddenham
Prof A Zuckerman

Secretariat:
Dr A Rejman
Mr J Canavan
Miss P Reenay

Observers:
Dr H Flett
Dr A McIntyre
Dr H Pickles
Dr J Purves
Dr F Rotblat

Chairman's Opening Remarks and Apologies for Absence

1. Dr Metters welcomed members, and Mr M Fuller who deals with pathology equipment and supplies in the Department's Procurement Directorate.

Apologies for Absence

2. These were received from Dr Lane and Dr Jacobs.

Minutes of the Last Meeting (6 November 1989)

3. These had been circulated, and were agreed to be an accurate record.

Matters Arising from the Minutes

4. There were no matters raised that are not covered under specific agenda items below.

Human Growth Hormone

5. Drs Gunson and Mitchell reported that as of 13 November 1989 recipients of pituitary-derived human growth hormone have been

permanently deferred from donating blood. Letters were sent to the RCS, RCP, RCPath, UKTS and all DMOs in England, and similar letters were issued by Welsh Office, SHHD and DHSS Northern Ireland. Dr Gunson said that there had been no noticeable response to these actions, and Dr Mitchell confirmed that the same applied in Scotland.

6. Dr Rotblat added that, as had been thought, all commercial companies had been excluding such donors since before 13 November.

7. Dr Rejman reported that the start of Prof Preece's study had been delayed. At the present time they were waiting for copies of their questionnaires to be sent to GPs. There was no fixed timescale for completion of the study.

ED Directive on Blood Products

8. Members had been given a copy of the draft paper stating the UK position with regard to the preparation of technical guidelines(ACVSB 5/1). Dr Purves explained that this was the result of two meetings that had taken place on 19 December and 2 January, in which members of the Committee participated. The paper was produced by MCA, after discussions with BTS, commercial producers and NIBSC.

9. Dr Purves confirmed that the final wording of section C1 would make it quite clear that church halls and like premises where blood donations were collected would be excluded from the requirements and inspections detailed.

10. Dr Minor tabled paper ACVSB 5/2. He explained that this was at a very early stage, and a new draft was currently in preparation. There had been no official consultation yet, and any comments members might have should be sent via the Secretariat.

HTLV1 Screening - UKBTS Pilot Study

11. Dr Gunson reminded the Committee that as the benefit of general screening had not yet been shown, a study was to be carried out on 100,000 donations. The initial part of the study would be at North London BTC. He explained that it was now thought likely that more than one center would be involved. Drs Mortimer and Tedder are agreeing a protocol, and arranging a method of transferring samples.

12. A submission , setting out the protocol and officially requesting funding, will be sent to the Department within the next few weeks.

Non-A Non-B Hepatitis

13. Dr Gunson spoke to paper ACVSB 5/3, which gave details of the pilot trial which had been financed by the Department's

Procurement Directorate.

14. The problems which caused the most concern were the number of tests (0.5 - 1%) that were in the "grey zone" - having a higher optical density than most of the negatives , but below the cut-off for positives - and weaker reactions observed with plasma as compared to sera. This was of importance in blood donations as Directors needed samples from the actual donation.The time taken to complete the test was also seen to be a disadvantage in relation to emergency release of products. In conclusion Dr Gunson said that these were some of the aspects that would have to be discussed with Ortho.

15. It was noted that Ortho were holding a symposium on Hepatitis C in London in February, on the same day that Abbott (who are expecting to produce a test shortly) will be holding one in Chicago. Members of the Committee would be attending both symposia.

Non-A Non-B Hepatitis Cost Benefit Analysis

16. The Chairman invited the Committee to address the question of whether the time has now come for the introduction of routine Hep C testing.

17. Prof Zuckerman spoke to paper ACVSB 5/4 - concerning the justification of the routine introduction of the test. He emphasised the problems posed by the lack of a confirmatory test, and the apparent high number of false positive reactions obtained when the test is applied to samples which had been frozen and then thawed. He advised that both in the US and Japan it had been found that some donors who show positive with the test have passed on disease.

18. In attempting to give an indication of the number of possible cases of chronic liver disease that could be prevented by the introduction of routine testing, Prof Zuckerman emphasised that his figures would represent gross assumptions and estimates. On that basis he offered a figure of 5,000 members of the donor population who could be excluded from donating, but 50% could be false negatives. As it was not possible to estimate how many recipients there would be for each donation it would be impossible to expand the estimate further.

19. Prof Zuckerman gave the Committee details of the work that had been carried out in Japan. He explained that of the 29 clones isolated, 16 did not react to US strains. The clones have been sequenced and clone 2 will detect both Japanese and US Hep C, but it was emphasised that the sensitivity must be improved. The conclusion was drawn that there was in fact another Hep C, which had been also been shown in chimpanzees in the Netherlands, which is a further complicating factor.

20. Prof Zuckerman felt that this strengthened the argument that we must keep an open mind about other tests, which should be

available within the next 12 months. He felt that is was unlikely that the FDA would license the Ortho test in the absence of a confirmatory test, and it would be difficult for us to approve a test which was not approved in its country of origin. The proposed Abbott test would not really be an independent test. Dr Rotblat added that it was also her understanding that the FDA was unlikely to approve the test at this stage.

21. Dr Tedder stated that it was very difficult to make any recommendations based on scientific criteria at this time, as so little was known about the virus and its antibody markers.

22. Prof Zuckerman added that he understood that the Japanese and US total sequences have now been published, and they are not the same. The virus has not been visualised yet and there is little published epidemiological details, as compared with what had been produced, for example, at an early stage with Australia Antigen.

23. Dr Minor posed the question: if 10% of the Ortho test positives transmit, how many of the Ortho negatives also transmit?

24. Dr Mortimer felt that as the perceived risk is higher than that of HIV, we would be inconsistent in our screening procedure if we did not introduce routine testing. If we began routine use of this test we should soon have a better test to move onto.

25. Dr Mitchell discussed the potential problem of handling donors. He felt that it was possible to deal with the donors who proved positive to the test without causing undue alarm.

26. Dr Gunson explained that the transfusion services were under a great deal of pressure, not just from Ortho but from the press, and increasingly from the clinicians in the field. He felt that each centre must now consider how to set up the test and what extra resources they would need to do so. He also highlighted the fact that as further tests are introduced the potential for labelling mistakes will increase to a point where the time may have come to introduce automation.

27. Dr Tuddenham explained that, to date, donors who have shown as positive have not been recalled, but will be retested on next appearance.

28. In answer to questions about the funding for the additional testing and counselling, the Chairman explained that the funding would have to be found from the existing health vote allocation.

29. The Chairman summed up the general consensus of the Committee as follows:

- routine testing should not be introduced in advance of the FDA decision;

- scientifically, not enough is known yet, but there is agreement that the test does detect some people who will transmit; and

- the overall prevalence figure of non-A non-B following blood transfusion, for the UK may be 10,000 pa, subject to very wide margins of error.

30. The Chairman then asked members for their opinions as to what action should be taken. Dr Tedder wanted it to be noted that he would not give an opinion before more scientific data had been generated. After further discussion the Committee agreed :

- the costs should be looked at now, with regions being called upon to consider the financial implications;

- Prof Zuckerman's figures would be further refined, to present as close an estimate of cases of potential infection as possible. This would undoubtedly be called for by Ministers;

- the Committee could give no further scientific advice at this point, but would discuss the matter further at the next meeting (April) which would be after the International Hepatitis Meeting in Houston.

31. Dr Pickles spoke to paper ACVSB 5/6, and explained that its purpose was to identify the considerations, and highlight the number of unknowns involved. She agreed to get together with Prof Zuckerman to calculate working estimates of numbers of possible preventions.

32. It was pointed out by Dr Gunson that another aspect that would have to be worked into the equation was the action to be taken regarding the positive donors once they were counselled. They could represent 8 - 10,000 annual referrals to gastroenterologists, along with concomitant treatment costs.

33. Mr Fuller added that Procurement Directorate will be talking formally to Ortho and informally to Abbott about their respective pricing policies and should be able to report back to the Secretariat before the next meeting.

34. Members were invited to send any further observations on this subject to the Secretariat, for discussion in at the April meeting.

35. It was agreed, that in view of media interest, a submission to Ministers should set out the present position and the Committee's views.

Combined HIV1 and HIV2 Testing

36. Drs Mitchell and Gunson had circulated the results of their evaluations of various combined test kits (ACVSB 5/7). They

explained that the Behring kit had only just been delivered, but they hoped to be able to give a full report by the next meeting. So far the Wellcome test had performed very well, as had the Abbott test. The Du Pont kit had been used for 5,000 tests at Manchester very satisfactorily. That centre currently uses the Du Pont HIV1 test, and had been informed that soon only the combined test would be available from that company. (Mr Fuller told the Committee that Du Pont had recently been acquired by Ortho Diagnostics, which might explain this.)

37. The Wellcome test is still being looked at in Southampton, while Behring is being evaluated at Glasgow. At North London four tests were being looked at. Abbott and Wellcome both showed 0.1% repeated reactivity, while that of Elavia was 1.5 - 2%. There were technical problems found with the Elavia test. The Behring Test was found to be very sensitive, but not on screening rate. All tests performed very satisfactorily on HIV1 samples. There were insufficient HIV 2 positive controls to assess performance on HIV 2 positive samples. The one comment that was emphasised was that Wellcome is immunometric and was found to be 10-100 times more sensitive at end-point dilution.

38. Mr Fuller explained that Procurement Directorate and PHLS have been looking at the combined tests. They did note that some of the tests did not have as strong a positive as the tests from which they had been developed. Dr Mortimer advised that specificity is something that can only be determined by the RTCs. From the point of sensitivity there was only one test, Pharmacia, which was looking unsatisfactory.

39. Dr Gunson concluded by stating that he felt that the combined test must be introduced as soon as possible.

40. The Committee agreed unanimously to recommend the intoduction of HIV2 testing on all donated blood, with a common date to be agreed within the UKBTS.

Extracts from UKBTS/NIBSC Guidelines

41. These extracts were circulated for the information of members. Dr Rejman explained that they had been prepared by a Liaison Group with several working parties, and were guidelines for use in RTCs in the UK. Comments were invited, and would be borne in mind for the second edition, which is due in two years time.

Any Other Business

42. Members were given ACVSB 5/10 - an extract from the PHLS document "Infections and Communicable Diseases in England and Wales 1989" - for information and discussion at the next meeting. There were no further items of business.

Date of Next Meeting

43. This was agreed for 1100hrs on Tuesday 24 April.

44. The meeting closed at 1315hrs.