BP's file 0030

SIXTH MEETING OF THE ADVISORY COMMITTEE ON VIROLOGICAL SAFETY OF BLOOD TUESDAY 24 APRIL 1990 AT 11.00 AM IN ROOM 84 HANNIBAL HOUSE, ELEPHANT AND CASTLE, LONDON

AGENDA

1	Chairman's Opening Remarks	
2	Apologies for Absence	
3	Minutes of the Meeting held on 17 January 1990	**(ACVSB 5/11)** already circulated
4	Matters arising from Minutes not covered by the Agenda	
5	EC Directive on Blood Products	
	- Oral report on current position	
6	HIV 1 and HIV 2 Testing	
	- Oral report from Dr Gunson	
7	HTLV 1	
	- Protocol - oral report from Dr Gunson	
8	Hepatitis C	
	- Ortho symposium - 8 February 1990	**(ACVSB 6/2)**
	- Abbott symposium	**(ACVSB 6/3)** to be tabled
	- FDA situation	**(ACVSB 6/4)** to be tabled
	- Hepatitis Conference Report(s)	**(ACVSB 6/5)** to be tabled
9	Any other business	
10	Date of next meeting	

? 24 July

To be confirmed

19 APR 1990

2031

Department of Health

Eileen House 80-94 Newington Causeway London SE1 6EFA

Telephone GRO-C

FAX — GRO-C

TO: All members and observers of the Advisory Committee on the Virological Safety of Blood

Your reference

Our reference GEB 1

Date 1 May 1990

Dear Member

I am writing to confirm that the next meeting of the Advisory Committee on the Virological Safety of Blood will be held

on: Tuesday ~~25~~ 24 July 1990

in: Room 63 Hannibal House
Elephant and Castle
London SE1

at: 11.00 am OCT NEXT ONE

Minutes of the 6th meeting held on Tuesday 24th April will be distributed as quickly as possible and an agenda for the July meeting will follow nearer the time.

Yours sincerely

GRO-C

J CANAVAN
For the Secretariat

Mark in
Diary please

Received - 8 MAY 1990
File No BP's office
R. PERRY

Dr. Perry 0032

CONFIDENTIAL TO COMMITTEE MEMBERS
NOT FOR PUBLICATION

ADVISORY COMMITTEE ON THE VIROLOGICAL SAFETY OF BLOOD

MINUTES OF THE 6TH MEETING HELD ON 24 APRIL 1990

PRESENT

Dr J Metters (Chairman)

Members: Dr Garrett (for Dr P Minor)
Dr H H Gunson
Dr R Lane
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

Observers: Dr A Flett
Mr M Fuller
Dr A McIntyre
Dr H Pickles
Dr F Rotblat
Mr J Sloggem (for Dr Purves)

15 JUN 1990

Apologies for Absence

1. These were received from Dr Jacobs, Dr Minor, Dr Purves, Dr Summerfield.

Minutes of the Last Meeting (17 January 1990

2. These had been circulated and were accepted as an accurate record.

Matters Arising from the Minutes

3. There were no matters raised.

EC Directive on Blood Products

4. Mr Sloggem reported that a small working group had been set up under the chairmanship of Dr Gunson to help prepare the UK input to the technical annex to the Directive and to the guidelines. The UK proposals for guidelines were based on those prepared jointly by NIBSC and the UKBTS.

HIV 1 and 2 Testing

5. Dr Gunson confirmed that the UK Blood Transfusion Services would introduce the combined HIV 1 and 2 test so that from 1 June 1990 all blood used would have been tested.

6. Dr Lane mentioned that blood products made from plasma which had been tested for HIV 1 but not for HIV 1 and 2 would be working through the distribution network for a considerable time. The Chairman said that the combined test had been introduced for blood not blood products. Dr Rolblat said that the MCA did not usually require the destruction of existing stock in the introduction of new tests. The Department would clarify the position on blood products for BPL.

HIV 1

7. Dr Gunson reported that the protocol for the pilot study would be submitted to the Department shortly.

Hepatitis C

Ortho symposium (ACVSB 6/2)

8. The abstracts from this symposium had been circulated with the secretariat's comments. Dr Rejman said the overall impression was that the test was not sensitive or specific enough for reliable testing. A confirmatory test and more information about the significance of positive test results were needed before the Ortho test could be used for the routine screening of healthy donors.

9. Dr Mortimer thought there had been an underlying feeling against screening because of the lack of confirmation. He thought confirmatory testing would become available within a reasonable time and that the routine screening of blood donors could not be delayed for a long time.

10. Professor Zuckerman showed disappointment at the outcome of the symposium and said the non specificity and sensitivity of the test had been the main talking points.

Abbott Symposium (ACVSB 6/3)

11. Dr Mitchell reported that following this symposium the American Association of Blood Banks had directed that testing for hepatitis C antibody should be introduced as soon as FDA approved the test. It was confirmed that approval had not yet been given. Concern about litigation was the main influence on the US Blood Banks. Dr Mitchell thought there would be problems counselling donors in view of the state of knowledge about the significance of a positive reaction to the test.

12. Dr Mitchell said papers presented at the symposium showed that the vast majority of hepatitis C cases were not transfusion related. Where high risk groups were tested concordance with hepatitis C positivity is high but among a cross section of blood donors concordance is much lower. He understood that the US would retain ALT and hepatitis B core antibody testing.

13. Professor Zuckerman stressed that the major cause of post transfusion hepatitis is non A non B virus, and even so not all cases were recognised.

Hepatitis Conference Report (ACVSB 6/9)

14. Professor Zuckerman would be preparing a full report in due course but he had provided some notes on anti HCV testing for the meeting.

15. In introducing the notes he said it was interesting that wide geographical differences had been found and that there was evidence of different strains of hepatitis C virus. These observations would have serious implications for diagnosis and the development of vaccines.

16. Professor Zuckerman drew attention to the main findings of the TTV study in the US recorded in his paper. This showed the predictive level of anti HCV positivity for infection to be about 77%. The Study recommended that positive donors should be deferred.

17. The RIBA test has confirmed positivity in 33% of ELISA positive donors who were not implicated in a hepatitis incident but among ELISA positive recipients of blood and implicated donors the rate of confirmation by RIBA was 88%. Professor Zuckerman remarked that RIBA was not good enough to use routinely as a confirmatory test.

18. Professor Zuckerman drew attention to the seroconversion table and said the findings should be improved by adding another epitope. Improvements were already being introduced. Abbott were synthesizing peptides and IGM testing was being developed.

19. Professor Zuckerman summed up the conference as having been rather promotional in character and the data had been generally well known. Little information had been given about the Japanese and Abbott tests.

Detection of Hepatitis C Viral Sequences by "Nested' PCR (ACVSB 6/7)

20. Dr Tedder had tabled this paper which would shortly be published. Commercial confidentiality had prevented earlier submission for discussion in the Committee. Dr Tedder said that the paper described an investigation of anti C100 positive donations using a modified PCR assay for the detection of HCV sequences. This study had shown this method to be a useful confirmatory test for viraemics and showed that true positivity of Hep C antigen was close to 1 in 1100 blood donors compared with the 1 in 200 shown positive by HIV antibody screening. Although the PCR assay in its present form was not suited to the mass screening needs of RTC laboratories recent modifications of PCR technology indicated its potential for large scale testing.

Discussion on Anti HCV Testing

21. Before opening up the subject of testing for general discussion the Chairman reported that France, Belguim and Luxembourg had introduced routine screening of blood for HCV antibody. Italy had introduced the test on a voluntary basis.

22. The Chairman also remarked that from the reports the science seemed to have advanced little from the time of the previous meeting. There were still questions whether the anti HCV test was reliable and a useful step forward or created too many problems at this stage.

23. Dr Mitchell mentioned a report from Harefield Hospital that 6 of the 7 hepatitis C positive donors identified in a study did not transmit infection and 4 had been found not to be positive after a year. He was concerned from the results of the study that screening might result in 1 200 donors being deferred but perhaps unnecessarily.

24. Professor Zuckerman was concerned that the Ortho test had a false positive rate of 50 per cent but that litigation concerns might force its use. He recalled, though, that in the early days of HIV 1 testing the UK had been prepared to accept high false positive rates. Professor Zuckerman thought viraemic testing could be developed with recombinant proteins being developed. A field trial could be run in RTCs using the prototypes and introduce them generally when sufficiently developed.

25. Dr Gunson said he found the US data about eliminating positive donors, in some series leading, to a 50% reduction in post transfusion NANB hepatitis, persuasive but he recognised there were problems in what to tell the donors. The RTCs had already listed 15,000 donations and found rates between 0.2% and 0.8% to be hepatitis C positive. Among 9000 frozen samples tested the rate had been 0.67%. His suggestion for a further study was that selected RTCs would use both Ortho and Abbott test and refer repeat positives to laboratories with access to recombinant proteins.

26. Dr Tedder said that the technology was already available to test which of the positives were reactive but irrelevant, which had other markers and which were viraemic.

27. Professor Zuckerman expressed the view that large scale experience was necessary to learn more about the prevalence of reactivity and the methods referred to for information of findings but he questioned whether donors should be told at this stage. He was still a little concerned, though, that the FDA had not approved the Ortho test.

28. Dr Mortimer considered that the argument now was not whether we should test for hepatitis C but whether the tests were adequate. He thought the Ortho and Abbott tests should be run together in some RTCs and the positive samples referred for PCR testing. A sample which would produce 50-100 reactive donors would be sufficient to get meaningful results. It was estimated this would require 25-50,000 donors..

29. The Chairman's summed up the discussion as follows:-

- there was inadequate scientific data to support the introduction of the Ortho test for routine screening;

- a confirmatory test was needed which could be used in the RTCs and not just specialised laboratories;

- the FDA had not yet approved the test and it would be reassuring if the regulatory authority in the country of origin had done so;

- there was a need to learn more about the donor panels and the significance of positive reaction to the hepatitis C antibody test;

- a prospective study involving 25-50,000 donors would generate sufficient positives for confirmatory testing.

It was agreed that a sub group of Dr Gunson, Dr Mitchell, Dr Mortimer and Dr Tedder would prepare a protocol for the pilot study and an estimate of the funds needed for the study and the laboratory services to support it.

30. The Chairman remarked that the paper by the Economic Advisor's Office (ACVSB6/6) reflected the lack of data.

31. A note would be prepared for Ministers telling them the outcome of the discussion.

Any Other Business

32. The Chairman said he was concerned that there should be no confusion over the roles of the ACVSB and the UKBTS Committee on Transfusion Transmitted Disease. He would, therefore, be writing to Dr Gunson Chairman for the UKBTS Committee so that they could agree the respective roles. The ACVSB advised Ministers on the virological safety of blood. The UKBTS Committee considered the operational implications of policy, gave the Department advice on safeguards against non-viral threats to blood and contributed to the advice on viral safety through input to the ACVSB. Dr Gunson confirmed that he shared this view of the roles and thought there was no conflict between the Committees.

33. Dr Mitchell spoke briefly about the HIV litigation and the question it raised about a scheme of no fault compensation. The Chairman said that Ministers had no plans for such a scheme.

Date of Next Meeting

34. This was set for 11.00 24 July 1990.

0033

COMMITTEE ON
SAFETY OF MEDICINES
FILE

Our Ref: BC/DMAL

24th April 1990

R. Whitbread
Assistant Secretary
Committee on Safety of Medicines
Market Towers
1 Nine Elms Lane
LONDON SW8 5NQ

Dear Sir/Madam,

THE PROVISION OF PLASMA POOL SAMPLES FOR THE CONTROL TESTING OF BLOOD PRODUCTS

In response to your letter of 18th April on this subject, I would advise you that NIBSC are already receiving samples from all plasma pools used in blood product manufacture. This policy will continue to be implemented and I am, therefore, happy to confirm that we will continue to comply with the recommendations of the Committee on Safety of Medicines.

Yours sincerely

DR B CUTHBERTSON
Quality Assurance Manager

)LBC0002.040 / LETTERS DISK

SP/7472m/12

0034

COMMITTEE ON SAFETY
OF MEDICINES

Market Towers, 1 Nine Elms Lane,
London SW8 5NQ.
Telephone: 01-720 2188
Fax: 01-627 2185

To Medical Director
Scottish National Blood Transfusion Service
Protein Fractionation Centre
21 Ellen's Glen
Edinburgh EH17 7QT

18 April 1990

Dear Sir/Madam

THE PROVISION OF PLASMA POOL SAMPLES FOR THE CONTROL TESTING OF BLOOD PRODUCTS

Blood products are well known to be capable of transmitting viruses to recipients. Patients receiving coagulation factors or some immunoglobulin preparations have developed therapy induced hepatitis B and non A, non B'. Both untreated factor VIII and IX concentrates have transmitted HIV to haemophiliacs.

The Committee on Safety of Medicines have recommended that in view of the limitations of testing for HB_sAg and antibodies to HIV in finished products and the greater sensitivity of tests on the plasma pool, manufacturers should submit formally to the National Institute for Biological Standards and Control samples of all plasma pools in addition to other samples and protocols required for batch release.

I would appreciate written confirmation of this at your earliest convenience.

Yours faithfully

GRO-C

L R WHITBREAD
Assistant Secretary

0065

2nd May 1990

Our ref: RJP/AWM

Professor J.D. Cash
National & Scientific Medical Director
S.N.B.T.S.
Livingstone House
39 Cowgate
Edinburgh
EH1 1JR

Dear John,

ACVSB

Somewhat belatedly I enclose some scribbled notes of a recent ACVSB meeting.

With kind regards.

Yours sincerely,

Dr. R.J. Perry
Director

Encl.

NOTES OF ADVISORY COMMITTEE ON VIRUS SAFETY OF BLOOD

1. EC DIRECTIVE ON BLOOD PRODUCTS

Blood product annexe to E.C. Directive 75/318 (draft) is now in Brussells for discussion by Working Party.

Has also been approved (U.K.) that the Directive will be supported by Guidelines document which basically consists of relevant chapters of UK/BTS document with UK references omitted. This UK initiative has been approved by "policy side of D.O.H." - whatever that means.

Draft directive attached.

2. HIV 1 + 2

Approval to proceed with combi-test confirmed June 1st to date for blood issues to be HIV 1/2 tested and thus introduction of testing before that date is requested.

2 centres in E+L (N. London, Oxford) already commenced testing as 'extended pilot study' using Welcome tests. Report expected in May (iu 20,000 donations).

Status of pre-existing plasma stocks discussed in light of previous experience with HIV-1. D.O.H. have agreed that plasma stocks collected before 1 June will continue to be acceptable for fractionation - no requirement to retrospectively test for HIV-2. R.S. Lane suggested that H.M. Government should state that all products will be derived from HIV 1/2 tested plasma from April 1991. Strongly resisted by R.J.P. D.O.H. also unhappy about specific dates and agreed that statement should be 'as soon as practicable'.

Report in Clinica (March 28 1990) that U.S. F.D.A. will not require HIV-2 testing as a routine screening procedure for blood on plasma!

3. HTLVI

Draft study/trial protocol ready for submission to D.O.H.

4. HCV TESTING

Main agenda item - dominated by reports and discussion by academic virologists!

General Comments

- tests do not have adequate specification for routine BTS use and there remains no effective confirmatory test.

- preference to recommend implementation once confirmatory test is in place and we have better understanding of the science.

  (ARC, AABB)

- U.S. have developed a set of guidelines for implementation once the test is F.D.A. approved.

- recent U.S. meeting concentrated on issues of litigation/liability and implications for donors.

- HCV testing in place in France, Belgium, Luxembourg, Finland and Australia.

- NIBSC reported that U.S. have not decided yet on whether HCV +ve donations will be included or excluded from plasma pools.

- U.S. will not give up ALT/HBc testing in event of HCV test.

- despite ill defined science of test, high false positive results, lack of correlation of test postivity with infectivity and confirmatory test there is good evidence in the U.S. that testing prevents 50% of P.T.H. NANB - compelling reason to introduce test.

CONCLUSION

Absence of F.D.A. approval, confirmatory test and unequivocal science led to conclusion that UK should not yet proceed with HCV testing at present time.

However it was agreed that Gunson, Tedder, Mortimer and Mitchell would organise a full trial of c 100,000 donors to gather more information on such matters as donor positivity and predictive value of HCV Ab with regard to infectivity.

H.G. and R.J.P. felt that there was sufficient data to justify testing now (based on U.S. data suggesting 50% reduction in PTH) but the majority and D.O.H. preferred more cautious approach.

More details from R.M.

GRO-C

Dr. R.J. Perry
30th April 1990

RPAM3004.90R