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NATIONAL DIRECTORATE OF NBTS

U.K. ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED DISEASES

Ad Hoc Group to Consider Implications of HCV Antibody Testing of Blood Donations

Minutes of a meeting held at the National Directorate on Friday 13th September 1991.

PRESENT: Dr. H.H. Gunson (in the Chair)
Prof. J.D. Cash
Dr. R. Mitchell
Prof. R.S. Tedder

1. Apologies for absence - Dr. Marcela Contreras

2. It was agreed that in order to answer questions which may arise in the future with respect to the timing of the introduction of HCV antibody testing of blood donations, the facts and decisions taken should be set out in chronological order in these minutes.

3. AVAILABILITY OF HCV ANTIBODY TESTS

Ortho Diagnostic Systems

3.1 1st September 1989. Arrangements were made by Dr. Gunson for Ortho to demonstrate their 1st generation test to RTCs in England and Wales.

At this time the test was available for research purposes only.

3.2 27th November 1989. Letters from the Product Development Manager, Ortho Diagnostic Systems to Dr. Gunson and Professor Cash gave the information that their HCV antibody ELISA test had received an Export Permit from FDA which allowed supply of the product for "in vitro diagnostic use" instead of "research use only".

This change in status would be effective from December 1989.

3.3 27th November 1989. Professor Cash was informed by the Group Vice-President and General Manager, Ortho Diagnostic Systems, that a 3-band RIBA confirmatory test was being evaluated. This test incorporated the C-100 antigen and a fragment of it, 5-1-1.

3.4 18th January 1990. Information from Ortho Diagnostics Systems that the Paul-Ehrlich Institute had registered the Ortho HCV antibody ELISA test for donor screening and diagnostic use.

3.5 2nd May 1990. FDA licensed the Ortho ELISA test system.

3.6 11th May 1990. Letter from Marketing Manager, Ortho Diagnostic Systems, announcing the availability of the RIBA test for HCV.

3.7 10th September 1990. Letter from Marketing Manager, Ortho Diagnostics Systems, enquiring if trials could be conducted on the 2nd generation Ortho ELISA test at North London RTC.

3.8 27th September 1990. Letter from Marketing Manager, Ortho Diagnostic Systems, stating that 2nd generation RIBA-HCV (4 band) would be sent to the confirmatory laboratories.

3.9 29th October 1990. Letter from Marketing Manager, Ortho Diagnostic Systems, stating that clinical trials would soon commence for the 2nd generation ELISA test.

3.10 21st March 1991. Letter from Marketing Manager, Ortho Diagnostic Systems, stating that the 2nd generation assay was to be introduced replacing the 1st generation assay.

Abbott Laboratories

3.11 17th August 1989. Abbott Laboratories concluded a collaboration agreement with Chiron Corporation and Ortho Diagnostics to develop and supply the HCV test.

3.12 23rd July 1990. Letter from Product Manager stating that FDA had approved the marketing of the Abbott HCV test.

3.13 2nd November 1990. Letter from Product Manager, Abbott Laboratories, announcing a scientific meeting to coincide with the launch of the Abbott HCV test on 6th December 1990.

3.14 8th April 1991. Undated letter from Product Manager, Abbott Laboratories (received on the date stated), announcing the launch of the 2nd generation HCV test.

4. INTRODUCTION OF HCV ANTIBODY TESTING OF BLOOD DONATIONS

4.1 At their meeting on 24th April 1990 the DH Advisory Committee on the Virological Safety of Blood (ACVSB) concluded:

(i) that there was inadequate scientific data to support the introduction of the Ortho test for routine screening

(ii) a confirmatory test was needed which could be used in the RTCs and not just specialised laboratories

(iii) there was need to learn more about the donor panels and the significance of positive reactions to the anti-HCV test

(iv) that a pilot trial of the Ortho and Abbott tests should be conducted and requested . Drs. Gunson, Mitchell, Mortimer and Tedder to prepare a protocol

4.2 At the ACVSB meeting on 2nd July 1990 it was recommended that:

(i) the U.K. should introduce hepatitis C testing but that first a pilot study using Ortho and Abbott tests was necessary to decide which was the better test for RTCs to use

(ii) there was general support for the protocol for the trial

4.3 The results of the trial were reported at the meeting of ACVSB on 21st November 1990.

The advice to the Committee was that anti-HCV testing should be introduced in RTCs as soon as practical. RTCs could decide individually whether to use the Ortho or Abbott tests. A submission would be made to Ministers regarding this significant policy decision and ME would consider the funding aspect.

The Chairman stressed the importance of a common date for introduction of testing throughout the U.K.

At this meeting Drs. Gunson and Mitchell informed ACVSB that both Ortho and Abbott were planning to introduce 2nd generation HCV antibody tests. Information given to RTCs should await Ministerial approval.

4.4 Dr. Gunson wrote to RTDs in England and Wales and to Professor Cash on 22nd January 1991 requesting from them a date from which they could commence routine anti-HCV screening of blood donations.

The responses received included the following points:

(i) at the time of the request for this information all RTCs were heavily committed to supplying blood for the Armed Forces in the Gulf. The introduction of an additional screening test whilst this work was in progress could be detrimental to GMP

(ii) there was concern amongst many RTDs about the funding for this additional test and that the introduction of testing would be dependent on this factor

(iii) one RTD preferred not to give a date at this time. Others gave dates which varied between 1st April 1991 and 1st October 1991. SNBTS agreed to commence at the same time as RTCs in England and Wales

(iv) Dr. Gunson wrote to RTDs on 15th February 1991 giving the date of 1st July 1991 for commencement of screening of blood donations

4.5 At the ACVSB meeting on 25th February 1991 it was reported that the 2nd generation tests would soon be the only ones available. Members agreed that it was important for the proper evaluation of the Ortho and Abbott 1 and 2 tests to be carried out before RTCs decided which test to adopt.

4.6 Dr. Gunson wrote to RTDs in England and Wales on 3rd April 1991 pointing out that "second-round" of evaluation had been delayed due to the unavailability and lack of supply of 2nd generation tests. The date of commencement of testing would have to be deferred from 1st July 1991 and the date to aim for was now 1st September 1991. Similar information was conveyed by Professor Cash to SNBTS Directors.

At this time Dr. J. Barbara had tested approximately 2000 samples with a 2nd generation ELISA test supplied by Ortho. It was found that this, in fact, was a pre-production batch. When the production batches were delivered it was discovered that the test had a different format from the pre-production batch and all the tests had to be repeated.

5. ADVICE TO BE GIVEN TO DONORS

5.1 It was clear from the trials of both 1st and 2nd generation tests that a significant proportion of repeatably reactive results using the ELISA test were falsely positive. It was apparent, also, that false negative results could occur.

5.2 It was not until the meeting of ACVSB on 24th November 1990 that Dr. Mortimer and Professor Tedder were able to report that a combination of RIBA and PCR could provide useful confirmatory tests.

5.3 As an indication of false positivity only 6 of the 65 repeatably reactive results found in both the first and

second phases of the multi-centre trials were RIBA positive/indeterminate and PCR positive.

5.4 The Blood Transfusion Service has an obligation to their donors to provide medical advice when this is necessary. The uncertainties of the significance of the HCV antibody positives by ELISA made it impossible to distinguish between false and true positives.

5.5 The second round of trials involving the 2nd generation Ortho and Abbott tests and the UBI test were concluded by the end of July 1991. At the meeting of the U.K. Advisory Committee on Transfusion Transmitted Diseases on 13th August 1991 it was concluded that the Ortho and Abbott 2nd generation tests appeared satisfactory.

Concern was expressed about the lack of reactivity with the UBI test against samples only reacting with c33c protein. However, it was agreed that there was insufficient evidence as yet to recommend that the test should not be used for routine screening of blood donations.

5.6 Arrangements were concluded to commence routine HCV antibody tests on blood donations on 1st September 1991.