Statement of Dr Brian McClelland : Topic B4

The decision not to use kits from the United States of America for testing donated blood for the virus as soon as they became available but, instead, to follow a process of evaluation of the kits before any such use.

Responses to the questions in the Schedule are shown in this font

1. On 23 April 1984, Dr Robert Gallo announced that he had isolated the virus that caused AIDS.

2. He subsequently provided an isolate of HTLV-III to Dr Tedder at the Middlesex Hospital for research purposes. When the DHSS asked if the isolate could be used to assist in developing a test for the UK market, permission was refused.

3. By 3 December 1984, Dr Tedder and Professor Weiss had prepared a local, independent isolate. A radioimmunoassay (RIA) from this isolate was also developed at the Middlesex. In order to develop a test kit for use by the blood transfusion services, the RIA needed to be scaled up and further work carried out to develop the actual test. The Centre for Applied Microbiology and Research at Porton Down was enlisted to help with the scaling up and Wellcome Diagnostics were to carry out the research and development necessary to achieve the test kit.

4. On 13 August 1984, Dr Alison Smithies forwarded a paper to Dr E Harris inviting him to consider the need for the formation of a working group of the Advisory Committee on the National Blood Transfusion Service [DHF.002.5897]. Dr Smithies' paper referred to the recent development of a RIA for HTLV-III by Drs Weiss and Tedder and proposals to extend the test to

all blood donors at the North London Regional Transfusion Centre and at least two other Regional Transfusion Centres. She noted that the information collected from the three centres would be used to "provide a basis on which to base policy decisions on extending the test more widely to the whole of the NBTS. We would therefore be in a strong position to make decisions about the need to buy from one of the five US pharmaceutical companies who have been licensed to produce a screening test and are likely to wish to start marketing these tests in the UK in the next few months".

Does Dr McClelland know what was meant by the statement "we would therefore be in a strong position to make decisions about the need to buy from one of the five US pharmaceutical companies"?

I have no personal knowledge of the meaning of Dr Alison Smithies' statement about "... decisions about the need to buy from one of the five US companies ..."

At that stage, was it intended that the commercial tests from the USA would only be brought into the UK in the event that the Middlesex/Wellcome test proved unsatisfactory for UK requirements?

I do not know if this was the intention.

Was there a preference for the Middlesex/Wellcome test? If so, why was there a preference?

I do not know. My reading of the documents suggests that there may have been different views. Concern about the cost of a test from the USA

seems to have been one fact seen to favour an indigenous test. Dr Harold Gunson stated in a letter to Dr Alison Smithies of DHSS dated 3rd July 1984 [SNB.006.5978]:

> "I have written at length about the possibilities of developing the test in the UK since the alternative will be to purchase kits from am American company such as Abbot Laboratories. I dread to think what the cost to the NHS will be under these circumstances"

The NBTS appears to have favoured a radioimmunassay of similar configuration to that then being used for HBsAg (Minute of EAGA 29th January 1985 [SNB.001.0002] Para 21). I imagine that this was on the grounds that it would be easier for the NBTS centres to adopt a test that was similar in operation to the test that NBTS was using at that time for Hepatitis B surface antigen

5. The working group of the Advisory Committee on the National Blood Transfusion Service was formed and met for the first time on 27 November 1984. Its terms of reference were "to consider the implications for the National Blood Transfusion Service of testing blood donations for antibody to HTLV-III and to report". The Inquiry does not have a copy of the minutes of the meeting. We note that Dr McClelland attended the working group and it seems that he made notes which he subsequently sent to Dr Cash [SNB.004.9180].

   Was this working group the first forum in which the introduction of donor screening for HTLV-III was discussed?

Donor screening for HTLV-III by the UK transfusion services had been discussed before 27th November 1984. The NBTS regional directors discussed AIDS at a meeting at CDSC Colindale on 11th July 1984 [DHF.002.9126]. The CBLA Research Committee had established an AIDS working group that met on 14th October 1983 [DHF.002.4834]. Dr Harold Gunson held a meeting on "HTLV-III and AIDS" on 28th June 1984, attended by Drs David Tyrell, Richard Tedder, Tim Wallington and Marcela Contreras. I had set off to attend the meeting on June 28th 1985 but travel problems prevented me from reaching London [SNB.006.5977]. The conclusions are detailed in the letter from Dr Gunson to Dr Smithies [SNB.006.5978].

> Does Dr McClelland have a copy of the minutes and/or notes of the meeting? If so, we would be grateful if he could provide copies to the Inquiry.

I have attached a copy of the notes that I made of the meeting on 27th November 1984 [PEN.012.1938] and the agenda, remit and membership [PEN.012.1942]. I do not have a copy of the minutes.

6. On 18 December 1984, Dr Tedder wrote to Dr Smithies at the DHSS asking for funding to pursue the following [DHF.001.8856]:

> (i) scale up of the Middlesex Hospital/Chester Beatty radioimmunoassay (MH/CB RIA);
> (ii) pilot studies in selected blood transfusion centres to confirm that the radioimmunoassay was compatible with the current BTS hepatitis testing;
> (iii) confirmatory testing and donor follow up; and
> (iv) monitoring of efficiency of the MH/CB RIA and forthcoming commercial kits

7. On 2 January 1985, Dr Smithies prepared a draft paper to go to the RLG (regulators liaison group) and enclosed Dr Tedder's letter of 18 December 1984 [DHF.001.9040].

8. Dr Smithies' draft paper appears to have been modified and sent in final form on 4 January 1985 [DHF.001.9036]. The final paper notes that after Dr Tedder's proposal was submitted "discussions were held with Dr Tedder to clarify some of the points made. As a result, some changes to the costings can be made and more information can be given". The summary of the paper states: "the proposal, which is strongly supported by Medical Division and STB3A, offers the opportunity to develop further a very sensitive British test for HTLV-III antibodies and to establish it for routine screening of blood donors for AIDS. The proposal also offers the opportunity to follow up in depth donations of blood from HTLV-III antibody-positive people. Finally, there is an opportunity to assess commercial products which will inevitably be introduced to capitalise on an established need".

   The paper of 4 January 1985 refers to discussions being held with Dr Tedder to clarify some of the points made in his original proposal. Does Dr McClelland know when these discussions took place and who was involved in these discussions?

I have no knowledge of the discussions referred to in the paper of January 4th 1985.

   The summary of the above-mentioned paper states "finally, there is an opportunity to assess commercial products which will inevitably be introduced to capitalise on an established need". At this point in time, which commercial products were intended to be subjected to the assessment (i.e. was it just USA commercial products or was it intended that the Middlesex/Wellcome test would also be assessed)?

I do not know what was intended at this point or to what extent the statement above represents a DHSS, as opposed to Dr Smithies' personal, view. However what happened was that during 1985, a comparative evaluation was carried out by PHLS using small numbers of samples from blood donors, from persons in a high risk group for AIDS, and from patients whose blood was considered likely to cause false positive results. This evaluation [SNB.004.8847] included tests supplied by Abbott Laboratories, Electronucleonics, Ortho diagnostics (USA) and by Organon and Wellcome (Europe), as well as two "in house" assays developed by PHLS. The completion of the first stage of the evaluation was announced by DHSS on August 1st 1985 [SGH.002.6967]. The report was dated September 1985 [SNB.004.8847]

> It appears to the Inquiry team that, as at 4 January 1985, the scaling up/development of the Middlesex Hospital/Chester Beatty Institute RIA and establishment of it for routine screening in the blood transfusion service was seen as a completely separate and parallel exercise from the evaluation. It seems as if any assessment was to be done on the commercial products from the USA and was not to include the MH/CB RIA. Is this understanding correct?

I have no knowledge of the intentions at the time. My reading of documents such as [DHF.001.9040], [DHF.001. 9036] and [SGH.002.7303] leaves me with the sense that some parties were working according to the assumption that the test developed in the UK was the natural choice. For example, [SGH.002.7304] contains the statement "The British test is

more sensitive and simpler to install at transfusion centres and is likely to be cheaper". I am not aware that there was substantial evidence to support these assertions about the performance and cost of the different tests at the time that document was written.

9. On 11 January 1985, Dr Smithies forwarded a draft submission for the CMO to consider before it was sent on to English Ministers [SGH.002.7303] and [SGH.002.7304]. The submission asked the Ministers "to agree in principle to the introduction of a screening test for AIDS antibody for all blood donations and to make an announcement to that effect at the appropriate moment indicating that the development of a test was being backed by the Department". The submission made no mention of an evaluation programme. The submission appears to have been sent to Mr A J Murray at the SHHD on 17 January 1985 [SGH.002.7302].

   Does Dr McClelland know why the English Ministers were not told about the evaluation programme at this stage?

I have no knowledge of this, but I note that [SGH.002.7302] suggests that Ministers were informed as it includes the statement "This has been endorsed by CMO and put to our Ministers".

Were Scottish Ministers told about the evaluation programme at this stage?

I have no knowledge about this.

Did the proposed meeting between DHSS and SHHD in Edinburgh which is referred to in [SGH.002.7302] take place? If so, does Dr McClelland know what was discussed?

I have no recollection of being aware of this meeting or of attending it. I do not know what was discussed.

10. On 16 January 1985, [X] in the Scientific and Technical Branch of the Department of Health sent a memo to an unknown recipient [DHF.001.9097]. The memo referred to a conversation that the two parties had previously had regarding setting up an evaluation programme on screening systems for AIDS markers. Attached to the memo was a draft letter which [X] proposed to send to each company known to be developing an AIDS test [DHF.001.9098].

    Does Dr McClelland know who the two parties referred to in this memo were?

    What was the background to this memo? Where did the idea for the DHSS evaluation programme come from? Which manufacturers were intended to be subjected to the evaluation programme? Who was intended to carry out the evaluation at this point in time?

I have no knowledge of the background to this memo.
I do not know where the DHSS evaluation programme originated but I note that among the documents provided – [DHF.001.9105] (17 01 1985) includes the statement that "All kits from any source including Middx (sic) Hospital and Wellcome will have to be tested to the same panel and protocol". This seems to be a very early reference to the evaluation.

    How much involvement did SNBTS/NBTS and SHHD have regarding the evaluation programme and the question of whether one was necessary?

I have no recollection of SNBTS discussions or actions relating to the evaluation of HTLV-III tests in late 1984 and early 1985. If SNBTS did

examine any of the tests, I think this would have been carried out in the West centre. Dr E Follet was advising SNBTS on virological matters at that time, and Dr Follet or Dr Brian Dow may also have relevant knowledge.

11. The Inquiry is in receipt of three responses to that memo [DHF.001.9105, DHF.001.9143 and DHF.002.7101].

In [DHF.001.9105] dated 17 January 1985, the author states "I am in favour of the proposed evaluation. All kit/test from any source including Middlesex Hospital and Wellcome will have to be tested to the same panel and protocol".

In [DHF.001.9143] dated 21 January 1985, the author states "Before the letter goes out I think it would be wise to establish [X] as an evaluation centre in order to be able to cope with the rush. At present, and even with R & D funding, he will see evaluations as a sideline. If we want him to do more we will have to put more resources his way – probably another MLSO".

Dr Smithies responded in a third memo dated 21 January 1985 [DHF.002.7101]. She noted "we also discussed whether or not any reference should be made to tests not being accepted in the UK unless they had FDA approval and decided that such a stipulation might not act in Wellcome's best interests in the short term".

The responses contained in [DHF.001.9105] and [DHF.001.9143] appear to be at odds. The earlier response states that the Wellcome/Middlesex test should be submitted to the evaluation whilst the latter response states that [Middlesex] should be established as an evaluation centre. Can the discrepancy between the two responses be explained? Does Dr McClelland know what was decided?

I do not understand the question being asked here. I do not see the inconsistencies among the responses. The statement in [DHF.001.9105] is about the choice of tests to be evaluated, while the statement in [DHF.001.9143] is about the choice of laboratory to perform the evaluation. It is evident from later correspondence that all manufacturers were invited to participate in the evaluation run by the Public Health Laboratory Service under the direction of Dr Philip Mortimer and that the Middlesex Hospital laboratory was ruled out as the evaluation centre on the grounds that it was a development centre for one of the tests to be evaluated

12. On 21 January 1985, the DHSS wrote to a number of manufacturers (including Wellcome) regarding the evaluation programme [see DHF.001.9140 for an example of the letter].

13. On 29 January 1985, Wellcome replied to the DHSS [DHF.002.7106]. The Wellcome representative noted "we will be very happy to submit our product for the evaluation you have requested in your letter but our main priority is to make available a test for use in the BTS as quickly as possible. We may have to accept that the volume of data to support the use of this test is rather limited for the time being but, of course, your evaluation will assist us in this respect".

    Can Dr McClelland explain why Wellcome seemed to view taking part in the evaluation as secondary to making the test available for use in the BTS? Was the purpose of the evaluation not to choose the most suitable test for the BTS?

I have no personal knowledge of the thinking in Wellcome Diagnostics that underlay this implication in their letter. As mentioned above, some of the documents provided appear to suggest that among some parties there was an assumption or an expectation that the obvious route to follow was to use the test developed in the UK. An example is a draft (undated) of the Submission to Ministers [PEN.012.1944] which contains the following text on page 3 [PEN.012.1948]:

> "Preliminary approaches already made by four of the USA pharmaceutical companies licensed to use the US isolate indicate that their tests are based on a different technique which is probably less sensitive... confirmation of positive findings with the US tests would require testing by the UK method...US tests will be more expensive than the UK test"

14. Also on 29 January 1985, the Expert Advisory Group on AIDS held its first meeting. The minutes note that the chairman, ME Abrams, said that the DHSS would ensure that all tests would be evaluated [SNB.001.0002].

    Were EAGA members aware that the decision to carry out the evaluation had already been made and that letters had been sent to all manufacturers? Why was the decision as to whether an evaluation was necessary not left to the EAGA?

I think it is unlikely that some members of EAGA as well as some of the Department personnel attending this meeting would not have known that the test evaluation programme was being planned. I cannot say why the decision on the need for an evaluation was not left to EAGA

other than that it appears to have been taken before EAGA was set up and held its first meeting. There are several references in the documents supplied (eg para 19 of [SNB.001.0002]) that indicate that the DHSS had accepted the recommendation of the Advisory Committee on the National Blood Transfusion Service formulated at its meeting on 27th November 1984. The minutes of the first EAGA meeting on 29th January 1985 indicate that there was agreement that blood donor screening should be introduced as soon as possible but I can see no reference to debate as to the acceptability or otherwise of delays caused by an evaluation programme. The need for an evaluation programme seems to have been accepted at this meeting (paras 18 and 21 of [SNB.001.0002]).

15. The DHSS responded to Wellcome's letter on 11 February 1985 [DHF.001.9175]. In their response the author states "the evaluation programme of AIDS kits will be organised through STB, with [X] looking after it. I think we would regard the commercialisation of the BTS test as quite separate from the evaluation programme that we are setting up".

    What was meant by "I think we would regard the commercialisation of the BTS test as quite separate from the evaluation programme that we are setting up"?

I do not know what meaning was intended. The writer appears to have felt it necessary to signal to Wellcome that while the commercial development of the test was a matter for Wellcome Diagnostics, a test system developed by Wellcome would be independently evaluated in the same way as offerings from any other manufacturer.

16. On 13 February 1985, there was a DHSS meeting. The Inquiry is in receipt of the notes of the meeting [DHF.001.9250] and an internal memo dated the same day [DHF.001.9212]. From the above-mentioned documents, it appears that by this time, go-ahead had been given for an R & D project at Middlesex Hospital with two objectives. These objectives were (1) to scale up the RIA and to carry out field trials with the co-operation of the NLBTC and (2) to carry out follow up studies on positive results. It had also been agreed that the Middlesex Hospital was not an appropriate site for evaluation of commercial kits because the staff had played a significant part in the development of the RIA. It was agreed that Dr Phillip Mortimer of the Public Health Reference Laboratory should co-ordinate the evaluations instead.

17. Why was the evaluation exercise not run in parallel with the introduction of testing, given that once the results of the evaluation had become available it would have been possible for blood transfusion centres to change to another test based on those results?

The documents I have reviewed do not appear to make any reference to this possibility having been considered. I do not know why the evaluation programme was not run in parallel with the start of routine testing. It is my recollection that supplies of test kits available to the UK from any manufacturer were limited in the early months of 1985. This may have been one of the reasons for not making an earlier start on routine testing.

18. The Inquiry is in receipt of a letter dated 24 January 1985 from Dr Cash to Dr Bell [SNB.005.7304] in which the former notes that Richard Lane had advised him that the CBLA had recently written to the DHSS conveying its serious disquiet about being deliberately excluded from a "secret meeting" between

DHSS officials, Professor Weiss, Dr Tedder and Wellcome Diagnostics. The Inquiry does not have a record of the CBLA letter.

Does Dr McClelland know anything about the "secret meeting"? When did it take place? Who was in attendance?

I have no knowledge of this meeting.

19. The Inquiry is aware that Dr Alison Smithies was heavily involved with the evaluation programme. Unfortunately, we have been unable to identify other DHSS personnel involved with this matter due to document redaction. We would be grateful if you would advise of any other DHSS personnel who were involved with the introduction of HTLV-III screening who may be of assistance to the Inquiry.

I am not able to identify other DHSS personnel who might be able to assist the Inquiry on this topic. It is possible that Dr John Barbara (microbiologist, now retired from NHSBT) may have had contacts with DHSS in relation to testing for HTLVIII antibody in the NBTS.

SNBTS evaluation

20. In the letter to Dr A E Bell dated 24 January 1985 [SNB.005.7304], Dr Cash noted:

> "The biggest anxiety of the NBTS Directors with regard to this problem is the Scots: that they will unilaterally move to come in line with American proposals. They're right: we are in detailed discussion with commercial (kit) companies, our technical staff are already looking at ways of introducing the technology within existing staff establishments, we have the Western Blot technique (HQ and SE Labs), we are already liaising with

local (Communicable Disease) physicians with a view to securing care for our positive donors and we are currently arranging our financial planning accordingly..."

21. On 25 January 1985, Dr Cash wrote to Dr Ruthven Mitchell (SNBTS Director Glasgow) [SNB.005.9713]. Dr Cash advised that WBTS should undertake, on behalf of the SNBTS, initial evaluation studies of commercial HTLV-III antibody kits.

22. At the SNBTS Co-ordinating Group meeting on 19 February 1985 [SNB.003.9171] it was decided that Dr Cash's letter should not be pursued at the present time.

What particular steps had the SNBTS taken with regard to the introduction of HTLV-III screening in Scotland as at 24 January 1985? When the SNBTS was considering its own evaluation, would this have occurred at the same time as the introduction of a commercial test or would a test have been introduced only after the evaluation had been completed? Did the SNBTS abandon its own evaluations altogether and await the DHSS evaluations and, if so, why? Was the decision to await the results of the DHSS evaluations made by the SNBTS or the SHHD? What discussions took place between the SNBTS and SHHD regarding this matter?

I do not recall what, if any, steps to evaluate HTLV-III tests had been taken by SNBTS as at 24th January 1985. I do not recall discussions within SNBTS about performing a separate evaluation in addition to that then being discussed by DHSS. I do not know what, if any, discussion took place with SHHD about this. It is likely that Dr Eddie Follett would have been involved, and Dr Brian Dow may have access to relevant information.

The Introduction of HTLV-III screening in Scotland

23. On 11 July 1985, the working party of the Regional Transfusion Directors' Committee produced a report, 'Screening of blood donations for anti HTLV-III in regional blood transfusion centres' [SNB.004.9046]. We note that Dr McClelland was a member of the working party. The report stated that routine screening tests should not be introduced until the proposed evaluation in the NBTS of different tests had enabled satisfactory system(s) to be selected.

24. A revised corrigendum [DHF.001.7532] altered this: the evaluation should take place but urgency precluded the completion of the NBTS evaluation prior to arrangements being taken for the introduction of routine screening. Directors were advised to make arrangements for the introduction of screening whilst the NBTS evaluation was being undertaken. The selection of kits should be made on the recommendations of the PHLS study. Long term contracts were to be avoided until the results of the NBTS evaluation were available.

25. Both the report and the corrigendum stated that the other steps necessary before the commencement of screening were: that reference centres had been established to carry out confirmatory tests on sera giving positive results, and that alternative venues for non blood donors to obtain testing had been established.

26. The first stage of the evaluation was completed on 30 July 1985.

27. HTLV-III screening of blood donors was introduced in Scotland (and the rest of the UK) on 14 October 1985.

Why did the working party amend the report and recommend that screening tests be introduced prior to the completion of the second stage of the evaluation?

I do not remember discussions that might have lead to this change of plan. I have been unable to find any document that helps to explain the reason for it. My recollection is that the first part of the evaluation took longer than planned, and as this was a period when there was a constant flow of disturbing information about AIDS, I think it is probable that it was felt that additional delay was not acceptable. Also, I think that by the time the first part of the evaluation had been completed, we were aware that "second generation" tests were being developed and could soon be available, so that if the second part of the planned evaluation had assessed the first generation tests, its findings may have been rapidly superseded.

> Why was HTLV-III screening not introduced in Scotland until 14 October 1985 given that the first stage of the evaluation was completed on 30 July 1985?

My recollection is that we were quite pressured to meet the timescales once the two kits had been designated as approved for use by UK BTS centres. SNBTS began testing donations well before 14th October 1985. In the SE region, the intention minuted on 19th August 1985 [PEN.012.1950] was to carry out a small "in house" assessment of the two kits that had been approved, and on completion of this to move directly on to start testing all donation samples. Routine testing in SE was to start on 23rd September 1985, [PEN.012.1951] so that all blood in stock, would be tested by the "official" start date of October 14th. This latter target was achieved across SNBTS [SNB.005.8091].

There had been preparation for the introduction of testing earlier than July 1985. I had prepared a short paper entitled "Introduction of testing for HTLVIII antibody…" [SNB.005.9600]. The covering letter for this [SNB.005.9598] is dated May 15th 1985 and was addressed to Dr Harold Gunson and copied to Dr Cash and Dr Gillon.

The day following the announcement of the results of the evaluation (August 1st 1985 [SGH.002.6967]), Dr Cash wrote to the SNBTS directors with a detailed account of the issues to be dealt with [SGH.002.6977]. On August 7th I assigned tasks to members of SE BTS staff [PEN.012.1949]. The minute of an SEBTS staff meeting about the implementation held on 19th August 1985 [PEN.012.1950] records that we intended to commence routine testing on 23rd September 1985.

> How long did it take to make arrangements for alternative testing venues in Scotland for non blood donors to obtain testing?

I am only able to answer this question for the SEBTS. During the spring and summer of 1985, Dr RP Brettle, then a Senior Registrar in Infectious Diseases, had returned to Edinburgh from a period in the United States where he had been studying the AIDS epidemic. He worked for some months in SEBTS before taking up post as Consultant in Infectious Diseases in the City Hospital, Edinburgh. On September 18th 1985 a grant proposal was submitted to SHHD by Drs Brettle, Gillon and McClelland for a study to evaluate a confidential self-referral clinic for AIDS testing [PEN.012.1956]. This clinic was in operation before the

commencement of routine HTLV-III donor screening by SEBTS. It was located in the Infectious Diseases Unit at Edinburgh City Hospital as it was felt that "worried well" individuals were more likely to attend there than at the Sexually Transmitted Diseases Unit which at that time retained the image of the "VD clinic" [PEN.012.1968].

Who was responsible for arranging alternative testing?

The DHSS appears to have issued advice on this topic to both NHS Managers and Regional Transfusion Directors. It is not clear to me on re-reading these documents what the Department's view was as to who precisely was responsible. A DHSS letter to Health Service Managers in England and Wales (copied to Regional Medical Officers and Regional Transfusion Directors) dated 1st August 1985 [SGH.002.6967] refers to earlier advice (Mr Hart to Regional General Managers, 30th July, [SGH.002.6965]) advising them "... of the need to set up alternative testing arrangements. This advice was reiterated in a letter of the same date (1st August 1985) to Regional Transfusion Directors in England and Wales [SGH.002.6963].

A booklet for doctors issued by the DHSS dated 1st October 1985 [SGH.002.7091] is prefaced by a letter from the Chief Medical Officer stating that as part of the introduction of HTLV-III testing of blood donors, "alternative facilities for providing antibody tests on a confidential basis will become available (a) at GUM clinics (b) by arrangement with the patient's general practitioner…"[DHF.001.8019].

SHHD issued advice in similar terms [SGH.002.7080 and SGH.002.7081].

28. The corrigendum recommended that long term contracts be avoided until the results of the NBTS evaluation were available. The minutes of the SNBTS Directors meeting on 2 October 1985 [SGH.001.6412] note that the South East and North regions had only purchased a 3 month supply.

With this in mind, could a short term supply contract have been entered into at an earlier date (i.e. whilst the first stage of the evaluation was being undertaken)?

I do not know if any suppliers would have been able to supply in the quantities required and I do not recall what enquiries were made about this apart from my letter to Wellcome [SNB.005.9501]

This appears to be supported by [DHF.001.8019] which includes the sentence "From a date in mid October to be announced, all blood donations will be screened at regional Transfusion Centres (RTCs) for HTLVIII antibody".

29. The Inquiry team is aware that by the time that HIV screening commenced in the UK (14 October 1985), Ruchill Hospital (Glasgow) and the Clinical Virology Laboratory (Edinburgh) had been established as reference centres to carry out confirmatory testing.

When exactly were these centres established and able to start carrying out confirmatory testing?

While I have seen no documentary evidence during the preparation of this statement, my recollection is that confirmatory testing was available to each of the SNBTS centres by the time that routine testing began.

Who was responsible for establishing them?

During August 1985, SNBTS made arrangements with Virology Departments in Glasgow and Edinburgh to undertake confirmatory testing [SNB.001.0344] [PEN.012.1969] [SNB.009.3415] [PEN.012.1971] [PEN.012.1972] [PEN.012.1973] [PEN.012.1974] and [PEN.012.1976]. The SHHD was party to these arrangements. It is minuted that at a meeting on 27th August 1985 Dr McIntyre "emphasised that no additional monies to AHB (sic) for their testing work". This statement appears in [PEN.012.1974] which is a note of a meeting held in SHHD on August 27th 1985 to discuss reference labs for HTLVIII antibody testing.

30. The minutes of the SNBTS Directors meeting on 2 October 1985 [SGH.001.6412] record that the East, South East, North and North East regions had all chosen the Wellcome test by that date.

Which test was chosen for the West?

I have consulted a member of SNBTS staff with long experience of virology testing (Mr Anthony Jordan) who states that to the best of his belief, West of Scotland RTC also used the Wellcome test when donor screening began.

Preference for the introduction of a "British test" into the NBTS

31. At the meeting of the EAGA on 29 January 1985 [SNB.001.0002], the preference for a radioimmunoassay was discussed The minutes state (paragraph 21) "on the type of test to be used, Dr Gunson said that there was an overwhelming preference for the use of a radioimmunoassay test in the NBTS whilst Professor Zuckerman stressed the need, first, for evaluation of other tests, including the ELISA test".

32. The subject was also discussed at the 16th meeting of the Central Blood Authority on 1 February 1985 [DHF.003.0219]. The minutes record "the Chairman stressed that revenue sparing was as important as saving. [X] emphasised that the enzyme assay was a US test and if the UK needed to be converted for enzyme testing it would pose a serious problem for the continuance of RIA testing. It was therefore considered vital that a British test be developed".

    Why was there an "overwhelming preference" for the use of the radioimmunoassay test in the NBTS? Was this preference shared by the SNBTS? Why did Professor Zuckerman want other tests, including the ELISA tests, evaluated?

I am not aware that a preference for a radioimmunoassay method for HTLVIII antibody testing was ever expressed in SNBTS. My understanding is that the preference in NBTS was to use an HTLV-III antibody test that was very similar in operation to the BPL RIA for HBsAg that was used by most or all NBTS centres.

I cannot speak for Professor Zuckerman's views. However, there was a substantial reason – in terms of minimising the use of ionising radiation

in the laboratories – to move to a form of assay that did not involve the use of radioactive isotopes.

33. We know that by July 1985 (when the first stage of the DHSS evaluation programme was completed) that Wellcome had switched from a radioimmunoassay to an ELISA test. The Inquiry is not aware of the reasons for the switch by Wellcome, nor at what point it occurred.

    Does Dr McClelland know when the switch occurred and/or why?

If this information is available, I imagine it would be in the archives of Wellcome Diagnostics – possibly as part of product licensing information. I think it is very likely that Wellcome judged that an enzyme based assay would be more acceptable on the market, because of the desire to avoid risks to health associated with the use of radioactive isotopes.

> What implications, if any, did the switch have for the NBTS and SNBTS? What, if anything, had changed between January/February 1985 and the date of the switch which made it acceptable for an ELISA test to be used within the blood transfusion services when it had not been acceptable beforehand?

Changing from RIA to ELISA testing was essentially a matter of using different equipment and protocols for the conduct of the analytical procedure. I cannot comment on factors that may have altered the acceptability of ELISA for the NBTS. My recollection is that SNBTS did not have any major issues about changing from RIA to ELISA methods over this period.

Consideration given to the idea of introducing commercial tests as an interim measure

34. On 21 February 1985, Dr Cash and others from the SNBTS and NBTS sent a letter to The Lancet [SNF.001.3361]. The letter stated "we the undersigned believe that the likely incidence of false positive HTLV-III antibody tests using the current generation of commercial kits in our voluntary blood donor populations will be high".

35. By comparison, Professor Bloom was anxious that one of the FDA licensed kits should be introduced immediately and wrote to the DHSS on 31 May 1985 to convey that view [DHF.002.5510]. With others (Charles Rizza and Charles Forbes), he wrote to the BMJ to similar effect, his letter being published on 22 June 1985 [LIT.001.0333].

36. It appears that the SNBTS/NBTS were concerned that the effect on donors would lead to a sizeable drop in the supply of blood and blood products.

    What was the SNBTS/NBTS "belief" that the current generation of commercial tests were likely to give a high rate of false positive results based on?

I think that we had seen data from the early introduction of routine HTLV-III testing in the USA using the Abbott Laboratories test that indicated that false positive rates were causing difficulty. Although I cannot recall the precise sources of that information I know that we had contacts with virologists working on HTLVIII tests including Professor Robin Weiss and his team and Dr Richard Tedder and members of SNBTS staff had attended meetings at which these matters were

discussed. I am sure that information about both sensitivity and specificity of tests would have been discussed during these contacts.

Crewdson[1] provides extensive information about the extent of the problems of false positivity (pages 188–189, 219, 228, 229) and false negativity (pages 251,279, 280–281) encountered by USA blood centres using the early Abbott tests, and by French laboratories evaluating these tests for routine donor screening (pages 447, 448). It may be relevant that the same source also indicates that Abbott Laboratories had difficulties in supplying sufficient tests for the USA during 1985 (pages 187, 448) and that the opening of their new German production facility, intended to produce supplies for Europe, was delayed until autumn of 1985 (Chapter 22 , note c, page 609) [see PEN.017.1057 for the above extracts]

What was considered a "high rate"?

During the first months of routine donor testing with the Abbott test in the USA, false positive rates of up to 99 false positives per 100 initial test positive samples were reported (Crewdson, page 219 [PEN.017.1057) I do not know if an acceptable upper limit of false positive results was defined at the time. I do know that there was awareness that the implications of the test performance were very dependent on (a) the prevalence of infection in the population tested and (b) the rates of true and false positive detection. This would have depended on the assumptions that

[1] Crewdson J (2002) *Science Fictions: A scientific mystery, a massive cover-up, and the dark legacy of Robert Gallo*; Little, Brown and Company; London

were made about the actual prevalence of anti-HTLV-III in the population tested. The 1985 PHLS/DHSS evaluation [SNB.004.8847] which appears to be the evidence on which the choice of tests to be used by the NBTS and SNBTS was based, employed small numbers of samples and does not appear to have proposed "acceptable" levels for false positive results. It did however show that among the tests evaluated, the Abbott test appeared much more likely to give positive or equivocal results with patient samples that the evaluators judged likely to give problems with false positivity.

> What, if anything, did the SNBTS/NBTS do to attempt to obtain information from larger blood transfusion services abroad in relation to the operation of the commercial tests?

I do not recall what was done about this. It is very likely that personnel from the UK transfusion services would have been aware of issues with test performance through links with other European blood services that had commenced testing earlier (possibly through participation in the Council of Europe Committee of Experts on Blood Transfusion and Haematology).

> What consideration, if any, did the SNBTS/NBTS give to how the effect on donors/transfusion recipients could be lessened, for example, by introducing testing without any public announcement or by deferring the giving of positive test results until the results had been confirmed by a reliable test method?

It was the practice from the start of testing to ensure that donors with a positive screening test were not informed until a confirmatory test had been done with a positive result. Much consideration was given to the practical aspects of communication of results and to management of the donor with an unconfirmed positive screening test both in SNBTS and in the various national committees. The conclusions eventually reached were (a) that donors must know in advance that they would be tested and must know that they would be informed of a positive test (b) that donors should not be informed of a positive test result unless it was beyond reasonable doubt that the result was a true positive rather than a false positive (c) that there must be a secure system to ensure that in the case of any donor who was still awaiting a confirmatory test and thus had not been informed, no donation from that individual could be transfused.

37. In a letter dated 8 January 1985 from Dr McClelland to Mr Madden (Wellcome Foundation) [SNB.005.9501], Dr McClelland states:

> "I would emphasise that in my own centre at least, we would be very prepared to use, in the interim, some form of test procedure which might be considered less than satisfactory for a large scale, long term screening programme".

It would be useful if Dr McClelland could explain what was envisaged here.

What I envisaged was that despite the fact that an early, possibly pre-production version of a test might perform less well in terms of sensitivity, specificity and convenience in use, it would be worth finding

ways to manage problems due to imperfect test performance to allow testing to begin before a definitive test was in production and available. The second element of my proposal was that with even a limited supply of tests it would be possible in the interests of patient safety to identify a subset of donors in which the risk of infection might be higher than the average in the donor. Had this approach been pursued, the subset might, for example, have been defined as donors from the city region, who were males between the ages of 18 and 30 years.

> Was any consideration given to the idea of introducing one of the US commercial tests as an interim measure at Dr McClelland's centre or more widely throughout the SNBTS?

I do not remember what consideration was given by SNBTS to the use of commercial tests – from USA, France or Netherlands. I think it is most likely that consideration would have been given to using any test that we believed would be available and would perform reasonably well.

DBL McClelland

14 September 2011