Issue 3:

The information given about the risk of AIDS (i) to patients (or their parents) before their treatment with blood or blood products and (ii) to patients who might have been infected and their families

Topics covered:

B5a) – The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products;

B5c) – The information given to patients who might have been infected, or who were found to be infected, and their families.

Issue 4:

The circumstances in which the Edinburgh Cohort became infected with HIV including the testing of such patients for HIV and the information given to them about their infection

Topics covered:

B5d) – The circumstances in which those patients known collectively as the Edinburgh Cohort became infected with HIV, the testing of such patients for HIV and the information given to them about their infection.

Topic B5a, B5c and B5d

PENROSE INQUIRY

Topics B5a, B5c and B5d

Evidence on this topic was given by:-

(1) Dr Mark Winter (Day 16);
(2) Dr Anna Pettigrew (Day 20);
(3) Professor Ian Hann (Days 21 and 31);
(4) Professor Charles Forbes (Day 33);
(5) Dr Alison Richardson (Day 29);
(6) Dr Patricia Wilkie (Day 32);
(7) Geraldine Brown (Day 34);
(8) Professor Christopher Ludlam (Day 35, 36 and 39);
(9) Dr Vivienne Nathanson (Day 37);
(10) Professor Gordon Lowe (Days 39 and 40) and
(11) Dr Brian McClelland (Day 40).

The relevant statements on this topic are:-

(1)	Dr Mark Winter	PEN.015.0292 (including written submission to the Archer Inquiry PEN.015.0283)
(2)	Dr Anna Pettigrew	PEN.015.0486 and PEN.012.0277
(3)	Professor Ian Hann	PEN.012.0270
(4)	Professor Charles Forbes	PEN.012.0411 and PEN.012.1328
(5)	Professor Christopher Ludlam	PEN.012.0351, PEN.012.0351, PEN.012.0187 and PEN.012.0774
(6)	Dr Brian McClelland	PEN.016.1239
(7)	Dr Alison Richardson	PEN.016.1284
(8)	Geraldine Brown	PEN.012.0401
(9)	Dr Patricia Wilkie	PEN.016.1297
(10)	Dr George Masterton	PEN.012.0366
(11)	Dr Vivienne Nathanson	PEN.012.0330
(12)	Christina Leitch	PEN.012.1430
(13)	Billie Reynolds	PEN.018.0810
(14)	Ishbel McDougall	PEN.018.1486
(15)	Christine Murphy	PEN.018.1149
(16)	Witness “A”	PEN.018.1367

As part of their evidence on the effects of infection with HIV, the question of information given to patients was also touched upon in the evidence of:- “Christine” (day 28), “Amy” (day 29); “Frances” (day 30); “David” (day 30); “Elaine” (day 31) and “Mark” (day 32).

TOPIC B5

B5a) The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products;

B5b) the tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products; and

B5c) the information given to patients who might have been infected, or who were found to be infected, and their families,

B5d) in particular, the circumstances in which those patients known collectively as the Edinburgh Cohort became infected with HIV, the testing of such patients for HIV and the information given to them about their infection.

Inquiry Counsel Issues Nos: 1,3,4 and 6

1. **The practice of obtaining blood samples from patients with haemophilia to monitor immunological abnormalities**

3. **The steps taken by haemophilia clinicians in Scotland to warn patients of the possible transmission of the HTLV III virus by blood products.**

4. **The response on the part of haemophilia clinicians in Glasgow and Edinburgh in the Autumn of 1984 to the results of tests showing that some of their patients had tested positive for the antibody to the HTLV III virus.**

6. **The way in which information about infection with the HTLV III (HIV) virus and prognosis was communicated by haemophilia clinicians to patients in the period 1985-90.**

In relation to this topic it is again proposed to concentrate upon the questions posed by Inquiry Counsel and to deal firstly with questions 1, 3, 4 and 6 which concern the practice of Haemophilia clinicians.

(1) <u>The practice of obtaining blood samples from patients with Haemophilia to monitor immunological abnormalities</u>

In his written submissions to the Archer Inquiry (PEN.015.0283) Dr Mark Winter describes the practice of Haemophilia doctors regularly monitoring their patients for the presence of new virus infections - see PEN.015.0287. In evidence (on day 16, page 102) he spoke of “the admirable practice of always storing blood on his patients whenever he saw them. He was having blood tests done anyway”.

In his statement PEN.012.0411 Professor Forbes describes the decision to store samples until tests became available (para. 7 at 0412). In his statement in relation to immunological testing in Glasgow (PEN.012.1328) he talks of having accumulated “a variety of stored samples from the Scottish Haemophiliacs that we had knowledge of and who attended GRI” (para. 2.1 at 1329). In evidence (day 33, page 110) Professor Forbes described how blood was obtained and confirms that written consent was not obtained

"because that really didn't exist at that time". See his statement PEN.012.1328 para. 2.3, "At that time it was not the policy of the department to get specific consent from those who had been included in studies for the publication to be submitted to a medical journal" and also statement PEN.012.0411, para. 9, "You ask specifically if consent and testing changed between 1984 and 1987 and the answer to that is of course it did. By 1987 specific consent was asked for. Often before that it was not". Clearly when samples were first obtained (thought to be about May 1983 - see day 33 page 114) there was only a suspicion by some that the as yet unidentified virus was transmitted in blood products. The purpose in collecting samples was in the anticipation/hope that one day a test would become available. See evidence day 33, pages 112 and 113.

In his statement PEN.012.0351 at para. 11, Professor Ludlam describes the same practice of taking blood from patients and the clinical reasons why this practice was appropriate and necessary. This was expanded upon in the "notes of meeting" statement PEN.012.0774 at paras. 5 and 6. Part of the background was of course the findings in 1982/1983 of immune abnormalities in asymptomatic, apparently well, Haemophilia patients in the USA. The cause of those immune changes was unknown. In para. 10 of statement of PEN.012.0351 Professor Ludlam describes his response, which was to liaise with a cell biologist for the purpose of more accurate lymphocyte monitoring. This was expanded upon at great length in evidence on day 35, pages 5-7, 21 and 25. The collaboration with Dr Steel referred to in statement PEN.012.0351, paras. 11 and 12 and PEN.012.0774, para. 4 was again explored in evidence - day 33 pages 34-40. The process of taking blood was explained - day 35 pages 60-67. This collaborative study enabled Professor Ludlam and his colleagues to respond to an international request for information about immune abnormalities in non-AIDS countries, explained fully on day 35 pages 71-81.

The question of whether the investigations carried out on the samples taken fell to be characterised as research or monitoring is of no consequence. It was the professional responsibility of Professors Forbes and Ludlam to do what they could to investigate the conundrum of immune abnormalities in their Haemophilia patients. As Professor Ludlam put it (day 35, page 62), "My responsibility was, as was everyone else grappling with these issues, to use whatever facilities we had available to try and monitor our patients and try and understand how their individual situations were". In line with the standards of the time, consent was not obtained for the publishing of the anonymised data, which standards changed rapidly as a direct result of the AIDS epidemic (see Professor Ludlam, day 35, pages 79-81 echoing Professor Forbes at day 33, page 130).

Dr Nathanson in her evidence (day 37, pages 92-96) confirmed that the testing without express consent of blood samples was common place and acceptable by the ethical standard of the time. In this regard see also Dr Winter on day 16, page 159. It is noteworthy that Professor Ludlam could not recall a single incident of any patient complaint of a sample being tested without consent. Indeed his decision to send samples to Dr Tedder and the results of that played a part in precipitating the meeting of the UKHCDO Reference Centre Directors, including Dr Forbes and Ludlam, with Prof Cash in attendance, at Elstree on 10th December 1984, which decided (by the narrowest of margins) to pursue heat treatment of Factor VIII (minutes of meeting - SNF.001.3850).

(3) The steps taken by Haemophilia clinicians in Scotland to warn patients of the possible transmission of the HTLV-III virus by blood products

Before examining the evidence of clinicians' practice it is vital to recognise the moving picture in relation to the appreciation that AIDS might be transmissible by blood products. Dr Winter discusses this in his statement to the Archer Inquiry PEN.015.0283 at 0284-7 and enlarged upon this with particular reference to knowledge within the UK on day 16 (the B5 discussion starting at page 146). The emerging picture has already been dealt with under Topic B2. After the suspicions were raised of the child in San Francisco being infected in April 1983, it appeared that (whatever was being said in Parliament) by late 1983 most Haemophilia clinicians were persuaded that AIDS was caused by an infectious agent which was transmissible by blood products. By November 1983, Dr Winter suggested that most Haemophilia doctors believed that commercial concentrates were capable of transmitting AIDS (day 16, page 88). See also statement by Professor Andrew Lever PEN.015.0517 at para. 8.25. During 1983 there remained the hope that any blood-borne infectious agent that was suspected of being transmissible by blood products was not present in British concentrates - see day 16, page 9. The minutes of the meeting of UKHCDO on 1st March 1983 revealed the current thinking (DHF.001.7178).

It is also necessary to recognise the extent of the uncertainty in relation to the perceived prognosis of the disease at that time. A useful aide memoire is the document "Historical Summary of AIDS in Haemophilia 1981-1985" (PEN.015.0468).

Professor Hann talked of the atmosphere of great puzzlement at the Second International Symposium on Infection of the Immunocompromised Host held at Stirling in June 1982 (day 21, page 42). At that stage AIDS was considered by many to be a problem of sexual transmission and possibly intravenous drug use (day 21, page 46). Although during the course of 1983 most Haemophilia clinicians subscribed to the view that the blood-borne infectious agent was probably transmissible by blood products, the consequences were far from clear. See Professor Bloom's letter to The Lancet of 30th June 1984 - LIT.001.0409. Further, as a reflection of the incomplete knowledge of the blood-borne infectious agent are the comments, subsequently shown to be inaccurate, contained in Dr Craske's letter of 30th November 1984 - LOT.003.4331, also PEN.015.0250.

Dr Forbes stated that it was his policy to discuss risks in treatment. He stated that patients would have been told - and it was well known - that there was a possibility of Hepatitis resulting from the use of concentrates or cryoprecipitate. When in 1983 it became appreciated that blood products might be capable of transmitting AIDS there was concern as to what to do, but to continue with treatment with concentrates or cryoprecipitate was considered the only viable option (day 33, page 100-101). The communication with patients was encapsulated at page 102-103. Although there were a number of protocols in place for the treatment of patients, Professor Lowe was unable to recall any specific written GRI protocol in relation to the warning of risks of possible transmission of AIDS (day 40, pages 8-23). This would not have been unusual for the time, nor did it prejudice patients. Professor Lowe's position was the same as Professor Forbes, that was to balance the unquantifiable potential risk of a blood borne

virus against the very major risk of bleeding. See also Professor Lowe's additional statement (PEN.018.0559).

At Yorkhill Professor Hann's position is set out in his statement PEN.012.0270 at para. 1.5 and 2.4 and he enlarged upon this in his evidence at day 21, pages 64 and 67 and day 31, page 5.

As regards ERI, see "notes of meeting" statement by Professor Ludlam PEN.012.0774, para. 2 and his evidence at day 35, page 16-22 and 25.

(4 & 6) <u>The response on the part of Haemophilia clinicians in Glasgow and Edinburgh in the Autumn of 1984 to the results of tests showing that some of their patients had tested positive for the antibody to the HTLV-III virus, and the way in which information about infection with the HTLV-III (HIV) virus and prognosis was communicated by Haemophilia clinicians to patients in the period 1985-1990</u>

The Inquiry has heard how Professor Ludlam, having heard in the Autumn of 1984 of the development of an anti HTLV-III assay by Professor Richard Tedder at Middlesex Hospital, sent stored samples to Professor Tedder and received the results by telephone on 26th October 1984. Further samples were sent and investigations were immediately undertaken to identify the solitary batch. (day 35, page 99-100). There followed a meeting at the SHHD between Haemophilia directors and the SNBTS on 29th November 1984 and thereafter the UKHCDO meeting at Elstree on 10th December 1984. This evidence is largely set out in the "notes of meeting" statement PEN.012.0774 and explored in evidence on day 35.

In Scotland, the SNBTS rapidly produced heat treated Factor VIII and recalled existing stocks, a process which, took only a matter of weeks and a recall notice was issued by the end of December 1984.

On his return from the Elstree meeting on 10th December 1984 Professor Ludlam was contacted by a journalist from The Yorkshire Post whose desire to publish his article precipitated the meeting held at Edinburgh Royal Infirmary on 19th December 1984. The circumstances which gave rise to that meeting were fully explained by Professor Ludlam on day 35, pages 111-117 and day 39, pages 89-91 and pages 102-104. Evidence about what was said at that meeting and who attended it came from Professor Ludlam day 35, page 126-135, day 36 pages 14-18 and 21-34; Professor Forbes, day 33, pages 143-149; Geraldine Brown, day 34, page 13-29 and Dr Brian McClelland day 40, pages 99-106 and statement PEN.016.1239. There is also now available the statement from "witness A" with her contemporaneous notes - PEN.018.1367. The statement of Witness A together with her notes entirely concur with the evidence of those involved in organising and running the meeting, and it is evident that for those patients and family members that attended, a great deal of helpful information was disseminated. Both at the meeting and in the circulars there was stressed the importance of the use of condoms and care with blood irrespective of their known HTLVIII status.

The purpose of the meeting was as Dr McClelland put it "to try to inform patients with Haemophilia that an event had occurred of enormous importance to them, which was that some of their number appeared to have become infected with this dreaded new virus" (day 40, page 99). The letter inviting patients to the meeting dated 12th December 1984 is now available

PEN.018.1405. That letter invited the recipients to make an appointment to speak to Professor Ludlam if they wished.

The Inquiry also heard of the results that Professor Forbes received from a Dr Mads Melbye and later from Dr E. Follett. The results from Dr Melbye appear to have been received before 29th November 1984 as Professor Forbes was able to advise the Haemophilia Directors/SNBTS joint meeting on 29th November 1984 of the results (SNS.001.0255, para. 4 - day 33, pages 134/5).

Albeit the method of giving test results to patients varied between Edinburgh and Glasgow, both were examples of good clinical practice. Following the meeting of 19th December 1984, Professor Ludlam sent a letter to his patients enclosing an advice sheet PEN.012.0495 (day 36, page 36). The advice sheet stated that tests were now available and "will be carried out on your routine visits to the centre" and also stated "if anyone wishes a further discussion please phone your centre director for a private chat". He also wrote to the patient's general practitioners - LOT.002.2489.

The advice sheet was drafted by Professors Ludlam and Forbes but the letter sent out from Glasgow took a slightly different approach. That letter is dated 8th January 1985 - LOT.003.4244 and letter enclosed an appointment in order that a test be carried out. Professor Ludlam's approach was, rather than arrange an appointment, to invite the patient to come in if they wished to be tested. Both approaches were entirely appropriate, and the reason for their difference is encapsulated by Professor Ludlam at day 36, page 53-54.

At a more fundamental level there was clearly debate about whether the patient should be told of a result at all. See Professor Forbes, day 33, page 140. The advice emanating from the Chairman of the UKHCDO meeting on 10th December 1984 was that "the test results should not be given automatically but if asked for", but it appeared to be recognised that the decision was to be left to the discretion of the individual clinician, who was best placed to make the decision. See also the advice from Dr Craske in a circular letter of 30th November 1984 - LOT.003.4331. Professor Forbes took the decision to tell his patients - day 33, page 131 and 136. Professor Ludlam sought to encourage patients to be tested but did not wish to pressurise the patients to have the results - day 36, page 61-64. This appears consistent with Dr Nathanson's view that "there is a right to know but there is not an obligation to know" - day 37, page 155. These approaches may be compared with the practice in certain parts of England. See statement by Dr Charles Hay PEN.018.1349 para. 8 and the evidence of Dr Winter on day 16, page 164-5. It is evident that all Scottish clinicians who gave evidence to the Inquiry gave serious consideration to the matter of telling patients their results and made decisions based on their clinical judgement.

At Yorkhill Dr Hann advised parents of the results as soon as the confirmatory tests became available PEN.012.0270 at para. 6.1 and 8.2.

Both Edinburgh and Glasgow were quick to appreciate the need for social work/ psychiatric/psychological input and make the appropriate provisions for this. In Glasgow Dr Patricia Wilkie assisted. Her evidence was that GRI was the first Haemophilia Centre to employ a counsellor. She indicated that she believes that the haemophilia patients received "superb clinical care at that time". - PEN.016.1297 at 1299 and 1303 - 1304.

In Edinburgh Dr Alison Richardson, Clinical Psychologist assisted with input from Dr George Masterton, Consultant Psychiatrist and Geraldine Brown, Social Worker. Their evidence describes the weekly multi-disciplinary meetings. Dr Richardson noted the importance placed upon counselling within the context of HIV-testing, stating "the kind of counselling for somebody who was to intending to have an HIV test was supposed to take about an hour…it was taken very, very seriously" Day 29 page 84.

There was a prompt response to the unprecedented challenge of HIV in the development of multidisciplinary care for infected patients. Clearly huge efforts were put into the care of infected patients.

The Inquiry has apparently received statements from patients which have not been exhibited to the core participants. It is understood that some suggest that they were not told of the results of their tests. There is a plethora of evidence from a number of clinicians about the ability of patients to absorb information, particularly bad news. See for example Dr Nathanson's statement PEN.012.0330 at page 9, "It is well known that when individuals are told difficult or bad news they may not remember the conversation, and are unlikely to remember in full the details. Research has shown that patients may deny ever discussing critical factors, and be astonished when shown a video recording of the interview in which not only were they told the information but engaged in some discussion about its implications". She spoke of this in evidence, day 37, page 107-109 but see also Dr Charles Hay's statement PEN.018.1186 at para. 53 and in evidence day 83, pages 108-110 and 114-116; Professor Gordon Lowe, day 80, page 113 and Professor Hann, day 21, page 66 among others. The preponderance of evidence strongly suggests that patients were told of their diagnosis. Professor Ludlam on Day 36, pages 67-71 explained, how to begin with, he did not force patients to know their test results if they did not want to do so, but later reviewed his policy once treatment which was likely to be beneficial to the patient became available.

In their interactions with patients, clinicians made every effort to communicate effectively in unprecedented circumstances.

Topic B5a and B5c

Inquiry Counsel Issue No 2

2. The steps taken by SNBTS to warn patients of the possible transmission of the HTLV III virus by their blood products.

Dr Perry provided evidence in the form of a witness statement on this topic (PEN.018.0543).
This evidence, which has been neither disputed nor challenged, describes the responsibilities and constraints of the SNBTS as a manufacturer of pharmaceutical products concerning the provision of product information and warnings. Accordingly the SNBTS did not and could not engage in any direct patient communication other than when specifically requested to do so by the Haemophilia Directors (eg the meeting with haemophilia patients on 19 December 1984 as referred to above).

In summary:

- The SNBTS was not in a position to provide warnings or information directly to patients concerning the risks of treatment with their products.
- At no time was the SNBTS requested or advised by regulatory authorities, government agencies or product users to provide specific AIDS/HTLVIII warnings in its product literature.
- The SNBTS did not include specific AIDS/HTLVIII warnings in its product literature reflecting the confused state of knowledge at the time.
- The SNBTS provided information to and cooperated with those responsible for patient care
- No evidence has been presented concerning possible actions or omissions of warnings by the SNBTS which may have influenced the decisions of prescribing doctors or advice given by them to patients.
- The SNBTS revised its product literature after the discovery of HTLVIII transmissions by its products in late 1984.

Topic B5d

Inquiry Counsel Issue No 5:

5. The response on the part of SNBTS in the Autumn of 1984 to the information that patients who had been treated exclusively with SNBTS factor concentrates had tested positive for the antibody to the HTLV III virus.

The SNBTS and the Health Boards (haematologists treating patients with haemophilia) worked together in responding to this information. There were also elements of the response that were undertaken by either the SNBTS or the Health Boards.

The first testing of patient samples for HTLVIII antibody was performed, at Dr Ludlam's request, very soon after a research test for the antibody became available in the laboratory of Dr Richard Tedder. (Oral evidence of Prof Ludlam, day 35, page 83)

The initial SNBTS responses were documented in contemporary records (SNB.006.5996 and PEN.012.1376). The results of the patients' tests were communicated immediately to the SNBTS by Dr Ludlam (PEN.012.1426 and transcripts of days 35, 37 and 40).

The first notification to the SNBTS of three positive recipients was on the evening of 26th October. The first suggestion that FVIII concentrate, batch NY3-0090 might be implicated in these 3 patients was received on either 29th or 30th October 1984. The report that further implicated this batch was received on 2nd November 1984. The batch recall was initiated on 3rd November. On 15th November Dr Perry, Dr Ludlam and Dr McClelland reviewed the data on other batches that some of the patients had received and concluded that they could not identify any other batch that was distinctively likely to be implicated (SNF.001.3624). On 28th November 1984 Dr McClelland wrote to Dr Tedder (PEN.012.1423) and to Dr Philip Mortimer asking if either was prepared to test the available archive samples from the donors who had contributed to FVIII concentrate batch NY3-0090, to which the answer was 'no'.

On 18th November 1984, the PFC commenced heat treatment of all its factor VIII stocks. The first batches were dispatched on 6th December 1984 and recall of all untreated product was initiated on that date also. By 10th December, the SNBTS had distributed heat treated factor VIII to all centres, had begun to withdraw all non heat treated factor VIII and replace stocks with the first generation of heat treated product.

PEN 012 .1335 is a timeline of events relating to batch NY3-0090.