CALL FOR PUBLIC INQUIRY IN RELATION TO HAEMOPHILIA TREATMENT
HEALTH COMMITTEE MEETING – 31 JANUARY 2006
BRIEFING

Infection of People with Haemophilia via Treatment with Blood Products

Haemophilia

- Haemophilia is an incurable, life-threatening disorder of blood coagulation. The condition is normally diagnosed in infancy.

- Without treatment, people with severe haemophilia had a life expectancy of 16 years. Those who survived were often crippled with a poor quality of life.

- During the 1920’s, it was discovered that the condition could be ameliorated by treatment with simple blood products. Patients continued to suffer pain and disability but life expectancy was increased to about 35 years.

- Cryoprecipitate (cryo) was developed in the late 1960’s, from single units of frozen plasma. Adults might need 20 bags of cryo per day to treat a bleed. This was an inconvenient and cumbersome treatment, but it was an important advance. Some children remained on cryo because their body weight allowed fewer units/treatment.

- During the early 1970’s specialist blood products became available; Factor VIII concentrate for the treatment of haemophilia A and Factor IX concentrate for the treatment of haemophilia B.

- The new concentrates were very effective. Life threatening bleeding and crippling injuries could be prevented. Pain and anxiety could be removed. Damaged joints were replaced. Normal education, employment and social activities became possible. A normal life-expectancy was envisaged.

- These benefits were judged by medical experts and by patient organisations, to greatly outweigh known risks of hepatitis infection from the use of these coagulation factor concentrates. Therefore, they were preferred to cryo.

- The challenges facing health professionals were to provide the quantities of coagulation factors needed to treat haemophilia effectively and to eliminate the infectious complications associated with the treatment.
• During the late 1970s and early 1980s, there was clear evidence of dialogue between the National UK NHS Haemophilia Directors and the Haemophilia Society and their members over the risk of hepatitis.

**Supply of Factor VIII Concentrate (1970’s-1980’s)**

• Factor VIII is a protein present in blood at trace levels. It is essential for normal blood coagulation. People with haemophilia A are deficient in factor VIII.

• Blood Transfusion Services were unable to provide the amount of Factor VIII concentrate needed to treat haemophilia patients effectively.

• Factor VIII concentrates prepared from USA paid donor plasma became available commercially in the early 1970’s.

• Commercial factor VIII concentrates were imported by the NHS following pleas by medical specialists, supported by the UK Haemophilia Society.

• From 1974-1984, use of Factor VIII concentrate in the UK increased 12-fold, with 60% of this being met by commercial imports.

• SNBTS increased its output of Factor VIII concentrate and, by 1983, was able to meet clinical demand in Scotland, enabling Scotland to be one of the few countries in the world to be self-sufficient in supply of Factor VIII.

• Most of the Factor VIII concentrate used in England & Wales was obtained from commercial sources until 1989; self-sufficiency was never achieved.

**Risk of Infection**

• The risk of a blood borne infection is an *intrinsic* feature of treatment with blood products.

• The degree of risk is related to the amount of blood product used by a patient. People with haemophilia are treated with large quantities of blood products.

• Concentrates derived from paid USA donors were regarded as more likely to be infected than those derived from unpaid UK blood donors, prior to effective virus inactivation (late 1980’s).

• SNBTS undertook research aimed at the discovery, detection, removal and inactivation of the agents responsible for blood borne infections.

**AIDS**

• The virus responsible (HIV) was identified by French and USA researchers in May 1984.

• Evidence that HIV might be destroyed by a level of heat that Factor VIII concentrates could withstand became available in November 1984.
• All Factor VIII issued by SNBTS from 10 December 1984 was heated in this manner. This enabled Scotland to be the first country in the world to make HIV-safe Factor VIII available routinely for all patients, within weeks of the knowledge being available.

• The UK Government introduced testing of blood donations for HIV infection in October 1985.

• To date, Medical Science has failed to develop either a vaccine or a cure. Public Health Authorities have failed to prevent the spread of disease.

• 44 million people are infected worldwide.

Post-Transfusion Hepatitis (PTH)

• The risk of hepatitis infection by blood products has been known since the late-1930’s.

• The risk to people with haemophilia was recognised following reports of infection by fibrinogen (1963), Factor IX concentrate (1969) and Factor VIII Concentrate (1972). Cryoprecipitate was also known to carry a risk of hepatitis transmission.

• Consequently all coagulation factor concentrates carried warnings concerning hepatitis.

Hepatitis B.

• The virus responsible (HBV) was identified in 1968.

• Testing of blood donations for HBV infection was introduced by SNBTS in 1970.

• It was believed that HBV was responsible for most cases of.

• A vaccine has been available in the UK since 1981.

• 350 million people are infected worldwide.

Non-A Non-B Hepatitis

• The hepatitis A virus (HAV) was discovered in 1973. HAV is a bowel and liver virus and is only very rarely transmitted by blood.

• Cases of PTH, which were not explained by HAV or HBV infection were reported in recipients of blood components (1974) and in people with haemophilia (1975).

• This condition was named non-A, non-B hepatitis (NANBH) and was presumed to be caused by a blood-born infection.
Hepatitis C

- The virus responsible (HCV) was discovered by USA researchers in 1989.

- HCV is now known to have been responsible for virtually all cases of NANBH and for 90% of PTH.

- Clinical evidence became available during 1983/84 that levels of heat which Factor VIII concentrates could tolerate were not able to destroy the agent responsible for NANBH.

- Preliminary clinical evidence became available in October 1986 that the agent responsible for NANBH might be destroyed by a higher level of heating.

- In April 1987, SNBTS began to routinely issue a new Factor VIII concentrate, which had been especially developed to withstand this higher level of heating. This advance enabled Scotland to be the first country in the world to supply sufficient HCV-safe Factor VIII concentrate for its haemophilia patients.

- A similar product (BY) had been used in a small proportion of haemophilia patients in England earlier than this, (see page 5).

- No other country or company developed a HCV-safe Factor VIII concentrate for some years. Detailed information on this was supplied by SNBTS in its evidence to the Investigation by the Scottish Executive.

- Testing of blood donations for HCV infection was introduced by the UK Government in September 1991.

- To-date, Medical Science has failed to develop either a vaccine or a cure. Public Health Authorities have failed to stop the spread of disease.

- 170 million people are infected worldwide.

Patient Information

- Patients have claimed that they were not informed of the risk of infection. SNBTS has previously provided the following documentation:
  - Leaflets supplied with SNBTS products warning of the risk of hepatitis.
  - Leaflets supplied with commercial products warning of the risk of hepatitis.
  - Warnings published in the medical literature and in presentations at conferences for haemophilia patients.

- Clinicians treating the patients have indicated that patients were informed of risks of infection (see report of Scottish Executive Investigation into the development of heat treatment, 2000).
In addition to leaflets supplied with its products, SNBTS has examples of the labels that were attached to vials of early SNBTS coagulation factor concentrates and of the carton in which the vials were packaged, all of which carried warnings of hepatitis infection.

SNBTS also has in its possession documents from the UK haemophilia Society, which indicate that patient representatives were aware of the risk of hepatitis, including a minute of a meeting of the Scottish Group of the Haemophilia Society, held on 29th March 1980 at which hepatitis was discussed.

Clinical Trials Consent


As far as 'written' consent is concerned, the 1983 and 1989 versions require "freely given informed consent, preferably in writing."

The 2004 version goes on to state "If the consent cannot be obtained in writing, then non-written consent must be formally documented and witnessed."

Self-Sufficiency and the Choice of Products

The SNBTS Factor VIII product was developed by SNBTS to improve the quality of, and in many cases, save the lives of, haemophiliac patients. Before Factor VIII concentrates became available during the 1970s, the life expectancy of a haemophiliac patient in the UK was about 40 years.

At all times during this period, it was well established that all Factor VIII products carried a risk of hepatitis transmission and SNBTS products were labelled carrying warnings to this effect (labels on the product bottle, carton and in package inserts).

The principles of unpaid volunteer donors and self-sufficiency were criteria fundamental to blood collection in Scotland. This was to avoid importing products from the plasma of paid donors from the US and elsewhere, products from these paid donors were known to present a higher risk of infection.

Scotland was one of the first countries in the world to achieve self-sufficiency in the supply of Factor VIII using donations from unpaid volunteers.

SNBTS is proud of the staff who worked hard to ensure that Scotland was able to have sufficient supplies of Factor VIII available to meet the demands of all Scottish patients by using plasma from unpaid volunteer donors resident in Scotland.

At the time when Scotland was already self-sufficient in the provision of HIV safe Factor VIII from unpaid donors, it also became the first country in the world to provide all of its haemophilia patients with Factor VIII, which was hepatitis C safe.
Comparative Safety of SNBTS and Commercial Factor VIII Products During the 1980s

- 1984: SNBTS Factor VIII product was prepared using heat treatment at 68°C for two hours. This was issued throughout Scotland on 10th December 1984 and prevented any further transmissions of HIV. Elsewhere in the UK heat treated Factor VIII was not generally available.

- 1985-87: By May 1985, unheated Factor VIII was still being used in at least 33 UK haemophilia centres outwith Scotland. A discovery by SNBTS enabled heating at 68°C to be extended to 24 hours giving a further margin of safety against HIV, which was demonstrated by the continued absence of HIV transmission. Commercially available products used heat treatment methods varying from 60°C for 10 hours to 68°C for 72 hours and in some cases these products continued to transmit HIV.

- In England, the Blood Products Laboratory (BPL, now called the Bio-Products Laboratory) began to issue heat treated Factor VIII routinely from September 1985 in the form of a new type of product which could tolerate heating for 72 hours at 80°C. Difficulty in preparing this meant that output from BPL fell to about 25-30% of the English requirement, resulting in increased importation of commercial Factor VIII from the USA.

Why this product could tolerate such severe heating was not known, even by scientists at BPL, and could not be reproduced by other manufacturers. Fortunately, SNBTS scientists discovered how this had been achieved and shared this information with BPL and with other manufacturers. SNBTS was then able to develop a new product equivalent to that being prepared at BPL.

- 1987 onwards: SNBTS Factor VIII was heated at 75°C and then 80°C for 72 hours, which in addition to preventing HIV transmission, was subsequently shown to make the product safe from HCV transmission also. Commercial products continued to be treated at 60°C and 68°C and transmissions of HIV and HCV persisted from some of these products.

- Throughout the 1980s, commercially produced Factor VIII concentrates imported into the UK continued to be associated with hepatitis transmission. Consequently, the achievements of SNBTS significantly reduced Scottish haemophilia patient exposure to the risk of virus transmissions.

Collection of Blood Donations from US Military Personnel

- SNBTS followed international policy and best practice in the selection of donors, which included the collection of blood from volunteer non-UK nationals resident in the UK. US citizenship has never been a criterion for donor exclusion in the UK or in any other country.

- It is primarily behaviour rather than country of origin that determines risk factors and this principle continues to be the basis for volunteer donor selection.

- US military as well as Scottish donors who exhibited risk behaviour were excluded from donating.
• SNBTS records show no evidence of any HIV positive donation being collected from US personnel.

• Epidemiological data now available indicates that collecting volunteer blood from American Military personnel based in Scotland, conveyed no greater risk of transmitting bloodborne viruses to patients receiving blood from donors indigenous to Scotland.

Collection of Blood from Prison Establishments

• Collection of blood from prisons and borstals during the 1970s and early 1980s was standard practice in the UK and in many countries worldwide. It was also Home Office approved policy, as this was seen to be a part of prisoner’s social inclusion and rehabilitation.

• This practice was phased out on advice of medical expert opinion in the early 1980s.

• No transmission of HIV by blood products in Scotland has ever been traced to prison donations.

• Even in retrospect, the use of prison donations did not have a significant effect on the safety of fractionated plasma products as the prevalence of hepatitis C in Scotland meant that infection of heavily treated patients, such as haemophiliacs, was virtually inevitable using donations from the normal population.

Facilities

• SNBTS sought voluntary inspection of its premises during a time when NHS facilities were under Crown Immunity. This was to ensure that SNBTS could fulfil the pharmaceutical standards for the operation of Hospital Blood Centres and attain licence criteria when Crown Immunity was removed in 1991.

• SNBTS had vastly increased throughput in its Donor Centres as part of the drive towards a self-sufficiency programme and this put the facilities under a great deal of pressure. The move from blood bank based activity to pharmaceutical style manufacture was achieved within a very short period.

• SNBTS was aware of the need to improve some of its facilities and those identified in the Inspectorate Reports were already being addressed at the time of the inspections. As part of these improvements, the PFC was upgraded, and because of these improvements, Scotland was able to increase its output and become the first country in the world to manufacture and to make available, hepatitis C safe Factor VIII products for all haemophiliac patients. In contrast, commercially produced Factor VIII products imported into the UK continued to be associated with hepatitis transmission.

• The actions taken by SNBTS, significantly reduced haemophilia patients to the risk of virus transmissions and SNBTS is proud of its achievements in making Factor VIII concentrate safe from these infections so early.
Council of Europe Recommendation No. R(83) issued to the Governments of Member States

- By 1983 SNBTS was producing sufficient FVIII concentrate to enable Scotland to be self-sufficient from unpaid donors, a key basic principle stated in the Recommendation. Information to substantiate this can be found in evidence submitted by SNBTS to the Investigation on Hepatitis C by the Scottish Executive (see additional information from SNBTS, Feb 2000, page 4, section 2.3).

- The objective of self-sufficiency was already the established policy of the UK Government (eg see Hansard, 15th December 1980, column 187).

- The fact that Scotland achieved self-sufficiency is recorded in Hansard (5th Feb 1985, column 498). *released under FoI and available on SNBTS website*

- Plasma pools at PFC were relatively small, being about half of the volume used at BPL (Elstree) and considerably smaller than those of commercial manufacturers (unpublished). It would have taken much longer to achieve self-sufficiency (a key objective recommended by the CE) with even smaller pool volumes.

SNBTS supplied cryoprecipitate according to clinical demand (and still does). Clinical preference was generally strongly in favour of concentrate over cryoprecipitate because this was more effective in adults in preventing death or disability from haemophilia.

*(note: the CE recommendation did not mention the use of cryoprecipitate)*

- SNBTS began to issue information on AIDS to blood donors in May/June 1983 (ie prior to the CE recommendation).

- Attending physicians were aware of the problem of AIDS prior to the CE recommendation (eg. see (b) below).

- Decisions on how best to treat and inform individual patients are the responsibility of the prescribing doctor. In the treatment of haemophilia, general guidance is provided by the UK Haemophilia Centre Directors who hold annual meetings for this purpose. These meetings are attended by Haemophilia Society Representatives. In Scotland these matters are also considered at annual meetings between SEHD (SHHD), Scottish Haemophilia Directors and SNBTS. For example:

(a) SHHD/HCD's/SNBTS, meeting, 21 January 1983 (minute, section 4a) *released under FoI and available on SNBTS website.*

SNBTS pointed out "PFC at present issued 2,000-3000 vials per month and at the present rate of uptake 6 months supply is held. Fears of a shortage were remote - - -" and SHHD stated, "in terms of national policy the purchase of commercial products should be avoided so far as possible."

*(This indicates that sufficient FVIII concentrate was available from SNBTS to meet Scottish needs from at least mid-1982)*
(b) SHHD/HCD’s/SNBTS meeting, 21 January 1983 (minute, section 6a) - released under FoI and available on SNBTS website.
SNBTS "drew members attention" to the "problem" of AIDS and it was noted, "in the UK a letter and questionnaire had been sent out to haemophilia directors."

(c) UK Haemophilia Directors meeting, 17 October 1983, (minute, section 9)
"After discussion it was agreed that patients should not be encouraged to go over to cryoprecipitate for home therapy but should continue to receive the NHS or commercial concentrates in their usual way." (emphasis in original minute)

(d) SHHD/HCD’s/SNBTS meeting, 2 Feb 1984. (minute, section 5.ii) - released under FoI and available on SNBTS website
The advice from haemophilia directors was "that cryoprecipitate was preferred in the treatment of children at present, because of the new danger of AIDS" and "It was agreed that a certain minimal amount of cryo was required." SNBTS advised that more cryoprecipitate could be produced "in emergencies."

(e) SHHD/HCD’s/SNBTS meeting, 2 Feb 1984 (minute, section 5.iv) - released under FoI and available on SNBTS website
Proposal from SNBTS that the number of batches of factor VIII that patients were being exposed to should be reduced.

(f) SHHD/HCD’s/SNBTS, 2 Feb 1984 (minute, section 5.v) - released under FoI and available on SNBTS website
SHHD statement: "that the aim of the SNBTS and of national policy was for Scotland to be self sufficient, and although the Department would not wish to intervene in what clinicians prescribed, it was not sensible to purchase imported material when suitable NHS product was available."

Destruction of Documentation

- As far as can be ascertained, SNBTS neither destroyed nor lost any documentation relating to this subject. However, if the DoH did destroy or lose documents relating to Scotland, these would be copies of documents already held by SNBTS or the Scottish Executive Health Department.

Scotsman Article, 14 January 2006.

- Although this is not mentioned in the agenda papers, it is possible that questions may be asked about an article entitled "Partial copies of destroyed files may hold key to cases of infected blood".

The article refers specifically to a letter dated 31st March 1972 "from the West of Scotland BTS to a Dr Biggs - - raising concerns about haemophiliacs and blood transfusions". It is claimed that this letter "indicates that the government knew as early as March 1972 there were serious problems with contaminated blood."

The letter was from Dr J Wallace, Director of the Glasgow and West of Scotland Blood Transfusion Service, to Dr G McDonald, Consultant Haematologist at Glasgow Royal Infirmary. Dr Wallace was simply informing Dr McDonald that the future treatment of haemophilia was being considered by a Medical Research Council Working Party, chaired by Dr Biggs.
Dr Wallace mentioned some of the issues being considered by the Working Party, one of which was the risk from hepatitis. This is not surprising. The risk of hepatitis being transmitted by blood products had been known since the 1940s. Testing of blood donors for hepatitis B had been introduced by SNBTS in 1970. There is therefore nothing new in this letter.

The report of this MRC Working Party was also released by the Scottish Executive in December 2005.

Safety of Anti-D Products as discussed by C. Leckie at the Health Committee,

- Antibodies for intramuscular administration, such as anti-D, are prepared from blood plasma. Although this product has been shown to be free from the risk of hepatitis transmission, hepatitis C was transmitted by anti-D prepared in the Irish Republic and in East Germany. No other country has reported such transmissions. Anti-D has been provided by SNBTS since 1988 with no evidence of hepatitis C being transmitted."

Hepatitis C Lookback Exercise

- SNBTS carried out a National health C virus lookback exercise during 1995-96. Clinicians and hospitals were notified by SNBTS of blood donations given prior to September 1991 from hepatitis C positive donors. These hepatitis C positive donors were detected by the four UK Blood Services following the introduction of routine HCV donor testing. Thereafter, it was the responsibility of clinicians to notify the recipients of the blood donations. GPs were informed by the Department of Health that any patients who had been transfused prior to 1991, and who were concerned about the risk of contracting HCV, should be offered a test.

SNBTS is aware that there may be a few donors who are HCV positive, but who have not returned to donate since HCV donor testing was introduced. Also, it is possible that clinicians were unable to identify through hospital records, living recipients of the contaminated donations.
DEBATE IN SCOTTISH PARLIAMENT: CAROLYN LECKIE  
22\textsuperscript{nd} DECEMBER, 2005

Points of Clarification.

1. **C Leckie. Col 22042, Council of Europe Recommendation R (83) 8.**

   The recommendation was issued to "Member States". Ms Leckie contends that this recommendation was not cascaded through the system (Col 22042) with the implication that patients suffered infection with HIV as a consequence.

   A draft version of the CE recommendation was contained in the papers released by SEHD in December 2005.

   SNBTS has not uncovered the document referred to, or any reference to it, in the SNBTS files. Current SNBTS management do not know if senior SNBTS staff at the time were aware of this recommendation or not. Nevertheless, SNBTS policies were consistent (not "compliant") with the recommendations.

2. **C Leckie. Col 22042. Informing patients of risk of exposure to HIV.**

   Patients were informed of the risk of AIDS by the Chairman of the UK Haemophilia Centre Directors Organisation in a letter distributed by the Haemophilia Society to its members on 4 May 1983. This letter advised patients to contact their Centre Director if they had further questions about AIDS and their own treatment programme.

   Ms Leckie is correct that a decision was taken in Scotland not to inform patients beyond this at this time. This subject was discussed at a meeting between HCDs, SNBTS and SHHD. As the risk from HIV was not known, Haemophilia Directors were concerned that patients might be worried unnecessarily.

   SNBTS acceded to this view as it felt that Haemophilia Directors were in a better position to judge what was best for their patients.

   The criticism is of course based on hindsight. Had it transpired that HIV was not a problem and patients had suffered death or injury because they had stopped treatment, Haemophilia Directors could have been accused of causing unnecessary panic.

3. **C Leckie. Col 22043. More sensitive screening of blood not undertaken because of unwillingness to provide funding.**

   This comment could refer to documents released by SEHD in December 2005 concerning funding, either for screening donors for hepatitis B by the third generation method or for ALT testing for NANBH.

   The infection of haemophiliacs with hepatitis would not have been prevented in either case, as the level of treatment required and the prevalence of
hepatitis infection in the Scottish population meant that people with haemophilia were at very high risk of infection, which could not have been prevented by these tests.

4. C Leckie, Col.22043. Facilities would not have been granted a licence if they had been commercial enterprises.

SNBTS believe that Ms. Leckie has misunderstood the statement made by the Inspector. SNBTS was under Crown Immunity and the Inspector was simply explaining what his powers would be had SNBTS been a commercial organisation. The Inspector was not indicating that a licence would not be granted per se, but that a licence would not be granted if the recommendations were not carried out. The recommendations were carried out and a licence was granted.

5. C Leckie, Col.22043. Crown Immunity was used to circumvent any need to upgrade facilities.

This clearly was not the case. SNBTS facilities, including PFC, were continually being upgraded throughout the 1980s. Documentation has previously been released on this matter.

6. C Leckie, Col.22043. Effective heat treatment of blood was delayed.

Ms Leckie appears to have misunderstood either the Report from the Scottish Executive, the evidence provided to the SE by SNBTS, the report from the HCCC or the Lindsay Tribunal.

The Lindsay Tribunal is important for a number of reasons:
- it was an independent public inquiry, undertaken out with UK.
- it recognised that providing safe treatment for haemophilia was a major challenge to health professionals world wide.
- it saw SNBTS as being at the forefront of this advance.

7. C Leckie, Col.220243. Patients continued to receive FVIII from stocks heated to 68°C.

This is correct. Batch dedication was in place to minimise exposure to donors (as per the Council of Europe recommendation) and it was felt that exposure should continue to be minimised by maintaining patients on the same batch of Factor VIII that they were already receiving until it was finished.

Patients not already being treated with a specific batch of 68°C Factor VIII were expected to be given the new 80°C product immediately.

This decision was taken because it was not known for certain if 80°C heating would be effective against HCV. Therefore, continuing to minimise exposure to donors remained an important safety measure.

Again the comment from Ms Leckie is based on hindsight. If 80°C heating had not worked against HCV, or had caused a high degree of inhibitor formation, then exposing patients to more batches of Factor VIII than necessary, would have presented a higher risk of complications.
8. C Leckie. Col. 22043. Quantity was favoured over quality.

This was not the case. Quantity (ie yield and output) was favoured over a minor reduction in convenience (ie reconstitution time). The overall quality of products from unpaid UK donors was higher than from commercial US donors with respect to infectious complications.

Without this approach, Scotland would not have achieved self-sufficiency as soon as it did and more patients would have been infected with HIV.

9. C Leckie. Col. 22043. Was it just a case of well-intentioned error, or is there culpability?

There were no “errors”. Decisions were made with the information available at the time (not with the benefit of hindsight). All of the decisions taken were reasonable on this basis, most were correct.

10. L Macdonald. Col. 22044. It must be enormously difficult to come to terms with a condition such as hepatitis C.

SNBTS has sympathy for anyone infected with hepatitis C. Nevertheless, it should be appreciated that haemophilia is an immediate threat to life and that patients were given the best treatment possible at the time.

11. L Macdonald. Col. 22044. The basic science that was involved was not understood.

It was not a lack of understanding, but a lack of knowledge that was important.

The viruses responsible for AIDS and for hepatitis C had not been discovered and suitable technology for destroying viruses in coagulation factors had not been developed.

Advances in scientific knowledge and technological innovation were needed to achieve a satisfactory treatment for haemophilia that was also safe from infectious complications.

12. N Milne. Col. 22047. Treatment was provided in good faith.

Factor VIII provided an effective treatment of haemophilia A for the first time, preventing disability and death, which previously had been inevitable.

Factor VIII was made safe from HIV within months of the virus responsible being discovered and then made safe from HCV, even before the virus responsible had been discovered.

These were considerable achievements from which patients were able to benefit.

Patients treated earlier benefited from the availability of Factor VIII, but not from the subsequent advances in safety.

Whenever there is an advance in medical science, patients treated earlier fail to benefit. That is the nature of progress.
13. S Robison, Col. 22049. Many questions remain to be answered.

The questions listed by Ms Robison have all been answered.

14. E Robson, Col. 22049. To say such a thing should never have happened is as obvious.

Given the nature of haemophilia, it was inevitable that if patients were treated for their disorder they would be exposed to blood borne viruses. If manufacturers had decided not to prepare Factor VIII before it had been made free from infectious complications, then safe preparations of Factor VIII could never have been developed.

Without the knowledge gained from plasma derived Factor VIII, recombinant Factor VIII could not have been developed and the treatment of haemophilia would still be in the dark ages.

All medical treatments carry a risk. It is the function of the treating physician to judge if the benefit of the treatment outweighs the risk.

15. E Robson, Col. 22050. Medical science was not aware of the risks and dangers at that time.

It would be more accurate to say that medical science was not fully aware of the degree of risk from infectious complications. Nevertheless, even if the risks had been fully known the benefit of treatment with Factor VIII would have still been substantial in the avoidance of life threatening bleeding.

16. E Scott, Col. 22052. A product that was supposed to be life saving but has ended up being life threatening.

The product was life saving. Without treatment with Factor VIII it is likely that patients surviving with haemophilia would have crippling joint problems and a life expectancy of 40 years.

17. E Scott, Col. 22053. Responsibility for the purchase of imported products lay with local health boards.

Central contracts for the purchase of commercial Factor VIII were held by the Department of Health from 1972 to 1979. These were discontinued on 30th April 1979 and individual Health Authorities were advised to purchase commercial products locally thereafter.

Detailed information on the use of commercial products was collected by UK Haemophilia Centre Directors Organisation and is held in the HCDO archive.
18. E Scott, Col. 22043. What went wrong at the beginning, both scientifically and in blood procurement?

Nothing went wrong. Patients were given the best possible treatment. The treatment of haemophilia advanced in line with increasing scientific knowledge and with innovations in manufacturing technology.

19. C Leckie, Col 22063. The HCCC was not able to access primary sources of evidence.

SNBTS offered to provide any evidence required. SNBTS is not aware of having refused to provide information, even before Fol. It is true that the HCCC did not take evidence from the doctors who were responsible for the patients who were complaining about their treatment.

20. B Adam, Col 22060. CMV - - has affected the life of one of my constituents extremely adversely.

Cytomegalovirus (CMV) is a herpes type virus that is very common. About 60% of the Scottish population have had CMV in the past, usually without knowing. Most people infected have live, but latent, CMV in their blood cells. This latent CMV can re-activate if the person's immune system becomes weak, or if their blood is transfused to an immune suppressed person. Patients with immune suppression must receive CMV negative blood because 60% of people are CMV positive. Blood supplies could not be sustained if all CMV positive donations were excluded.

Doctors caring for immune suppressed patients must request CMV negative blood, which is readily available. If CMV unscreened blood is transfused to an immune suppressed person, there will be a risk of CMV infection (blindness, lung disease most common).

Removal of white cells from blood (leucocyte depletion) is also an effective way of reducing risk from CMV in blood.

Correspondence in possession of SNBTS suggests that CMV negative blood was not requested in this case, and prior to 1998, blood would not normally have white cells removed unless a request was made. Many countries, including U.S.A. still do not remove white cells routinely.
AGENDA PAPERS –HEALTH COMMITTEE MEETING –
31ST DECEMBER, 2006

Points for Noting.

1. Submission from the Minister for Health and Community Care: HC/52/06/3/06

1.1 Para 3. The World Federation of Haemophilia (WFA) Congress is not an annual meeting but normally takes place every two years.

1.2 Para 4. In addition to having two warnings about hepatitis within its product information leaflets, SNBTS products carried a warning of hepatitis on the bottle label and two warnings on the box containing the bottles.

2. Submission from Scottish Haemophilia Forum: HC/S2/06/3/03.

2.1 Ireland (page 2)

The point being made by the Scottish Haemophilia Forum is that the Irish Government has not accepted wrongdoing with respect to the treatment of haemophiliacs. This may be correct, but the Irish Government did accept that the Irish Blood Transfusion Service (BTB) was at fault in the preparation of Anti-D and payments were subsequently extended “to cover all those who had contracted hepatitis C from a blood transfusion or blood product administered within the State” as explained in the letter appended from Anne McGrane.

2.2 “Prisons and Borstals (page 2)

When the SNBTS gave evidence before the Health Committee members raised concern about America using blood from prisoners. The representatives from (sic) did not acknowledge that in Scotland they were collecting blood from Scottish Prisons - - -.”

The is no record of anyone raising concern about “America using blood from prisoners” either in the transcript of the meeting or in any of the written submissions to the Committee.

A question was asked about American “skid row blood”. This was interpreted by the Convener as meaning importation of products from the USA. The representatives of SNBTS were not allowed to respond to the question due to time constraints but were requested to submit a written response.

SNBTS submitted a detailed written response on the importation of commercial coagulation factor concentrates into the UK. However, as SNBTS was not responsible for commercial imports, it does not know the origin of the plasma used, nor if any of the plasma used was obtained from prison donors in the USA. (Note: the collection of blood from prisons was banned by FDA in June 1995).

SNBTS answered all of the questions put by the Committee and subsequently wrote to the Convener offering to answer any further questions. No additional questions have been put to SNBTS.
2.3 (page 2) “Why did it take one full year from the time the Medicines Inspector had commented adversely on the collecting of blood in prisons (sic) borstal institutions before the practice of taking blood from these institutions ceased and who made the final decision?”

The Medicines Inspector did not say the practice should cease, but did advise that SNBTS should reconsider the collection of blood in prisons. The issue was considered by SNBTS Directors at their next meeting. As this practice existed throughout the UK (as well as in many other countries) and was encouraged by the Home Office, the SNBTS Directors decided to take the issue to the UK Working Party on the Selection and Care of Blood Donors. The Medicines Inspectorate was informed of this action and no objection was raised.

As a result of the action taken by the SNBTS, the collection of blood in prisons ceased not only in Scotland but also throughout the UK.

The collection of blood from prisons and borstals has never been formally banned in the UK and decisions to cease such collections were a matter for Regional Directors of Blood Transfusion Centres.

2.4 “US Troops (page 3) Why were SNBTS extracting blood from US troops?” etc.

SNBTS collected blood from people resident in the UK who satisfied UK donor selection criteria. Neither USA citizens, nor US troops have ever been deferred from giving blood on this basis alone (either in the UK or elsewhere).

In March 1983, following the emergence of AIDS in the USA, ‘high-risk’ categories of people from whom blood donations should not be taken were identified by the US Public Health Service (covering CDC, NIH and FDA). SNBTS implemented this guidance. Neither troops nor prisoners were named as high-risk categories by the US Public Health Service.

SNBTS has evidence that hepatitis infection associated with US troops in the UK was no greater than in the normal population.

3. Submission from Scottish Haemophilia Forum – background to the Hepatitis Campaign

3.1 (page 9) “In 1975 Lord David Owen - - - set aside money to improve the screening of blood - - - about a year ago Lord Owen stated - - - official had decided not to proceed “ and “ - - minutes of the 1975 meeting had been shredded - -“.

In 1975, following a television report from ‘World in Action’ concerning the risk of hepatitis from commercial blood products, then Minister for Health David Owen, announced in parliament that he was making available £500 000 to achieve UK self-sufficiency in blood products (not for “the screening of blood” as Mr Dolan states). A substantial increase in the production of NHS-Factor VIII followed, suggesting that this money was spent in the manner intended. However, output of NHS Factor VIII was unable to keep pace with a continued increase in demand for treatment, which greatly exceeded expectations. Consequently, the sum allocated by Lord Owen was not enough to achieve UK self-sufficiency against this escalation in demand.

Figures for the production of NHS Factor VIII since 1969 are readily available and suggest that Lord Owen’s memory of these events may not necessarily be correct.
As the relevant minutes have been destroyed, there would appear to be no evidence to support the version of events described by Mr Dolan.

3.2 (page 9) "About 1985 the Blood Transfusion Service in England - - - discovered that by heat treating blood products to 80% (sic) they were not only able to kill off HIV but also Hepatitis C virus."

This presumably refers to 80°C heat treated Factor VIII concentrate, which was issued routinely from the Blood Products Laboratory (BPL), Elstree from September 1985.

At the time (1985), there was no information on the ability of this treatment to inactivate the agents responsible for non-A, non-B hepatitis (NANBH). The hepatitis C virus had not been discovered. In addition, the treatment could not be tolerated by any established Factor VIII concentrate. Why this new Factor VIII concentrate from BPL could tolerate such a high degree of heating was not known (even by scientists at BPL) and could not be reproduced by other organisations at that time.

Reasonable evidence that 80°C treatment could destroy NANBH was not available until 1988, and was not confirmed until 1993.

3.3 (page 9) “In 2001, the High Court in London awarded compensation to people who had been infected with hepatitis C as a result of blood transfusions” and "only those who received blood transfusions on or after March 1988 were eligible."

There are two points to note:

1) All of the cases concerned treatment with blood components; none of the cases concerned haemophilia or treatment with factor concentrates.

2) The date of the award was determined by the date at which the Consumer Protection Act entered into law in the UK. Justice Burton was not in a position to backdate the law.

3.4 (page 9) “two doctors appearing in the Irish Court in July this year”

The individuals who appeared in court were Mrs C Cunningham (not a medical practitioner) and Dr T Walsh. In both cases the charges against them concern the preparation of anti-D and the transmission of HCV. The charges are not related to the treatment of haemophilia.

3.5 (page 10) The Expert Group Chaired by Lord Ross

In putting forward the recommendation of this group Mr Dolan makes the point that the Expert Group “included medical, nursing, legal and health service management, as well as patient representation,”

It should be noted that the Expert Group did not include any experts in the treatment of haemophilia, or experts in Transfusion Medicine or experts in the development or the preparation of coagulation factor concentrates. One of the patient representatives was a person with haemophilia.

4. Submission from Scottish Haemophilia Forum addendum HC/S2/06/3/04 (page 1)
Most key points have been addressed above. However Mr Dolan complains that the Scottish Executive investigation “did not meet patient or patient organisations” “Nor did it look at those who had been infected by blood transfusions.”

The investigation was established at the request of the Haemophilia Society to examine its allegations that SNBTS had delayed the introduction of heat treatment. There was no suggestion at the time that the investigation should also encompass those infected by blood transfusion (a matter that was due to be heard in court in England). The report of the investigation notes that meetings were held with the Haemophilia Society and with Haemophilia Directors. (note: no meetings were held with SNBTS who provided written evidence only).

It should also be noted that SNBTS met with the Haemophilia Society in November 1999 in order to address the allegations being made by the Society.

5. Submission from Mr Robert Mackie HC/S2/06/3/05

Mr Mackie quotes with the benefit of hindsight. For example, he refers to the Lindsay Tribunal, but quotes testimony to the Tribunal, rather than giving the considered opinion of the Tribunal after all of the evidence had been taken. Mr. Mackie has not provided references for his citations, making it impossible to verify his sources and quotations.

As much of the submission from Mr Mackie concerns HIV infection, it is not clear how this relates to a request to the HCCC for a public inquiry into infection with hepatitis C.

Comments will be restricted to points not already covered above.

5.1 page 3, para 3. "Why did clinicians not warn us about the serious and fatal risk of AIDS, when the risks became known by the beginning of 1983- -.”

UK haemophiliacs were first advised of the risk of AIDS in May 1983 by the chairman of the UK Haemophilia Directors Organisation in a letter distributed by the UK Haemophilia Society. This letter also mentioned the risk from hepatitis. Patients were advised to speak to their local Haemophilia Director if they wished to discuss this further in respect of their own treatment programme.

SNBTS first took action to exclude donors at high-risk from AIDS infection in May 1983.

The conclusions of the Lindsay Tribunal (page number?) (page 61) on the state of knowledge at this time were:

“It is important not to overstate the information which was available by the middle of 1983. Although the evidence in favour of the hypothesis of a transmissible infectious agent seemed to be growing, there was still uncertainty. Other hypotheses to explain the condition of AIDS continued to be advanced. The debate was not over. The infectious agent had not been identified.”

“- it was not known how widely the infectious agent was distributed in the population or whether exposure to it would lead inevitably to the development of the condition of AIDS.”
"In their May 1983 article Montaginier (sic) and Others did not claim to have identified a virus causative of AIDS."

"The breakthrough of the identification of a virus causative of AIDS came with the publication by Dr. Robert Gallo in May 1984."

5.2. page 4, para 5. "By the beginning of 1985 patients throughout the world were beginning to be told of their HTLVIII status, personally and individually by their clinicians, but the practice in Edinburgh was different, why were we not informed of our infection of HTLVIII (AIDS) until years later."

This is of course a matter for the treating physician. Nevertheless, by his own admission on page 19 of his submission, Mr Mackie did attend a meeting at which Professor Ludlam informed his patients that they were HTLV III positive.

5.3. page 6, para 5. "When and why was Crown Immunity imposed on the PFC in Scotland?"

Mr Mackie appears to be claiming that haemophiliacs were infected with HIV or with hepatitis C as a result of Crown Immunity and the resultant standards of operation at PFC.

This rationale is not consistent with the fact the HIV and HCV were transmitted by Factor VIII concentrates produced by all manufacturers world-wide and that Scottish Factor VIII carried a lower risk of infection than equivalent products prepared by other manufacturers.

Despite this inconsistency it might be helpful to explain the situation in Scotland. When PFC opened in 1975 it was not clear if Crown Immunity applied to the NHS in Scotland or not. Therefore PFC applied for, and was granted, a Manufacturers Licence and Product Licences for Factor VIII and for Factor IX concentrates.

In 1981, legal advice concluded that Crown Immunity did apply to PFC. Nevertheless Product Licences for Factor VIII and Factor IX concentrate were renewed in 1983 and in 1984 respectively. However, it was decided that PFC should not apply for renewal of its Manufacturers Licence and informal inspections and dialogue with the Medicines Inspectorate took place instead.

Advice given by the Medicines Inspectorate was acted on at all times.

Crown Immunity was removed from the NHS from 1st April 1991 and PFC's Manufacturers Licence was renewed.

5.4. page 6, para 3. "—why - - did they all fail the minimum standards for manufacturing Licences and Product Licences — why were they allowed to continue production."

The PFC facility did not "fail the minimum standards". The Medicines Inspectorate did make suggestions for improvement. This is normal in any inspection. The advice of the inspectors was acted on at all times.

It is standard practice for an inspection report to state that a Licence would not be granted if the points raised by the inspector are not addressed.
As PFC operated under Crown Immunity, the Inspector explained what his legal powers would have been if PFC had been a commercial company. This should not be interpreted as meaning that PFC was operating at a lower standard than an equivalent commercial organisation.

5.5 page 6, para 4. "PFC has manufactured product which has unequivocally endangered the lives of patients - - I have authorised the issue of products which failed to meet specifications - - - on the basis of breaches of GMP PFCs continued function rested on the provision of crown immunity."

These quotations are taken from a letter written in 1988 in which the author is doing his utmost to persuade officials at SHHD that Crown Immunity should be removed from PFC (and BPL). In presenting his case, the author has argued from an aggressive viewpoint in order to make his point as forcefully as possible.

For example, a procedure for authorising the issue of products, which marginally failed to meet specification, was included in the Product Licence for PFC’s Factor VIII and was therefore a practice which was approved by the licensing authority.

A more detailed explanation of the various points made in this letter is available from SNBTS.

5.6, page 15, para 1. "- - were the patients who took part in these studies informed that the UK had not tested on animals before they decided to proceed directly to human subjects."

The products used in these trials were subjected to all of the tests required for product release before they were given to patients, including relevant animal safety tests for toxicity and for reactions of a pyrogenic nature.

The animal testing to which Mr Mackie refers concerns experiments to determine if the heat treatment employed was effective in destroying the agents responsible for NANB hepatitis.

Chimpanzees were the only animal model thought suitable for this type of experiment. Access to chimpanzees for this purpose was extremely limited and was not available to SNBTS. Some commercial manufacturers in the USA were able to perform experiments of this type in chimpanzees, however the results were misleading as human recipients continued to be infected with hepatitis after being given products that had been found to be safe in chimpanzees.

These findings led international experts to decide that monitoring of products in patients who had not been treated previously was the only way in which safety from NANB hepatitis could properly be determined. SNBTS undertook the studies recommended once a suitable product had been developed.

5.7, page 23, para 2, Safety of Treatment. - “Russian Roulette”

This section of the submission relates to correspondence between Professor Ludlam and Dr Boultin and Professor Cash of SNBTS during the introduction of Z8 (PFC’s 80°C heated Factor VIII).
Both SNBTS and Professor Ludlam had been seeking written assurances from SHHD that patients involved in clinical trials would be eligible for compensation if harm should result.

Although written assurance was provided, Professor Ludlam continued to have concerns over matters of detail and wished to have this resolved before Z8 was issued routinely.

However PFC had ceased preparation of 68°C heated Factor VIII in mid-1986 and stocks of this product were almost exhausted. The expression "Russian roulette" was used by Professor Cash to emphasise the severity of the supply situation and that patients would be at risk from bleeding. Once this was appreciated, Professor Ludlam agreed to Z8 being issued routinely to his patients.

This was essentially a misunderstanding of the supply situation, which has been misinterpreted by Mr Mackie.

5.8. page 24, para 4. "Richard Titmuss - - argued strongly against the use of prisoners as blood donors - - ."

Titmuss argued strongly against the use of paid prison donors in the USA. His views on the use of prison donors in the UK are less clear. He places them in the category of "The Captive Voluntary Donor," and states, "In England the policy is to treat prisoners (and prison staff) like other members of the community and give them the opportunity to volunteer if they wish to do so. It is made clear, according to official policy, that whether they do or do not will not affect their prison sentences or grading; there are no tangible rewards, monetary or non-monetary." He goes on to state, "In terms of ethical principles, therefore, there is a fundamental difference in the official policies adopted in regard to prison donors in the United States and England."

5.9. page 24, para 5 "By 1971 - - Canadian Red Cross Society stopped collecting donations from prison inmates - - ."

This decision did not prevent Canadian blood products from having a worse record than Scotland in transmitting infections.

5.10 page 24, para 6 "In America in 1982 - - the director of the Office of Biologics of the Food and Drug Administration- - asked them not to use plasma collected from prisons."

Mr Mackie acknowledges that this was an informal agreement with four US fractionators. This informal agreement was not made public and did not become official FDA policy until 1995.

5.11 page 25, para 3 "extract from hazards of Transfusion Therapy".

Although no reference is given for this quotation it may be of interest to note that it is taken from a textbook that was published in 1977 which describes the accepted UK policy of the time.

1st February, 2006