IRISH HAEMOPHILIA SOCIETY

TRIBUNAL NEWS

ISSUE 3

TRIBUNAL OF INQUIRY

(Into the Infection with HIV and Hepatitis C of Persons with Haemophilia and Related Matters)

PROCEEDINGS: JUNE 20th, 2000 – DAY 12

The Proceedings opened before her Honour Judge Lindsay on the above date at The Distillery Building 141 – 145 Church Street, Dublin 7.

The Irish Haemophilia Society was represented by Mr John Trainor, S.C., Mr Martin Hayden B.L., Mr Jim McCullough B.L., instructed by Mr Raymond Bradley of Malcomson Law, Solicitors.

Mr John Finlay S.C., for the Tribunal set out the procedure for the forthcoming division of the Tribunal's work. He said it is intended that the Tribunal should deal with Terms of Reference 1, 2 and 4 and 3, 5, 6 and 7 with respect to the Blood Transfusion Service Board, its servants, agents or employees. This division will require the Tribunal to ascertain which blood products or blood components administered to persons in the State, treating them for Haemophilia or other blood clotting disorders caused or probably caused the infection of such persons with HIV or Hepatitis C and, to examine the role of the BTSB in the manufacture or selection of such products, with particular reference to the adequacy of steps taken to avoid or minimise the risk of such infection and to deal with the situation which arose when both the risk of and the fact of such infection became known.

Mr Finlay gave a brief history of Haemophilia and the treatments available for it. He told the Tribunal how from 1973 onward the BTSB issued Factor IX fractionated from Irish Plasma and how from 1974 Factor VIII and Factor IX, which had been commercially fractionated, became available in Ireland. He said that while the BTSB had never itself produced a high purity Factor VIII Concentrate comparable to commercially produced Concentrates, it had produced a freeze dried cryoprecipitate in 1976. Between 1981 and 1984 BTSB had planned for and experimented with the production of an intermediate purity concentrate. This concentrate was never put into full production. The BTSB subsequently entered into contract fractionation arrangements whereby Irish Plasma was fractionated into Factor VIII and Factor IX and supplied to the BTSB for distribution in the State.

Mr Finlay said that an important element of the Tribunal's investigation would be the consideration of different viral inactivation techniques employed by commercial fractionators and the BTSB in the preparation of concentrates. The following viral inactivation techniques were listed:-

(a) Dry Heat Treatment
(b) Super Dry Heat Treatment
(c) Wet Heat Treatment
(d) Heating in a solution or pasteurisation
(e) Solvent Detergent
(f) The use of ultra violet light combined with the addition of a purifying concentrate.

Mr Finlay indicated that the issues involved in viral inactivation would necessarily require expert evidence.

The legislation under which the BTSB was established was set out for the Tribunal and it was noted that the BTSB has recently changed its name to the Irish Blood Transfusion Service however, for the purposes of this Tribunal the organisation will be known by its former name, BTSB.

The Tribunal was told that the National Haemophilia Treatment Centre was established in 1971. At the same time the National Haemophilia Treatment Centre Council was also established. This

Council was succeeded by the National Haemophilia Services Co-Ordinating Committee in 1977. The NHSCC continued to meet until the 27th January 1989. There are no records of any NHSCC Committee Meeting after that date and it is not clear why the Committee ceased to meet. Mr Finlay said it is clear from the representation on the Committee that it provided a forum and an opportunity for most of the persons who would be relevant to the treatment of persons with Haemophilia to meet and discuss their needs. An examination of the work of the NHSCC will form part of the Tribunal.

Mr Finlay told the Tribunal that the Irish Haemophilia Society was founded in or around 1967. An inaugural meeting of the Society was held on October 7th, 1968. The I.H.S. is a voluntary organisation dedicated to promoting the interests of persons with Haemophilia.

The National Drugs Advisory Board was established by an Order of the Minister for Health in 1966 under the Health (Corporate Bodies) Act, 1961. The NDAB was not a licensing authority and was replaced in 1995 by the Irish Medicines Board.

The above organisations in conjunction with the Department of Health were the principal bodies dealing with persons with Haemophilia during the relevant period, said Mr Finlay. The Department of Health had an important role to play in the fortunes of people with Haemophilia in that all significant expenditure incurred by the above public bodies required the sanction of the Department. Mr Finlay noted that it was not unusual for certain individuals to be members of more than one of the above committees or groups, for instance, Professor Temperley was a member of the Board of the BTSB from 1987 to 1999 while he was at the same time Medical Director of the National Haemophilia Treatment Centre.

Mr Finlay said that a number of bodies were likely to be referred to on a continual basis throughout the Tribunal. These were the UK Haemophilia Centre Directors, CDC, MMWR, FDA, National Haemophilia Foundation, American Association of Blood Banks, World Health Organisation and various Committees of the Council of Europe and in particular, the Committee of Experts on Blood Transfusion and Immunohaematology.

Mr Finlay said in considering the BTSB's role it would be convenient to follow a chronological order, i.e:-

1. The period prior to the 1st January 1981

2. The period from 1st January 1981 to 1st January 1987

3. The period from 1st January 1987 to 1st January 1990

Mr Finlay said in the period prior to the 1st January 1981 there was no knowledge of evidence of the virus now known as HIV or the condition now known as AIDS. He also said that while this specific condition of Hepatitis C was not generally known and referred to during this period, it was known from approximately 1975 that a form of Hepatitis Non A Non B was generally known in the medical and scientific community. By 1975 Hepatitis A and Hepatitis B had been identified and at around the same time it was known that a further form of Hepatitis neither A nor B existed.

Mr Finlay said it seems appropriate that the Tribunal should investigate the steps which were taken to deal with the risk of infection with the condition when it was known as Non A Non B Hepatitis.

A further key issue which would have to be examined in respect of the first chronological issue is whether the BTSB should have achieved a situation of self sufficiency in respect of blood products. The Tribunal defined self sufficiency as a situation in which the BTSB was supplying all the blood products required for the treatment of persons with Haemophilia in this State from blood or plasma donated in this State. The Tribunal noted that if self sufficiency had been achieved prior to January 1981 a significant amount of the infection of persons with Haemophilia with HIV which occurred in

the second period between 1981 and 1987 could have been avoided. While self sufficiency would not of itself have prevented all HIV infection, it would have led to a much lesser degree of infection among people with Haemophilia in Ireland. Mr Finlay said the Tribunal would also look at the extent to which self sufficiency would have protected or failed to protect against the infection of persons with Hepatitis Non A Non B or Hepatitis C as it subsequently became known.

The Tribunal would not come to conclusions with regards to self sufficiency up to 1981 by judging the decisions of the BTSB in light of events which occurred after that date. The Tribunal would not rely on hindsight to come to its conclusions said Mr Finlay. However, he noted that the general desirability of self sufficiency was well established. As early as 1975 the World Health Organisation urged member states to promote the development of National Blood Services based on voluntary non remunerated donations of blood.

These views were echoed by Dr O'Riordan, National Director of the BTSB when he spoke to the World Federation of Haemophilia at its Conference in July 1975. It was noted that this view point was supported by ethical considerations. These ethical considerations were based in the desire to avoid the exploitation of Third World countries, exploitation of paid donors and the desire to prevent commercial organisations becoming involved in the preparation of blood products using paid donors.

The sentiments were further echoed by the World Health Organisation in December 1977 and by the Council of Europe's Committee of Experts on Blood Transfusion and Immunohaematology in May 1978 and further in Recommendation R85 adopted by the European Council's Committee of Ministers on April 30th, 1980.

With regard to adopting a policy of self sufficiency the Tribunal noted that the achievement of such a policy was contingent upon the BTSB producing a product of at least comparable convenience and efficacy to that provided by concentrate. Up to this time the BTSB had from 1973 produced Factor IX and freeze dried cryoprecipitate from 1976. To achieve self sufficiency as defined by the Tribunal, the BTSB would be required to produce a high quality concentrate or enter an arrangement with a commercial fractionator to custom fractionate plasma from Irish donors. It was noted that in 1975 the Scottish Blood Transfusion Organisation contacted the BTSB with a proposal that it fractionate Irish plasma. The BTSB did not appear to be willing to enter into a custom fractionation arrangement at this stage. The BTSB's version of self sufficiency appears to have been to embark upon a plan to produce its own Factor VIII Concentrate, however no step had been taken to achieve this objective by January 1981.

Another matter which appears to be of relevance to the Tribunal was the relationship between treating doctors and the BTSB in the selection of concentrate and the formulation of policy on how concentrates should be used. This policy was in the first instance formulated by the NHSCC in November 1979 and adopted by it with some amendments in January 1980. This policy provided that the Director of the National Haemophilia Treatment Centre and the Regional Directors in consultation with the National Drugs Advisory Board and the BTSB would recommend to the NHSCC Factor VIII and Factor IX products to be purchased for each year. Professor Temperley was the Director of the NHTC and a Member of the NHSCC. Dr O'Riordan was Chairman of the NHSCC and National Director of the BTSB during this time.

Between January 1st 1981 and January 1st 1987 a total of 105 people with Haemophilia became infected with HIV as a result of receiving blood products in the State. Of these:-

1. 97 persons with Haemophilia A appeared to have been infected prior to 1st April 1985.

2. Seven people with Haemophilia B were found to be HIV antibody positive at various dates between July 1985 and August 1986.

3. One person with Haemophilia A appears to have been infected on a date between April 10th, 1985 and December 11th, 1986.

Of the first group, those with Haemophilia A of whom 97 were infected with HIV, 51 have since died. Of the second group, those with Haemophilia B, 5 have died. The person with Haemophilia A who became infected after the 10th April, 1985 has since died. The above deaths have been notified to the National Haemophilia Treatment Centre. From the evidence at the disposal of the Tribunal it is possible that some further persons with Haemophilia infected with HIV who are not patients of the NHTC have also died.

Of the 97 people with Haemophilia A in the first group it is likely that the majority, or perhaps all, were infected as a result of being treated with commercial concentrates provided to them for their treatment prior to the 1st January, 1985.

January 1st, 1985 is a significant date in that after this date commercial concentrates supplied in this State were heat treated, said Mr Finlay.

Another possible source of infection to the above may be freeze dried cryo provided by the BTSB. With regard to this issue, evidence given in personal testimony from two persons with Haemophilia who became infected with HIV after being treated with cryo only, is of great significance. The Tribunal is in the process of investigating this matter. The Tribunal listed the products supplied to patients for the years 1980 to 1984. These products were supplied through the BTSB. The Tribunal also noted the practice of individual doctors retaining the right to order products for patients other than through the BTSB. Given the state of the evidence available to the Tribunal, it would not be possible for it to identify which product was responsible for the infection of each individual member of the group of 97 persons with Haemophilia A. The Tribunal will look at the adequacy or otherwise of the role played by the BTSB and the adequacy or otherwise of the steps which it took to avoid or minimise the risk of the infection which occurred to these 97 people.

Another avenue of investigation for the Tribunal was the development of the state of knowledge concerning AIDS during the period from 1981 to 1985. One of the first reports of the condition which later became known as AIDS was contained in an Article in the MMWR of June 5th, 1981. Thereafter a number of articles appeared in various journals describing a disease which subsequently became known as AIDS. On the 10th December 1982 the MMWR reported four or five further cases of the AIDS in persons with Haemophilia. The journal suggested AIDS might be caused by an infectious agent transmitted sexually or through exposure to blood or blood products. In May 1983 Drs Montagnier and Gallo, separately identified a virus which appeared to be associated with the AIDS condition. The Tribunal set out a number of land marks which traced the development of AIDS during the period up to 1983. By the beginning of 1983 the suspicion that AIDS was transmissible through blood products was being converted into a likelihood, although not a certainty, and the means of transmission had not been identified. The emergence of AIDS gave a greater urgency to the need for self sufficiency.

The BTSB's Factor VIII project had reached the stage where Mr Sean Hanratty of the BTSB and Professor Temperley could draft a letter to the Lancet describing the production of an intermediate Factor VIII Concentrate based on the method of Gail Rock. The draft letter suggested that the results were excellent.

A specific issue to be examined by the Tribunal is the supply of Kryobulin by Immuno, a German/Austrian company. Immuno offered to supply Factor VIII concentrates derived from either European or US donors, European product being the more expensive of the two. Mr Finlay said it seemed reasonable for the Tribunal to enquire whether during the 1982 – 83 period the BTSB gave any consideration to trying to obtain concentrate fractionated from a source other that US remunerated plasma donors.

The Tribunal will also examine the introduction of heat treated products from January 1985. The Tribunal would look at the decision-making process which led to the introduction of heat treated products and to the continued distribution of non heat treated products after this date.

The issue of heat treatment as an effective form of viral inactivation against HIV during 1983 and 1984 was a matter for expert evidence said Mr Finlay. From the evidence at his disposal Mr Finlay thought it likely that a consensus that heat treatment was effective in eradicating the AIDS virus emerged some time between September and December 1984.

With regard to the seven people with Haemophilia B who became infected as a result of treatment with Factor IX in the 1985/86 period, Dr Emer Lawlor of the BTSB has indicated that as a matter of probability these persons were infected with HIV as a result of treatment with Factor IX produced by the BTSB. This straightforward acknowledgement by the BTSB through the evidence of Dr Lawlor has greatly assisted the work of the Tribunal said Mr Finlay.

Two batches of plasma are identified as the source of infection, batch number 90633 which was donated between the 14th March 1984 and 27th March 1984 and batch 90753. The evidence available to the Tribunal is that unheated BTSB Factor IX continued to be issued until December 1985. No formal recall of BTSB Factor IX was carried out until June 1986. During the period November 1984 until February 1986 when BTSB Factor IX was still in circulation, commercial heat-treated Factor IX concentrate was available for distribution by the BTSB.

In 1985 the BTSB's custom fractionation programme was under way and individual testing for HIV was started in October of that year. The issue of testing forms part of the subject matter of paragraph 2 of the Terms of Reference of the Tribunal. It is also directly referred to at paragraph 10. This will be considered as part of the second division of the Tribunal's investigation.

While the donor testing issue will be considered in the second division of the Tribunal, Mr Finlay noted that commercial kits for carrying out such testing were available from March 1985 and that the BTSB commenced testing donations from all donors in October 1985.

Mr Finlay said that Dr Emer Lawlor will give detailed evidence concerning the individual Haemophilia A patient who was HIV negative on a sample taken from him on the 10th April 1985 and HIV antibody positive in a test carried out in December 1986. Evidence will apparently show that this person received a number of different products including Cyro and Hemofil. This evidence will show that this person received a single treatment of Armour Factor VIII A28306 on the 21st February 1986.

Dr Lawlor will express an opinion that it is most likely that the Armour product infected this person. An issue arises as to whether or not this batch was purchased directly by the BTSB and supplied to St. James's or whether it was purchased directly by St. James's Hospital. It has been suggested to the Tribunal by the I.H.S. that at least 10 people were infected as a result of the use of Armour Factor VIII A28306, said Mr Finlay. The Tribunal has asked the Society to provide whatever evidence is the basis for this understanding on their part. The Tribunal notes that the Society has not yet done so.

It is the Tribunal's position that there is no evidence to suggest that any person with Haemophilia or other blood clotting disorder became infected with HIV after the 1st January 1987 as a result of being treated with blood or blood products in this State. However, people with Haemophilia and others continued to be infected with Hepatitis C in respect of the period after the 1st January 1987. The Tribunal will therefore focus on the risk of infection with Non A Non B Hepatitis or Hepatitis C. While the Hepatitis C Virus was not identified until 1989, there were considerable advances in the knowledge of the nature of the condition in the period after 1981 and in particular of the capacity for chronic Non A Non B infection to progress to severe liver disease. This will be a matter for expert evidence.

With respect to Hepatitis C the Tribunal will again look at the issue of viral inactivation. Under this heading it will consider:-

1. Pasteurisation.
2. Super Dry Heat Treatment.
3. Vapour Heating developed in approximately 1986.
4. Solvent Detergent.
5. Monoclonal Antibody Purification.

The BTSB's custom fractionation plans firstly with Travenol and then with Armour will be examined by the Tribunal with respect to the priority accorded to viral inactivation of concentrates for Non A Non B and for HIV.

Mr Finlay described how the BTSB came to an agreement with Armour in December 1987. In January 1988, Armour indicated it was unhappy with the agreement and had decided that it would only fractionate monoclonal products and that it did not wish to continue with its arrangement with the BTSB beyond the end of 1988.

With regard to the Board's custom fractionation arrangement with Octapharma under which Octapharma would produce Factor VIII and Factor IX for the BTSB using a viral inactivation method called solvent detergent, the Tribunal will investigate if it ought to have been possible for the BTSB to move more quickly and decisively into an arrangement with Octapharma after the initial contract had been made with that company.

The Tribunal will not investigate the introduction of generalised testing for HCV Antibodies which was introduced in October 1991. It will however inquire into the policy adopted by the BTSB in relation to surrogate testing of blood and plasma donations in order to detect donations at risk of transmission of Non A Non B Hepatitis or Hepatitis C.

The Tribunal has received information from the NHTC to the effect that since the introduction of second generation Eliza tests in June 1991, 191 persons with coagulation disorders have tested HCV Antibody (+). Of the 191 person proved positive, 44 have since died. Of this group of 44, 32 were also infected with HIV.

People with Haemophilia who received products prior to 1990 which had not been virally inactivated against the transmission of Non A Non B Hepatitis or Hepatitis C were exposed to potentially infectious products. For those receiving regular treatment over a long period of time it would be virtually impossible to identify the particular product or products responsible for the infection. For those with mild Haemophilia who received products after 1985 on a limited number of occasions, it may be possible to identify the products concerned.

Since 1985, 22 Children have been born with Haemophilia A, none of these children is infected with HCV, said Mr Finlay. During this period 4 children with Haemophilia B have been born, each of these children is infected with HCV from a batch of BTSB Factor IX fractionated from supernatent returned to the BTSB by Armour under the custom fractionation agreement.

Mr Finlay concluded his opening statement by noting that recombinant Factor VIII and Factor IX are now available for the treatment of Haemophilia in Ireland and that this product is safe against HIV or Hepatitis C. It is to be hoped that persons with Haemophilia and their families will never again be struck with the disaster of the kind into which the Tribunal in enquiring.

Following an adjournment for lunch Dr Emer Lawlor of the BTSB was called and sworn. Dr Lawlor outlined her own professional qualifications and described the structure of the BTSB and she outlined

the personnel who occupied the various posts in the BTSB during the time under investigation. Dr Lawlor described the early treatment of Haemophilia and the BTSB's early attempts to manufacture its own cryoprecipitate.

With respect to the arrival of Factor Concentrates, Mr Finlay directed Dr Lawlor's attention to a letter from Travenol to the Department of Health in 1973 where the company was looking for a license. In a written response to the Department, Dr O'Riordan of the BTSB on the 26th November 1973 raises no objection to the application by Travenol for a license for Factor Concentrates. However, a record of a telephone conversation in the Department of Health Discovery reveals a different opinion regarding Travenol's application for a license to import Hemofil.

The note said Dr O'Riordan of the BTSB was on the phone, he was worried about a license to import Hemofil which he believed to come from Hyland's US laboratory.. He said the Board was producing the essential Factors VIII and IX for Haemophilia Treatment. He admitted that there was a very odd occasion when other factors were required but the Board was able to get this from Sweden where Irish Plasma was used for the production. The Board was able to meet all requirements. Dr O'Riordan said Hyland was trying to corner the market here. The market was worth £50,000 and with Hyland's prices that might double. He also objected that their donors were not voluntary but were "skid row types" in the US and native populations in the Caribbean. He also objected to high pressure salesmanship which might result in doctors other than those attached to the National Haemophilia Centre, the Meath and Harcourt Street Hospitals undertaking treatment.

Dr Lawlor said this type of communication typified tensions between Blood Bankers who issued blood, plasma and platelets and fractionators who deal in very high purity products.

She said that while Factor IX was relatively easy to make, Factor VIII presents tremendous problems. These sentiments were reiterated to a Mr Cusack of the Dublin Voluntary Hospitals on the 31st May 1974, when Dr O'Riordan continues to protest about the continued use of Hemofil at a cost of £250,000 per annum compared to the cost of cryoprecipitate at £100,000 per annum. Dr O'Riordan also informed Mr Cusack that the BTSB proposed to produce its own Factor VIII. Therefore for a period in the 1970's Dr O'Riordan was firmly opposed to the introduction of Factor Concentrates and stated that the BTSB would go on to produce Factor VIII in the form of dried cryoprecipitate.

In the late 1970's concern existed about the question of Hepatitis. While Hepatitis B was feared it did not seem as severe among patients with Haemophilia. It was, said Dr Lawlor, accepted as a "side effect of treatment and people sort of accepted it".

While evidence of Hepatitis was readily seen in those using concentrates however, the convenience of using Concentrates outweighed the risk of contracting Hepatitis. Dr Lawlor said it was not until quite a bit later that people realised that Hepatitis was actually causing chronic problems. However, the Tribunal pointed out there was quite a bit of concern about Hepatitis at the end of the 1970s and pointed to the Council of Europe Committee of Experts' first meeting from the 8th to 11th May 1978, at which Professor Hassig of Switzerland delivered a paper. This paper pointed out that Viral Hepatitis remains the most frequent and most serious complication of blood transfusion. In the United States of America, some 30,000 clinically recorded cases were reported per year, of which about 1,500 cases were fatal. Mr Finlay referred Dr Lawlor to a report appended to a Council of Europe meeting. The report can be summarised in the following guidelines:-

1. Don't use blood products from high risk areas if sufficient alternative is available.

2. Treat Haemophilia A of minor and intermediate severity with small pool cryoprecipitates as their bleed is episodic.

3. Fibrinogen products originally from large plasma pools should no longer be used, they should be replaced by small pool preparations.

4. P.P.S.B Factor IX Concentrates should only be used for Haemophilia B Patients.

Mr Finlay pointed out that the Council of Europe paper would seem to indicate that Professor Hassig was very concerned about Hepatitis B. Dr Lawlor agreed but said that up until the mid 1980's Europe was unable to produce concentrates which were in any way comparable to what the commercial US companies were producing.

Mr Finlay then directed Dr Lawlor to a series of communications between Professor Temperley and Dr O'Riordan concerning the price charged by the BTSB for commercial factor VIII. In addition to the discussions on price, the activities of the NHSCC were also scrutinised by Mr Finlay.

Dr O'Riordan did not defend the price being charged for factor concentrates, instead he expressed the hope that freeze dried cryo would take over from concentrates as the treatment of choice of the National Haemophilia Treatment Centre. The dispute between Professor Temperley and Dr O'Riordan appears to have been resolved whereby the Blood Transfusion Services Board would continue to be the central purchasing and distributing body for commercial supplies of intermediate and high purity Factor Concentrates. A number of other recommendations were made including a direction that the BTSB be requested to produce more Factor VIII Concentrate. Mr Finlay asked Dr Lawlor did the BTSB do anything in the calendar year of 1980 to follow up on this direction. The BTSB's response to this direction was more apparent in 1982 when it undertook its own Factor VIII production using the Rock Palmer method. However this did not turn out to be a viable enterprise. With respect to the purchase of Factor Concentrates it was directed that 50 per cent of the concentrates be purchased from Baxter Hyland and 50 per cent from Immuno.

The proceedings closed with Mr Finlay referring to the Department of Health's response to the National Haemophilia Service Co-Ordinating Committee's draft Policy Document which directed the BTSB to produce more Factor VIII. The Department agreed that the recommendations were within the BTSB's

Mr John Finlay S.C., continued with the direct evidence of powers under its Establishment Order. The Department directed that in view of the general economic circumstances it should be informed of the additional resources which will be needed to undertake this work, the costs involved and how the Board would propose to meet those costs.

The Tribunal adjourned at 4:00pm.

Dr Emer Lawlor of the BTSB.

Dr Lawlor commenced the continuation of her evidence by considering the status of recommendations from the Committee of Ministers of the Council of Europe and described these as aspirational documents. Counsel for the Tribunal put it to Dr Lawlor that while these documents did not have any regulatory effect would it be correct to say that they are simply inspirational? Dr Lawlor insisted that this was the case.

Dr Lawlor did not agree that a Council of Europe Recommendation could be the foundation of a policy which once agreed by Council members was in any way binding on those who had agreed it.

Dr Lawlor was then referred to the Minutes of the NHSCC of September 1980 which dealt with the supply of concentrates by two commercial firms. The report to the NHSCC indicated that the BTSB was attempting to achieve self sufficiency by producing a more concentrated form of freeze dried cryo. Dr Lawlor said she was unable to answer any questions concerning production of a more concentrated product in and around September 1980.

Mr Finlay said that despite Dr O'Riordan's anxiety that there should be self sufficiency and his dislike of the notion of commercial concentrates taking a hold, it was a fact that Factor VIII was being used increasingly as time went on. Examining a document from the BTSB discovery Counsel for the Tribunal noted a record of cryoprecipitate issued and imported commercial concentrates supplied in various years. It was noted that in 1980 the use of commercial concentrates had increased three fold from their introduction in 1975, as the use of commercial concentrates increased the use of cryoprecipitate decreased.

In January 1981 the BTSB put together a plan which was designed to replace imported Factor VIII Concentrate with locally produced Factor VIII. The plan set out Mr Sean Hanratty stated that a large proportion of high concentrate Factor VIII could be replaced by an intermediate product made locally using well established procedures. The well established procedures to which he was referring appeared to be the Rock Palmer method of Factor VIII production in a heparin solution.

In response to a question as to whether or not this method was a well established procedure, Dr Lawlor said this matter was an issue for expert witnesses.

This evidence would seem to be directed at establishing when the BTSB decided to embark upon its own production of Factor VIII Concentrate. Preliminary planning for the production of BTSB Factor VIII Concentrate would therefore appear to have started in April 1980. At a meeting of the NHSCC of the 9th October 1981 Mr Hanratty of the BTSB presented a document on the National Production of Concentrate Product. The document sets out the cost, savings and equipment required using a new method of fractionation.

Mr Hanratty explained that Professor Temperley would be required to evaluate the new method. The Irish Haemophilia Society was to be asked to provide some of the equipment required for the Factor VIII production. Dr Lawlor agreed that this plan referred to the Gail Rock Heparin method of Factor VIII production which would result in an intermediate purity product without having to go through full scale fractionation.

In September 1982 the NHSCC considered the issue of commercial concentrate procurement by the BTSB. Mr Hanratty reported that laboratory trials for home produced Factor VIII had been satisfactorily completed. Mr Hanratty was congratulated on behalf of the Committee by Professor Temperley and it was decided that should the Department of Health fail to support the project serious consideration should be given to it as a commercial enterprise.

Dr Lawlor agreed with Mr Finlay that a Factor VIII project was still being viewed optimistically at this time.

By September 1982 a condition known as AIDS had been reported in four people in the US in June or July of that year.

While a general air of optimism appeared to surround the Factor VIII project being conducted by the BTSB, Dr Egan at a BTSB Board meeting was anxious to know of any progress being made on the issue of self sufficiency.

At a January 1983 meeting of the NHSCC it was indicated that trials for BTSB Factor VIII would be completed in three months time allowing for the introduction of home produced concentrates in about six months. In addition to the general air of optimism surrounding the project and Mr Hanratty's favourable reports, the National Director of the BTSB, Dr O'Riordan in response to a further query from Dr Egan relating to Factor VIII production said that the BTSB was currently working on the production of a purified concentrate more convenient and suitable for home therapy. A successful outcome would result in very substantial savings to the country by virtue of non importation of costly products from abroad.

Mr Finlay put it to Dr Lawlor that despite all the positive reports on the BTSB's Factor VIII production, the project had not proceeded very far by October 1982.

Dr Lawlor said "that's correct, it's a bit like alchemy, it's like turning lead into gold and it's just not going to work". The heparin idea didn't work, said Dr Lawlor, the only way you could have produced an intermediate factor concentrate was either going to process fractionation somewhere else or building a plant here which would have been uneconomic. A Fractionation Plant would cost between £20 million and £60 million.

In short Dr Lawlor's assessment of the BTSB's Factor VIII project was that it was totally unrealistic but, despite this the option of custom fractionation had not been examined by the BTSB in late 1982.

By January 1983 serious concern existed about the risk of AIDS infection in blood products.

Dr Lawlor said that while there was concern, there was still a lot of debate actually going on. Knowledge of the threat from AIDS was well established by May 1983. The Blood Transfusion Service Board at this time was contemplating its Message to Donors leaflet. An Article appeared in *The Irish Times* in May 1983 in which both Professor Temperley and Dr O'Riordan are quoted in relation to the possibility of donors being questioned about their sexual orientation in relation to giving donations of blood in order to exclude the risk of donations being given by persons who are homosexual. Dr Lawlor agreed with this proposition.

Therefore, while the situation regarding AIDS was changing throughout the period, the risk had become very apparent in everybody's mind, said Mr Finlay. Dr Lawlor agreed with this suggestion.

In this regard Mr Finlay referred Dr Lawlor to Brian O'Mahony's note of a conversation he had with Mr Hanratty in May 1983. Mr O'Mahony wrote –

"I informed him of the Committee's concern over AIDS and the use of imported American blood products which could lead to cases of AIDS in Ireland. He agreed that American blood products because of the payments system and the nature of the donor panel are of inferior quality to the BTSB products. I asked him was there any reason why we could not use Irish products exclusively?. He replied that the use of American products was first pushed by this Committee because of their suitability for home therapy. There is no problem in immediately supplying all our needs for Factor IX. They are developing a new Factor VIII product which would be an improvement on

cryoprecipitate. However, this work is proceeding slowly and he felt that any pressure we might bring would be useful in speeding things up. He sees no reason why the needs of Irish Haemophiliacs can not be met totally by BTSB products. This should decrease the risk of AIDS, Hepatitis and other blood borne diseases which may surface. He recommended that we discuss the matter with Professor Temperley and not quote him i.e. seemed to communicate our misgivings with Temperley in the first instance".

This note indicates Mr Hanratty was firmly of the view that the BTSB could produce enough product to meet the needs of people with Haemophilia. Dr Lawlor agreed with this idea. This note would also indicate that Mr Hanratty had a fully developed view of the dangers posed to people with Haemophilia with a continued use of imported US blood products. Mr Finlay's questioning of Dr Lawlor on these points appears to seek to establish:-

1. Why the BTSB embarked upon its own Factor VIII production; and

2. Why it took almost four years for the BTSB to realise the plan would not work?, and

3. That during this time the BTSB, in keeping with everybody else, came to realise the dangers posed by AIDS to people with Haemophilia.

The level of the BTSB's state of knowledge with regards to the threat of AIDS is illustrated at a Board Meeting on the 20th July 1983. During a discussion on the BTSB's leaflet "An Important Message to Donors", it was indicated by the National Director, Dr O'Riordan that there is an element of risk in continuing to use imported high purity concentrate of Factor VIII for the treatment of Haemophilia A but, the Haemophiliacs currently wish to continue with its use for home as distinct from hospital therapy.

Dr O'Riordan also noted that the BTSB's own Factor VIII project was yielding promising results and it is hoped that in the future it may be possible to enter into large scale production to cater for the entire needs of this country. Dr O'Riordan quoted the Council of Europe's Recommendation that each country should be self sufficient in support of his position.

Mr Finlay referred to a draft letter which was intended for publication in the Lancet. The letter sets out details of the BTSB's Factor VIII experiment and commenced by saying that in view of the threat now posed by AIDS the method used in the BTSB Factor VIII trials may be considered to be a further and possibly decisive argument in favour of a policy of national self sufficiency. Mr Finlay noted that the draft letter appeared to present the BTSB Factor VIII experiment as essentially a response to the emergence of the threat of AIDS, appeared to be suggesting that this method of Factor VIII production might provide a solution not only for the BTSB but for other people who are to be self sufficient in blood products. Dr Lawlor responded to this by saying that it was obvious that the Factor VIII experiment was premature and that it was likely that it just turned out not to be as good as it was hoped to be.

On July 12th, 1983 a copy of a leaflet called "A Message to Donors" was sent from Dr O'Riordan to the Secretary of the Department of Health. Appended to the letter was a press statement, part of the statement contained a reiteration of the BTSB's commitment to self sufficiency and declared that with the advent of home as distinct from hospital therapy for the treatment of Haemophilia A, Factor VIII deficiency, imported high concentrate products which can be administered at home by the patient or a family member were required. The statement said that the BTSB was on the point of making a big breakthrough with regard to the question of home production of Factor VIII. The breakthrough should make it easier to achieve complete self sufficiency.

According to Dr Lawlor the breakthrough was the anticipated transfer from pilot stage to an actual production stage processing BTSB Factor VIII. According to Dr Lawlor, there were no real resources within the BTSB at this time to realise anything like full scale production of Factor VIII.

At a Board meeting on the 20th July 1983 while discussing the contents of the "Message to Donors" leaflet Dr O'Riordan, National Director of the BTSB noted that there was an element of risk in continuing to use imported Factor VIII in the treatment of Haemophilia A. But the Haemophiliacs wished to continue with its use for home as distinct from hospital therapy.

Dr Lawlor was asked if, in her investigation into the BTSB's documentation, anything supported the contention that Haemophiliacs wished to continue with concentrate use for home therapy. Dr Lawlor said she had found no documentation which would support that view point but she expected that it would have been a generally held view at the time.

Up until the end of 1983 the BTSB continued to hold out the Factor VIII experiment as a viable proposition and as a method which would lead to self sufficiency. During this time the use of imported Factor VIII Concentrate continued to increase.

Mr Finlay's questioning of Dr Lawlor on the BTSB's plans to produce its own Factor VIII reveal that the project, which took three years to complete, was not a feasible proposition.

This is evident in the response, first of all to Dr Egan and secondly to Brian O'Mahony, who spoke to Dr O'Riordan on the 24th November 1983 seeking to know the amount of Factor VIII imported in the last year and the cost of these concentrates. He also wanted similar figures for Factor IX. The I.H.S. wanted to know if production of sufficient Factor VIII and Factor IX to satisfy the requirements of Irish Haemophiliacs was a feasible proposition. They also wanted to know the cost of realising such a proposition. Dr O'Riordan's response was to talk to Mr O'Mahony on the phone, tell him he could not give him the information and that a meeting of the NHSCC would be held sometime after Christmas at which these matters may be discussed.

At the end of 1983 up to 15 people were involved in the trial of BTSB Factor VIII. Up until this point it would appear that Dr O'Riordan continued to be completely committed to the project of producing BTSB concentrate. Dr Lawlor agreed with this proposition.

The NHSCC did not get to hear of the BTSB's plans to produce its own Factor VIII until the 13th January 1984. Dr O'Riordan wrote to the Irish Medical Times. The letter stated that the treatment of Haemophilia A Factor VIII deficiency called for the use of high concentrate product which can be administered by the patient or a family Member. There was no mention in this letter of the BTSB producing such a concentrate.

By the 18th January 1984 the Board of the BTSB heard that a gene that produces Factor VIII had been discovered and in these circumstances artificial Factor VIII would be available for therapeutic trial in three to five years. The Board also heard that custom fractionation of BTSB cryoprecipitate by a commercial company was being pursued.

BTSB's own project to manufacture Factor VIII appears to have been abandoned from this point. At the NHSCC on the 3rd February 1984 Mr Hanratty told the Committee that in the short term it would be in the best interests of everybody to develop a system to obtain sufficient plasma from the Irish donor population to produce Factor VIII.

Dr Lawlor said she agreed that it had taken a long time for the BTSB to realise that its Factor VIII project would not provide the basis for a viable Factor VIII production option. Dr Lawlor said that the delay incurred by embarking upon the Factor VIII project did not have any great practical consequences, in the sense that commercial fractionation would not have been an option at an earlier period. Dr Lawlor said that while commercial fractionators would have been perfectly happy to take Irish plasma, they may not have been prepared to fractionate it as one batch.

The different options facing the BTSB concerning the production of Factor VIII or custom fractionation were discussed at a meeting of the NHSCC attended by Brian O'Mahony. Mr Hanratty summed up the options facing the BTSB. They could either go ahead with home production or get Factor VIII produced on a contract basis using Irish plasma. The meeting concluded that there was no chance of any Factor VIII being produced from Irish sources in the year for 1984. Contracts had already been signed for the purchase of commercial concentrate for that year.

After some experimentation in fractionating cryoprecipitate by Travenol, the Board of the BTSB decided to embark upon a plasma procurement programme. At this stage the estimated cost of producing custom fractionated plasma from Irish donated plasma would be around £100,000. The cost of importing commercial concentrates at this time was around £300,000. Custom fractionation of Irish plasma was therefore an attractive financial proposition.

In May 1984 Mr Hanratty spoke to Dr O'Riordan regarding his request for a quotation for the carrying out of contract fractionation of plasma secured by the BTSB in the Republic of Ireland. Immuno offered to pay £5 per litre for Irish Plasma and provide the Factor VIII concentrate fractionated from Irish Plasma as part of a contract fractionation agreement.

Mr Finlay said that this sort of deal indicated that commercial fractionation companies had great interest in obtaining fresh supplies of plasma. Dr Lawlor agreed that this was the case. Was there any reason, asked Mr Finlay why such an arrangement could not have been entered into a year or two earlier? Dr Lawlor said that this was a matter he should discuss with a fractionation expert.

Mr Finlay noted that having apparently decided to opt for contract fractionation of Irish Plasma, the Board of the BTSB then embarked upon a tortuous to-ing and fro-ing between the Board of the BTSB and the NHSCC, the NDAB and the Department of Health and the employees of the BTSB as to how such arrangements could be put in place.

On the 28th November 1984 Dr O'Riordan wrote to Mr McCartney of the Department of Health enclosing detailed costings of the procurement of plasma on contract fractionation for Factor VIII concentrate production. Also in this letter reference to very recent events in light of which Dr O'Riordan would like to discuss arrangements for a meeting with the Department on Monday 10th December at 10:00am, reference to recent events, was a reference to a Haemophilia patient with AIDS in St James Hospital.

On the 17th December 1984 Professor Temperley wrote to Dr O'Riordan and informed him that it had been decided that only heat treated products would be used in 1985 and in this context Professor Temperley reminded Dr O'Riordan of his suggestion that those concerned with the treatment of Haemophiliacs should be involved in policy relating to new concepts introduction in the BTSB.

Mr Finlay noted having gone through the whole history of the BTSB's self sufficiency strategies at the end of 1984, that products supplied by the BTSB hadn't in fact progressed beyond the production of lyophilised cryo which was first produced in 1976. Dr Lawlor agreed that progress had not been made but, she said progress had not been made in other countries either. She said that looking back it was not really feasible to be self sufficient in anything other than freeze dried cryo for a country of our size.

When asked were there other countries of a similar size who did manage to achieve that, Dr Lawlor answered "no, there weren't". She then went on to say Finland was using cryo largely, it did have some concentrate but not a huge amount. And Belgium were using cryo all the time and in fact probably not producing really enough. But, fortunately for them they avoided getting HIV by having a freeze dried cryo programme.

Dr Lawlor said that by being self sufficient in plasma by 1984 there was no guarantee that it was actually free of HIV. Mr Finlay asked Dr Lawlor was it not the case as a matter of probability that the

level of infection would have been significantly less if there had been less exposure to commercial concentrates and more availability of an acceptable home produced product. To which Dr Lawlor responded: “absolutely, yes”.

PROCEEDINGS: THURSDAY JUNE 22nd, 2000 – DAY 14

John Finlay S.C., continued his examination in chief of Dr. Emer Lawlor of the BTSB. Mr. Finlay took Dr. Lawlor through her evidence in four areas covering the period 1981 to 1985. Examined were:-

1. BTSB State of Knowledge during this period regarding the development of AIDS

2. Viral inactivation

3. Product Selection

4. Donor Screening

5. HIV infection

1. State of Knowledge 1981 – 1985

The condition which later came to be know as AIDS was first reported in an Article in the MMWR on June 6th 1981. Dr. Lawlor said that the BTSB did not receive the MMWR in June1981 but it does now. In the summer of 1982, three haemophilia patients in the USA are noted by the CDC to have an AIDS related cancer. In July 1982 *Haemophilia News Notes Medical Bulletin* commented on the three cases reported by the CDC and asked for reports of Kaposi's Sarcoma.

Mr. Finlay noted that the article was not recommending any change in blood product use and went on to say that a panel of experts would be set up. Dr. Lawlor noted that the article stated twice that no change in the treatment regimen was suggest. Mr Finlay referred to an American Association of Blood Banks publication which had been supplied to the Tribunal as part of the BTSB discovery. The article refers to a deadly new disease which deifies analysis and reports that the Centre for Disease Control statistics show the disease known as AIDS has affected 471 men and women from 24 States and eight foreign countries, of those 184 are dead. The article describes the symptoms of the disease and notes a further four persons who are infected are persons with Haemophilia.

Mr Finlay then referred Dr Lawlor to the New England Journal of Medicine of January 1983 which deals with the information that has emerged about AIDS in persons with Haemophilia and the conclusion of the article being that Haemophiliacs are at a clear risk of AIDS. This article notes that if the use of cryoprecipitate will minimise the risk, the current home based infusion programme needs to be revised. Mr Finlay said he was not suggesting that the article in the New England Journal of Medicine portrayed consensus among those treating Haemophilia that there should be a return to cryoprecipitate. The Article did however suggest that the matter should be viewed in a very serious light and as a threat to persons with Haemophilia.

Dr Lawlor said it would not have been generally accepted among haematologists or haemophilia treators at that time that a reassessment of home treatment should be undertaken. He also noted that the New England Journal of Medicine published a number of letters in response to these points. Mr Finlay said he accepted there was no consensus but it was clear that there is now beginning a debate about treatment and also that there is a cause for serious concern.

In June 1983, Hyland Travenol wrote to Dr O'Riordan, among others, warning that a donor with AIDS had contributed to its plasma pool in the United States. The products derived from this plasma pool had not been shipped to Europe and all the products had been recalled.

2. Viral Inactivation

In addition to warning about the presence of AIDS in its plasma pools and the potential presence of AIDS in its blood products, Travenol offered a new heat-treated product, Hemofil P. While it did not offer a guarantee against the threat of AIDS, heat treatment had been shown to reduce viral contamination in blood products.

Dr. Lawlor agreed that the issue of heat treatment had been raised and that Travenol had written to Dr. O'Riordan informing him of the benefits of heat treatment with respect to Non-A Non-B. There is no record at this time of the issue of heat treatment being addressed by Dr. O'Riordan. Dr. Lawlor stated that heat treatment was not seen by anybody as providing an answer to the AIDS problem at this stage. There was also concern that by heat treating Factor VIII yield would be reduced but, more importantly, the molecule shape would be changed and encourage the development of antibodies to Factor VIII making patients extremely difficult to treat.

With regard to the viral inactivation of Factor VIII by heat treatment Mr Finlay noted a report on a Conference held in Rio de Janeiro on heat inactivation. This paper was presented by Mr Hanratty of the BTSB. Mr Finlay asked did Sean Hanratty attend the Rio Conference? Dr Lawlor was unable to confirm this.

In May 1983, Dr Montagnier in Paris isolated the AIDS virus to be followed a year later by Dr Gallo, who in May 1984 identified the virus and produced a test which can locate the virus in blood. This study was published in *Science* magazine on May 4th 1984. Mr Finlay asked Dr Lawlor if she would accept that by the Autumn of 1984 it was accepted that heat treatment of blood products would provide adequate viral inactivation with respect to HIV. Dr Lawlor agreed with this proposition.

Mr Finlay then asked was there any record at this time of Dr O'Riordan or anybody else in the BTSB following developments in relation to viral inactivation. Dr Lawlor said she hadn't found any records but was sure that it was being followed. Dr Lawlor was asked did the Scientific Committee of the BTSB follow these developments. She responded by saying she was unsure if any Scientific Committee meetings took place at this time. In any event she had found no records of viral inactivation being discussed.

3. Product Selection

Mr Finlay directed Dr Lawlor to a letter from Professor Temperley to Mr Hanratty dated 1st December 1981. Following this communication Mr Hanratty ordered Factor VIII concentrate from three sources for the following year, Immuno, Travenol and Cutter.

Dr Lawlor appears to say that once it had been decided which products to obtain and each of these products was a licensed product, there wasn't really any difference between them with respect to Hepatitis. Each product was made from a multi-donor plasma pool, viral inactivation was not an issue. Essentially the issue came down to one of price.

In considering the issue of product selection Mr Finlay directed Dr Lawlor's attention to the policy of bulk purchasing - the BTSB's purchase of products from, Armour, Cutter, Travenol and Immuno. Mr Finlay enquired whether or not the situation where AIDS infection had been reported among people with Haemophilia in the US was considered by the Treating Doctors and Dr O'Riordan and Mr Hanratty when the issue of which product to buy was discussed.

Mr Finlay said he wanted to know if those who were organising bulk purchase of factor concentrates considered the risk of AIDS when making their deliberations. Dr. Lawlor said that the whole scientific community got it wrong at that stage including regulators, fractionators, haemophilia treatment doctors and haemophilia patients or at least certainly their representative bodies. In any

event the bulk of infections were occurring at this time and nothing anyone was doing was going to make any difference to that. Dr. Lawlor said everybody was slow to react to the situation.

The answer to Mr. Finlay's question would appear to be that no consideration was given to the risk of AIDS when considering the bulk purchase of Factor Concentrates.

4. Donor Screening:

The Tribunal considered a leaflet produced by the BTSB in 1983 called "A Message to Donors" and compared this leaflet with similar leaflets issued in the United States which were in fact a precedent of the BTSB's leaflet. The BTSB's leaflet identifies at risk groups. The same at risk groups are identified in the US leaflets however, the difference between the BTSB's leaflet and those issued in the US is that BTSB no made reference to the symptoms and signs suggestive of AIDS.

Dr Lawlor said that the difference between Ireland and the US was that in the US people with AIDS were queuing up at Blood Centres to make donations. In Ireland, on the other hand, the incidence of HIV and AIDS was very low. In addition to this consideration if the symptoms associated with AIDS which were included in the US leaflets such as severe night sweats, unexplained fevers, unexpected weight loss, swollen glands or Kaposi's Sarcoma – a rare cancer, were listed in the Irish leaflet up to 10 per cent of the population would defer when it came to giving blood.

Donor screening during the period 1981 to 1985 consisted entirely of self exclusion by donors who considered themselves at risk after reading a leaflet, the shortcomings of which were:-

(a) the symptoms of AIDS were not included in the leaflet;
(b) Donors had to publicly exclude themselves from making a donation.

5. HIV Infections:

John Finlay set out the statistics supplied by the National Haemophilia Treatment Centre of those infected with HIV. Mr Finlay said 105 persons with Haemophilia became infected with HIV during the period. Of this group 98 of the 105 were persons with Haemophilia A, the remaining seven being persons with Haemophilia B.

According to Dr Lawlor one person with Haemophilia A was infected between the 10th April 1985 and the 11th December 1986. The remaining 97 persons with Haemophilia A were infected from 1980 onwards. Infections continued in 1982 and by the end 1983 virtually all of this group was infected. Dr Lawlor said this group was infected with imported American concentrates.

Dr Lawlor said that she was not aware of any individual patient who had received cryo only becoming infected with HIV.

Persons with Haemophilia B who became infected did so sometime after January 1985 according to Dr Lawlor. Seven people with haemophilia B who became infected with HIV were infected with two batches of Factor IX which were un-heat treated and which were issued between June and December 1985. This BTSB FIX was made from plasma collected in 1984.

Dr Lawlor identified the infectious batches as batch 90633 and batch 90753. Mr Finlay took Dr Lawlor through the contents of a chart which traced the destination of the infected batches.

Mr Finlay then turned to the issue of heat treatment raised in a letter from Professor Temperley dated 17th December 1984. This letter informed Dr O'Riordan, that Dr Cotter, Professor Temperley and Dr Walsh of the Department of Health had agreed to purchase only heat treated coagulation Factor VIII and Factor IX concentrates from commercial firms in 1985. The letter also asked Dr O'Riordan to urgently consider the question of heat treating all BTSB products produced for the treatment of

Haemophiliacs. Mr Finlay said it did not appear from the documents that there was any indication that Dr O'Riordan or anybody else in the BTSB had ever considered the question of heat treating product even at this stage. Dr Lawlor said that heat treated Factor IX only became available even in the US in late October/November 1984. Heat treated Factor IX was not generally available until mid-1985 said Dr Lawlor.

The question of heat treating BTSB product did not arise until around December 1984 when Ms Cunningham was in touch with Elstree. However, Mr Finlay pointed out that Ms Cunningham's contact with Elstree on the 24th December 1985 probably came about as a result of Dr Temperley's letter of the 17th December, it would therefore appear that there was no independent initiative on the heat treatment of Factor IX from the BTSB. Dr Lawlor agreed there was no such initiative.

Dr Lawlor said because Factor IX was an Irish product it was not seen as a problem. Mr Finlay then pointed out the BTSB had in fact received commercial Factor IX Konyne in February of 1985.

Dr Lawlor then said one of the difficulties with heat treated Factor IX was that there were concerns about thrombogenicity. Following Professor Temperley's December 1984 letter, commercial companies removed non-heat treated Factor VIII from stocks held by the BTSB and the treatment centres and replaced it with heat treated Factor VIII.

Dr Lawlor and Mr Finlay then attempted to decipher a handwritten note of which Cecily Cunningham is the author. The note concerns viral inactivation of Factor IX by heat treatment. It also contains a reference about the dangers of heat treating Factor IX. The note contains the words *"as worried about thrombosis as AIDS"*.

Dr O'Riordan replied to Professor Temperley on the 2nd January 1985 and advised him that the question of heat treatment of all products for the treatment of Haemophiliacs is being given urgent attention by the Board. Mr Finlay wanted to know what sort of urgent attention was being given to the issue of heat treatment. Dr Lawlor said that the big problem of heat treating Factor IX was that of thrombogenicity.

The BTSB's position would therefore appear to be that it was justified in issuing un-heat treated Factor IX during 1985/1986 as the thrombogenic effects of heat treating Factor IX were as yet undetermined. However, it would appear that the BTSB had obtained and distributed commercial heat treated Factor IX in the form of Konyne from Cutter early in 1985.

Mr Finlay asked Dr Lawlor to point to him anywhere where the matter of heat treatment had been considered by the Board of the BTSB at this time. The matter of heat treatment was discussed at a Board Meeting of the BTSB on the 16th January 1985, said Dr Lawlor. This discussion by the Board consisted of Dr O'Riordan informing the Board of the Department of Health requirements both in relation to heat treatment of Factor VIII and IX products and the necessity for the early attainment of self sufficiency in regard to such products.

Mr Finlay then referred Dr Lawlor to the debate in the medical literature concerning the merits or otherwise of heat treating Factor VIII and Factor IX.

It would now appear that the BTSB will defend its decision to issue un-heat treated Factor IX in 1985 and 1986. While there has been a straight forward admission by the BTSB that BTSB Factor IX infected seven haemophilia patients with HIV, the BTSB was nevertheless justified in issuing un-heat treated Factor IX on the basis that heat treatment gave rise to a risk of thrombogenicity.

PROCEEDINGS: FRIDAY JUNE 23rd, 2000 – DAY 15

Mr John Finlay, S.C., continued the direct evidence of Dr Emer Lawlor of the BTSB.

The proceedings commenced with the Tribunal continuing its investigation as to why the BTSB delayed in introducing heat treated factor IX in 1985/1986. The reason for the delay introducing heat treated factor IX was, according to Dr Lawlor, BTSB was awaiting developments in England, particularly with regard to the thrombogenic effect of heat treating factor IX.

Dr Lawlor maintains that heat treated factor IX was not introduced in England until October of 1985. Documents available to the Tribunal indicate that heat treated factor IX became available in the UK in August and September of 1985. By early October, issues of unheated factor IX from Elstree, BPL were discontinued. Dr Lawlor disagreed with this proposition.

Mr Finlay asked Dr Lawlor, was there any evidence to support the viewpoint that the BTSB was awaiting developments or was conducting enquiries into the thrombogenic effect of heat treated factor IX. Dr Lawlor conceded that, apart from a handwritten note by Miss Cunningham, there was no written evidence to support her position.

Mr Finlay noted there was indeed no evidence of communication between the BTSB and any other party regarding the effects of heat treated factor IX, and in particular there was no evidence of any communication between the BTSB and Prof. Temperley on this subject. This was despite Prof. Temperley's letter of December 1984, requesting that only heat-treated products be used in future. In fact, Prof. Temperley's letter of January 17, 1985 to Dr Scott of the NBAB, indicated that only heat-treated factor VIII and IX will be used in 1985, the products to be supplied by Armour and Cutter. Dr Temperley also said the BTSB would supply heat-treated cryoprecipitate during 1985. However it later transpired that cryoprecipitate could not be heat-treated.

Mr Finlay referred Dr Lawlor to three separate documents:

1) A communication between Mr Cann of the BTSB and Prof. Temperley,

2) An article by Bloom, et al, and

3) An article by John Craske.

Each of these articles was supportive of the position of heat treating factor VIII and factor IX as a viral inactivation method against HIV. The articles were all written in the early part of 1985. Mr Finlay put it to Dr Lawlor that, by May/June of 1985, the benefits of heat treated product were generally recognised, and the results of switching to heat treated product were beginning to become available. Dr Lawlor said this was true for factor VIII, but was not true for factor IX.

Dr Lawlor agreed that commercially fractionated factor IX was available in early 1985. The BTSB stocked such a product, but there is no record of any discussion taking place as to whether or not it was advisable to switch completely to commercial factor IX.

The Tribunal then moved to consider the events of August 1985. On the 13th of that month, Dr Helena Daly, Prof. Temperley's locum, met Dr O'Riordan and Mr Hanratty of the BTSB. She was concerned about the continued use of un-heat treated factor IX. Subsequent to this meeting, Dr Daly wrote to Prof. Temperley and told him what had occurred at the meeting. She reported that she told Dr O'Riordan and Mr Hanratty that it was unethical to continue using any products for haemophilia except heat treated products, and that a change over to heat treated products should happen as soon as possible. She proposed that St. James' discontinue using freeze-dried cryo and BTSB factor IX concentrate.

Mr Finlay indicated that Dr Daly would now say, she considered the use of the word "unethical" to be the wrong word in the circumstances. She did not now think this was a fair phrase to use.

Dr Daly noted in her letter that the BTSB had indicated it was not happy to cease using cryo, as it had large stocks in place. Neither was it happy to consider heat treating cryo, as to do so would waste a large proportion of the stock. If the BTSB terminated cryo production it would require yet more plasma for its custom fractionation plans. The increased plasma need would present the BTSB with unexpected production and financial difficulties. Dr Daly also said that the BTSB would have to heat treat its factor IX. As a result of Dr Daly's letter, and a subsequent meeting with Dr Daly in London, Prof. Temperley wrote to Dr O'Riordan.

Prof. Temperley's letter to Dr O'Riordan said: "I thought I had made it plain we would require all therapy to be heat treated. Commercial companies were advised to do so forthwith, and Pelican House was to be given time to cope with the technical problems. In the end, all product given to haemophiliacs would require heat treatment." The letter pointed out that, by November 1st, when Prof. Temperley returned from sabbatical, the BTSB would have had eleven months to sort out the problem. This would imply that Prof. Temperley was of the impression that he had issued an instruction in December of 1984 that all products should be heat treated.

Following Prof. Temperley's letter, the BTSB commenced heat treating factor IX. This was in or around August 20th 1985. Mr Finlay noted that heat treatment commenced without any questions of safety or thrombogenicity being raised.

The BTSB commenced heat treating in August 1985. Product heat treated in August 1985 was issued in October 1985. The first batch was heated to 68^0 centigrade for 72 hours. Miss Cunningham, who had undertaken the heat treatment, noted that the next four batches would be heat treated at 60^0 Centigrade for 20 hours. Unrecorded published sources are cited as the authority for the heat treatment protocol selected. Miss Cunningham's handwritten note finished by seeking permission to issue the heat treated product.

From October to the end of December of 1985, the BTSB continued to issue un-heat treated factor IX and heat treated factor IX. According to Dr Lawlor, it was about half and half. Half of the factor IX issued was heat treated, and half of the factor IX issued was un-heat treated. Dr Lawlor agreed that the BTSB was in a position to issue only heat treated factor IX from October of 1985. She said it was a cause of concern that non-heat treated factor IX continued to be issued during this period.

On 15th October 1985 the BTSB commenced testing donors for HIV. On 25th October 1985 the first HIV positive donor was recorded. Mr Finlay made the point, from this date, the Irish blood supply could not be regarded as safe with respect to HIV. Dr Lawlor agreed with this point of view. Nevertheless, the BTSB continued to issue un-heat treated factor IX for the remainder of the year. It also failed to recall un-heat treated factor IX it had issued until June 1986.

The discovery of a HIV positive donor shortly after the introduction of HTLV-III testing, gave an urgency to the issue of recalling all blood and blood products which were derived from the blood of untested donors. A decision to recall blood and blood products would have significant financial implications for the BTSB. Dr Barry, Chief Medical Consultant, so informed Mr Flanagan of the Department of Health, in a letter of 22nd January 1986. Mr Flanagan responded by saying it was imperative that all blood products issued to hospitals prior to the introduction of HTLV-III antibody testing, and still held in stock by them, should now be withdrawn. He directed that immediate steps be taken to effect withdrawal, and said that the financial implications of this action should be taken into account by the BTSB, in determining its 1986 overall budget.

A notice subsequently issued to hospitals did not, in fact, recall BTSB factor IX. Dr Lawlor agreed there was no formal recall of these products, and said an informal recall took place. Drogheda,

Galway and St. James' returned some BTSB factor IX. No returns were made from Cork. A Haemophilia B patient being treated from St. James' continued to use the BTSB factor IX into February of 1986. Asked whether this situation could have been avoided by a more timely and formal recall, Dr Lawlor responded by saying that, in 1986, the recall went to the hospitals and it would have been up to the hospitals to recall further from home, she said.

The Tribunal referred to a letter received by Dr Lawlor from Mr Snape of the BPL. This letter says October 2nd 1985 is the date upon which heat treated factor IX was issued in the United Kingdom. He gathered that some un-heated product was also in use after this date in the UK. While there was no record within the BTSB of any discussions taking place regarding heat treatment of factor IX and thrombogenic effects, Dr Lawlor said she was nevertheless sure it was discussed, but she agreed that there were no formal records.

Mr Finlay referred Dr Lawlor to the policy in Scotland in relation to heat treated factor IX. In the course of her preparation for the Tribunal, Dr Lawlor prepared a chart indicating dates when heat treated factor IX was introduced by various countries. The chart indicates that the Scottish Blood Transfusion Service suspended the issue of its own factor IX in February of 1985. During the period of suspension of its own factor IX the Scots investigated the thrombogenic effect of heat treating the product. In October 1985, they had overcome the difficulties and went back into production of heat treated factor IX. Mr Finlay asked, was this option not open to the BTSB? Dr Lawlor agreed that this option was in fact open to the BTSB.

Mr Finlay then turned to the circumstances of the infection with HIV of a person with haemophilia A in 1986. Dr Lawlor said she thought this person was a patient at Harcourt Street, National Children's Hospital. He was treated with cryo, Hemofil made from Irish plasma, Hemofil made from non-Irish plasma, an unknown product and Armour batch A28306.

Dr Lawlor says she thinks the infection was likely to be caused by the Armour batch on the 21st February 1986. The only other possibility she could think of, was that a unit of cryo had been infectious, but that was much less likely, she said. Dr Lawlor said the Armour product was heat treated at 60^0 Centigrade for 30 hours and was made from the plasma of untested donors. It had been associated with something like 12 cases of late seroconversion. These seroconversions took place in Birmingham, the Netherlands, the U.S. and Canada. Dr Lawlor said that Armour A28306 did not have the same batch number as the product which infected boys in Birmingham, but it was made from the same untested plasma, and it was the same type of product. Dr Lawlor said the BTSB did not stock Armour product after December 1985.

Dr Lawlor said the BTSB received a total of 450 vials of Armour product in November and December of 1985. It was then decided that the hospitals would order their own product and 350 vials were sent back to Armour. Dr Lawlor said it appears as if the returned product was re-issued to the hospital from Armour.