IRISH HAEMOPHILIA SOCIETY

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CONTENTS:

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TRIBUNAL OF INQUIRY

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

PROCEEDINGS: TUESDAY 24th OCTOBER, 2000 – DAY 60

Mr Martin Hayden continued his cross-examination of Mr John Cann, former chief technical officer of the BTSB.

Mr Hayden referred Mr Cann to a letter of the 9th May 1983 from Mr Barrell of Travenol to Dr O'Riordan. The letter, concerning Hemofil T, informed Dr O'Riordan that the company believed heat treated product, designed to reduce active viral content, may increase patient and centre personnel safety. Mr Cann said that he had also seen this letter. Mr Cann agreed that in general, it was known from May 1983 that heat treatment would increase product safety.

Mr Hayden then referred Mr Cann to the scientific meeting of June 9th 1983. Mr Hayden directed Mr Cann's attention to his own note relating to the use of cryoprecipitate. Mr Cann's note of the meeting records that more cryo should be used pending the introduction of intermediate concentrate. Mr Hayden asked Mr Cann, was the scientific meeting a forum at which BTSB experts discussed technical and medical matters with a view to directing the board on these issues. MrCann agreed with this description and said that it would be unlikely that the board would second guess the scientific meeting's recommendations, should such recommendations issue from the scientific meeting.

A handwritten note of the meeting records a discussion on T4/T8 ratios. Mr Cann agreed that T4/T8 ratios were a measurement of immune dysfunction. Mr Cann said he had a very limited understanding of what T4/T8 measurement was recording. Mr Cann said he did not know whether T4/T8 referred to an earlier discussion on hepatitis or on any discussion on HIV, but he agreed that in general terms T4/T8 measured immune dysfunction.

Mr Cann said he did not recollect any discussion on Council of Europe recommendations at the June 9th meeting. With respect to why he noted that the BTSB should use more cryo pending the introduction of intermediate concentrate, Mr Hayden asked Mr Cann would it be the case, given the information at the BTSB's disposal arising from Mr Barrell's letter of 9th May 1983 concerning the heat treatment of factor concentrate, that the BTSB was discussing the issue with a view to viral inactivation and safety?

Mr Hayden then referred Mr Cann to a letter to Dr O'Riordan of 17th June 1983, which informed Dr O'Riordan that the FDA had approved newly developed heat treatment to reduce infectious agents in blood products required by haemophilia sufferers. Mr Hayden put to Mr Cann the sequence of events from the Council of Europe

recommendations, information from the CDC, information from Travenol all of which were at the disposal of Mr Cann as chief technical officer, and in this context was the BTSB scientific meeting of June 1983 discussing the issues surrounding heat treatment and HIV and advocating that cryo should be used pending the clarification or resolution of potential health risks? Mr Cann said it was always the BTSB's view that cryo should be used where it was acceptable to the clinician. Mr Cann agreed that if the treaters had been happy to accept cryo, the BTSB would have supplied it.

In this context, asked Mr Hayden, did the BTSB pass on their concerns to the treaters, concerns which had been raised by the letter from Travenol, information from the CDC, and Council of Europe recommendations concerning HIV and heat treatment. Mr Cann said to his knowledge such information was not passed on to the treaters. Mr Cann said he had no direct knowledge that information was passed on, but he believed that it was done.

Mr Hayden referred Mr Cann to a scientific meeting of October 13th 1983, with regard to a discussion on hepatitis B surface antigen. Mr Cann said the discussion took place in the context of hepatitis B becoming more prevalent in haemophiliacs. On the question of why hepatitis B coming through in their patients was causing concern to haemophiliac treaters, Mr Hayden asked Mr Cann was hepatitis B at this stage being used as a surrogate marker for HIV? Mr Cann said there had been talk about it coming from the States, possibly because of the association with the donor environment rather than the association with the disease itself.

Mr Hayden referred Mr Cann to the evidence of Prof. Temperley. Prof. Temperley had stated that Mr Cann had attended a meeting of the Federated Dublin Voluntary Hospitals on 14th February 1985, at which he said Irish unheat-treated factor VIII concentrate was safer than U.S. heat-treated factor VIII concentrate in terms of HIV. Mr Cann said he was quite definitely not in accord with this recollection of events. Mr Cann said he could not possibly see how he could have been connected with this meeting.

Mr Hayden also referred Mr Cann to discrepancies in the records of plasma despatched to Kabi and the amount of plasma acknowledged to have been received by Kabi in the years 1982 and 1983.

Mr Hayden referred Mr Cann to the issue of the BTSB stock of unheat treated factor IX in the latter half of 1985, and the issue of whether or not the stock had been subjected to a run-down. Mr Cann said he had no recollection of a stock run-down. He could not be specific about what was said at the time. Mr Cann said he did not recollect being given instructions to run down the stock

Mr Cann was then examined by Mr Butler S.C. for Prof. Temperley. Mr Cann said he was not aware of any pressure from the treaters with respect to the issue of heat treatment. He had no knowledge of this issue other than the record of what he had read in the files prepared for the Tribunal. Mr Cann said he did not know Dr Daly had had a meeting with Dr O'Riordan and Mr Hanratty on 13th August 1985. Mr Cann said his

recollection of the events was based on the minutes he had read with respect to the decision to heat treat factor IX. He had no recollection of the type of heat treatment decided.

With respect to the issue of thrombogenicity and the visit by Dr Lane and Mr Pettit of BPL, Mr Cann said the issue of thrombogenicity had been considered for a long time prior to this meeting.

Mr Cann was then examined by Mr Meenan for Dr Egan, Dr Walsh and Dr Power. Mr Meenan asked Mr Cann how long it would have taken the BTSB to produce tested donations following the introduction of HIV testing in 1985. Mr Cann said that factor IX from tested donations should have been available one month after the introduction of testing in 1985. Such factor IX would have been prepared from Pelican House cryoprecipitate. Factor IX prepared from concentrate may have taken longer to produce. Mr Cann said that the purported withdrawal of products conducted by Dr Walsh on 22nd January 1986 was designed to withdraw non-heat treated and non-tested product. It did not refer only to non-tested product, said Mr Cann.

The letter issued by Dr Walsh on 27th June 1986 was the recall notice for factor IX, according to Dr Walsh, not the January notice.

Mr Cann was also examined by Mr Brennan for the Department of Health.

PROCEEDINGS: WEDNESDAY 25th OCTOBER, 2000 – DAY 61

Mr Gerry Durcan S.C. for the Tribunal examined Mrs. Cecily Cunningham, formerly head of the BTSB fractionation unit.

Mrs. Cunningham told Mr Durcan that she started her career with the BTSB in 1968 with the fractionation unit. She attended scientific committee meetings and was answerable to Mr Cann, the chief technical officer. Mrs. Cunningham said she reported to Mr Cann on a daily basis. She also reported to his deputy, Mr Sean Hanratty, who specialised in coagulation factors. Mrs. Cunningham said she worked in unison with both Mr Hanratty and Mr Cann in those days.

In 1981 when the BTSB moved to Mespil Road, Mr Hanratty became much more involved in the work of the fractionation unit because factor IX became a much larger proportion of the work, said Mrs. Cunningham. Mrs. Cunningham was appointed principle biochemist and was paid on the biochemist scale, however she did not enjoy extensive powers. Mrs. Cunningham said she got her directions from the scientific meeting and she would discuss her work with Mr Cann on a daily basis. She said she was not independent, although would have been involved in the ordering of equipment, dealing with staff and personnel issues and overseeing the work of the fractionation department.

Mrs. Cunningham said her early days in the BTSB were happy times for her. Later, said Mrs. Cunningham, her conditions in the BTSB deteriorated and she experienced a very hard time there.

Mrs. Cunningham said her main involvement with concentrate was the manufacture of factor IX. She was also involved in the production of Anti-D for the BTSB. Mrs. Cunningham said, while she tried to keep abreast of developments in her area of expertise, she was generally not permitted to travel abroad to attend conferences. Mrs. Cunningham said she did travel to Edinburgh in her own time to examine their factor IX fractionation method.

Mrs. Cunningham said in October 1983 she attended the I.H.S. AGM but was later advised by Mr Hanratty not to become emotionally involved with the plight of people with haemophilia.

In October 1983 Mrs. Cunningham said she travelled to Oxford to see at first hand their plasma fractionation laboratory. Mrs. Cunningham indicated she came away from this visit with a firm view that thrombogenicity posed a danger to those using heat treated factor IX. Mrs. Cunningham said she had no medical training or clinical experience and was not involved in policy making decisions. She may have had an input into making policy decisions and contributed to the debate, but she did not make these decisions.

With respect to the BTSB's own factor VIII production, Mrs. Cunningham said Sean Hanratty derived this method from that published by Gail Rock. Mr Hanratty took this on as a research project. Mrs. Cunningham said she was not involved in the project other than to make up some buffer solutions. This was her only involvement. The project was discussed at the scientific committee meeting but not in any great detail, and Mr Hanratty was left to carry on with this work. Mrs. Cunningham said she knew very little about the BTSB's own factor VIII production plans, but she did know that Prof. Temperley didn't want heparin in the finished product.

Mr Durcan directed Mrs. Cunningham to a note of the June scientific meeting in 1983. The note says "use more cryo pending intermediate concentrate". Mrs. Cunningham said it was always Dr O'Riordan's opinion that cryo should be used. Mrs. Cunningham said it was known that cryo was more awkward to use, but it was made from the plasma of one donor. The attraction of this situation was if one donor was infected with AIDS, it meant that the person receiving the plasma would be at risk from infection, whereas with concentrate thousands of donors would contribute to one plasma pool, resulting in hundreds of infections if one donor was HIV positive. It was therefore a good idea to use cryo.

Mr Durcan asked Mrs. Cunningham wasit the case in mid-1983 that the BTSB was concerned about AIDS? Mrs. Cunningham said the scientific meeting kept in touch with international developments, and Dr O'Riordan would report from the Council of Europe.

Mrs. Cunningham described for the Tribunal the manufacture of factor IX. Mr Durcan then referred Mrs. Cunningham to her visit to Oxford on 28th October 1983. In her note of this visit Mrs. Cunningham records an AIDS risk, and also notes that the incidence of hepatitis was up to 100 per cent in people with haemophilia. The short and long term effects of hepatitis were discussed, however Mrs. Cunningham said she thought at this time NANB was very mild and she didn't know about any long term complications which may arise.

With respect to factor IX and the risk of thrombogenicity, Mrs. Cunningham said it was believed at this time that the factor IX was safer with respect to AIDS. The heat treatment of factor IX, said Mrs. Cunningham, may affect the cascade of coagulation factors, in that they may be activated in sequence. The risk of activating proteins in factor IX was always a concern, said Mrs. Cunningham. The issue was discussed in great detail and Mrs. Cunningham agreed with Mr Durcan that her note contained a verbatim account of this discussion.

Commercial heat-treated products, said Mrs. Cunningham, became available after December 1984. At this time experimental heat treatment of factor IX was also taking place. Mrs. Cunningham recorded the experiments in the fractionation department workbook. The purpose of the experiment, said Mrs. Cunningham, was to see how BTSB factor IX would withstand heat treatment. Mrs. Cunningham said this experiment was carried out because she realised heat treatment may be helpful. Mrs. Cunningham said she could not recollect who may have instructed her to heat treat factor IX, but this was

just a sample. The scientific meeting may have discussed it, said Mrs. Cunningham, in December 1984.

Mrs. Cunningham said the results of the experimental heat treatment of factor IX were considered to be unsatisfactory. There was a loss of yield but more importantly, the danger of the negative or destroyed part of the product inducing inhibitors was considered dangerous. This was discussed at the scientific meeting.

Following the experimental heat treatment in December 1984 Mrs. Cunningham noted in a telephone memo with Dr Smith that it was very dangerous to heat treat factor IX. Mrs Cunningham observed that the danger of thrombosis was considered to be more pressing than the danger of AIDS at this time. Mrs. Cunningham said that telephone contact with Dr Smith and other parties was on-going during January 1985. These enquiries were of an informal nature but were reported back to the scientific committee. During this time Mrs. Cunningham noted that Mr Hanratty was anxious to heat treat his factor VIII product.

Mrs. Cunningham said that in the spring of 1985 the heat treatment of factor IX and the risk of thrombosis therefrom was of greater concern than AIDS. Mrs. Cunningham said the BTSB had heat treated factor IX since 1972 and they had had no reactions. It was also reckoned that the manufacturing process was eliminating different viruses. Mrs. Cunningham said that this was considered to be the case despite the fact that she had earlier noted that all people with haemophilia would get hepatitis. Mr Durcan asked Mrs. Cunningham was there a belief at this time that the manufacturing process would reduce the risk of AIDS. Mrs. Cunningham agreed that this was the case. Mrs. Cunningham could not recall if this had been discussed at a scientific meeting. Mrs. Cunningham said there was a balance of risk with regard to heat treating factor IX, the balance being between the dangers of thrombogenicity and the belief that by the heat treating process viral inactivation would take place.

Mr Durcan referred Mrs. Cunningham to a work sheet of BTSB batch 90753 heated 16 hours at 68-70 degrees. Mrs. Cunningham said batch 90753 heat-treated was an experiment carried out on approximately 10 vials of factor IX. Mrs. Cunningham said that other than loss of factor IX it was difficult to say how heat treatment affected the experimental batch of 90753.

Mr Durcan asked Mrs. Cunningham was there any thrombogenic significance in her results. Mrs. Cunningham said at this stage both the UK and Scotland still thought thrombogenicity was a problem. Mr Durcan asked her was this known to her by her own personal contact or did she read this in the literature? Mrs. Cunningham said that Dr O'Riordan and Mr Hanratty were in contact with their counterparts in the United Kingdom. Mrs. Cunningham said at this stage in 1984 and 1985 scientific meetings were held on an irregular basis.

Mr Durcan asked Mrs. Cunningham who did she contact other than Dr Smith. Mrs. Cunningham said there were no notes other than her note of the telephone memo

conversation. She thought that Mr Hanratty and Dr O'Riordan were in contact with colleagues abroad. This was verbal contact only. With respect to the memo of her conversation with Dr Smith, Mrs. Cunningham said she was asked to make this call and that is why the outcome was recorded.

Mr Durcan asked Mrs. Cunningham was there any sense of urgency on the issue of heat treatment. Mrs. Cunningham said heat treatment would only be conducted if possible. Mrs. Cunningham said she was unaware of Prof. Temperley's communication to the BTSB concerning the first AIDS patient in Ireland on 18th December 1984. Mrs. Cunningham said she realised it looked like she was aware of this particular correspondence but she was not aware of it. She was acting independently and did not know Prof. Temperley had written.

Mr Durcan drew Mrs. Cunningham's attention to her letter of 24th December 1984 to Dr Snape, where she says we are all very anxious about AIDS and wish to heat treat our product as soon as possible. Mr Durcan noted Mrs. Cunningham's careful note of the conversations she had had with Dr Smith. However, no further notes of any conversation with BPL or Scotland appear.

Mr Durcan drew Mrs. Cunningham's attention to records of heat treating experiments taking place in July 1985. He asked Mrs. Cunningham did the BTSB change its view as to what should happen regarding the heat treatment of factor IX in the summer of 1985. Mrs. Cunningham said that this occurred sometime in August.

Mr Durcan pointed Mrs. Cunningham to Mr Cann's note that a decision to heat treat factor IX was taken on 14th August 1985. Mrs. Cunningham said she was merely told the decision was made, and to go ahead and heat treat the factor IX.. She said she was surprised at the ease with which this was done. Mrs. Cunningham said Mr Hanratty instructed her to heat treat factor IX. His instructions were not in writing; they were oral instructions. Mr Hanratty's instructions were to heat treat a batch of factor IX and she did so on the next available batch.

Mrs. Cunningham said that an incubator was made available to heat treat the factor IX. No discussion took place prior to the arrival of the incubator, said Mrs. Cunningham.

The first batch of heat-treated BTSB factor IX was heat treated at 68 degrees for 72 hours. Thereafter the instructions issued from Mr Hanratty that the heat treatment was to be effected at 60 degrees for 20 hours. Mrs. Cunningham said some batches remained unheat treated and remained available to allow a "clinical trial" of the heat treated batches to take place. Mrs. Cunningham said this was a form of clinical trial but a very limited one. Mrs. Cunningham said the clinical trial consisted of comparing the reaction of those treated with heat treated to those being treated with unheat treated product. The rises of factor IX would be compared and reactions would be observed.

Mrs. Cunningham said unheat treated product was retained in stock at St. James' Hospital. Both heat treated and unheat treated product continued to be used. The clinical

trial of BTSB heat treated product was conducted at St. James' Hospital. Other hospitals were supplied with BTSB factor IX unheat treated.

Mr Durcan put it to Mrs. Cunningham that the question of product in hospitals was thus addressed at this time. Mrs. Cunningham agreed this was the case. Mrs. Cunningham said the trial began in October 1985, and the arrangement continued for around three months thereafter. Mrs. Cunningham said the medical directorate at the BTSB took this decision. Mr Hanratty must have told Mrs. Cunningham that this decision was made by the medical directorate and she implemented the decision. Mrs. Cunningham said it was intended to leave unheat treated and heat treated product in St. James' Hospital to be used. In respect of Mr Hanratty's instructions, Mrs. Cunningham wrote a note to Dr O'Riordan asking his permission to issue the heat treated product.

Mr Durcan asked Mrs. Cunningham why did she write to Dr O'Riordan concerning Mr Hanratty's instructions. Mrs. Cunningham said she was concerned that Dr O'Riordan did not know the actual detail of what was proposed, and that there was no scientific meeting at this time. She wrote to Dr O'Riordan. She did not discuss this issue with Dr O'Riordan and upon his approving the instructions she proceeded to implement the decision to heat treat the factor IX.

Mr Durcan referred Mrs. Cunningham to the *British Medical Journal* of 22nd June 1985, wherein Prof. Bloom writes that the use of cryoprecipitate and non-heat treated products was no longer justified. Mrs. Cunningham said she asked why a decision had now been made to heat treat the factor IX, but she got no response. Towards the end of 1985 all BTSB plasma was being despatched to Travenol in respect of contract fractionation. Mrs. Cunningham said there would be an occasional batch of cryo supernatent available, but by and large the production of cryo had ceased at this stage. Mrs. Cunningham said stock batches of factor IX in the BTSB had been drawn from non-tested donors. Tested plasma was now going to Travenol. The amount of plasma available from tested donors was limited, said Mrs. Cunningham.

Mrs. Cunningham said in November 1985 she was testing batches with respect to non-HTLV-III. Mrs. Cunningham said the intention of testing a batch from each run was to test for HTLV-III antibody. However, a lot of plasma was from non-tested donors.

Mr Durcan asked Mrs. Cunningham was she aware that as of 1st January 1985, instruction had issued from Prof. Temperley that only heat treated product should be used? Mrs. Cunningham said she was not sure of the exact date, but as from January 1986 all BTSB factor IX was to be heat treated. At this stage the clinical trial was at an end and the product was deemed satisfactory. No report is available on the outcome of the clinical trial.

In January 1986, said Mrs. Cunningham, she was not aware of any step to recall non-heat treated product prior to the order that only heat treated product should be used in January 1986. During this period unheat treated product continued to be used. In January 1986 Mrs. Cunningham said she recalled some 30 units from a batch issued to Drogheda. The

30 unit consignment was restored to its original batch and the whole batch was heat treated. Mrs. Cunningham said no other recall of unheat treated factor IX from hospitals took place at this time, ie. January 1986.

With respect to batch 90753, Mrs. Cunningham said she got a phone call from Galway regarding the testing of batches. When she went to Dr Walsh and Mr Hanratty they had a report sheet concerning 90753 at their disposal.

Mrs. Cunningham said she tested 90753 for HIV by conducting a batch test. Mrs. Cunningham said she was aware of the letter of April 22nd 1986 from Prof. Temperley to Dr Walsh, which informed Dr Walsh that persons with haemophilia B were seroconverting to HTLV-III. These persons had been treated with commercial factor IX and with BTSB factor IX, and had been treated with the products after the date when heat treatment was due to have been applied to all products. Mrs. Cunningham said this letter was brought to her attention by Mr Cann. He asked her to provide a record of BTSB stocks, which she did. Mrs. Cunningham said she thought an investigation was taking place.

In June of 1986 Mrs. Cunningham said she read a report in a newspaper concerning a seminar at which Prof. Temperley indicated that seroconversion of factor IX's had taken place, and may have been caused by products made by native plasma. With respect to a letter from Dr Walsh on June 27th 1986, concerning an investigation of the BTSB product, Mrs. Cunningham said she did not link this letter with the newspaper report. Mrs. Cunningham said nobody in the BTSB told her that a BTSB product had caused HIV seroconversation in 1985 and 1986. Mrs. Cunningham said she did not know this until last year, ie. 1999.

With respect to the meeting of 1st July 1986 at which Mrs. Cunningham attended concerning heat treatment of BTSB factor IX, Mrs. Cunningham said the reason she was there was that she had been to Travenol and had seen how they contract fractionated the factor IX. The meeting was called to consider a change in the heat treatment protocol for factor IX. Mrs. Cunningham said that if a new international standard was adopted for factor IX, the BTSB would introduce the standard. Mrs. Cunningham said that Mr Keating put the matter strongly.

With respect to product recall Mrs. Cunningham said she did not deal with recalls. Mr Durcan referred Mrs. Cunningham to a note of a visit by Dr Hoppe. Mrs Cunningham is the author of the note. With respect to an observation that the use of cryo was declining and the increase in risk of AIDS, it was observed that the BTSB should "push cryo for a while" and that Dr Daly's decision should be rescinded. Mrs. Cunningham said she did not know who Dr Daly was at this stage, nor did she know of any decision that might be rescinded pertaining to Dr Daly. Mrs. Cunningham said while she was the author of the note, she could not remember the content of the meeting. However, it was likely that the whole system of blood banking was discussed, including the testing of Anti-D donors.

PROCEEDINGS: THURSDAY 26th OCTOBER, 2000 – DAY 62

Mr Durcan, continuing his cross-examination, referred Mrs. Cunningham to her visit to Travenol and the material that was returned by Travenol for fractionation by the BTSB into factor IX. Mrs. Cunningham said that this material was unsatisfactory as it clotted. Likewise, factor IX concentrate from cryo by Armour was also unsatisfactory.

Mr Durcan referred Mrs. Cunningham to batch 9885, BTSB factor IX derived from material initially prepared by Armour arising from the Armour contract in 1987. The BTSB carried out the heat treatment on this factor IX. Mr Durcan asked Mrs. Cunningham was any discussion entered into concerning hepatitis C. Mrs. Cunningham said there was no discussion on this matter. There were no scientific meetings at this stage that she could remember, so hepatitis C was not discussed. Mr Durcan asked Mrs. Cunningham was she now aware that hepatitis C was caused by those batches.

Mrs. Cunningham was then cross-examined by Mr Jim McCullough on behalf of the Irish Haemophilia Society. Mr McCullough asked Mrs Cunningham was there any outside consultation available to BTSB scientific meeting. Mrs. Cunningham said she could not remember such representation at the scientific meetings.

Mr McCullough referred Mrs. Cunningham to the BTSB's scientific meeting of June 1983. Mrs. Cunningham said the meeting was discussing the question of a leaflet entitled "*An important message to donors*" in the context of producing a leaflet for all donors to read before they donated blood. The leaflet talked about AIDS and at-risk groups, and the necessity for such groups to exclude themselves from blood donation.

With respect to a note recording the issue of surrogate testing, Mrs. Cunningham said the surrogate testing may relate to ALT testing with respect to hepatitis. In that an ALT test, while not testing for the virus, gives an indication that a person might have a viral infection or a liver infection of some kind.

With respect to a note of T4/T8 ratios, Mrs. Cunningham said there was a lot of discussion on this subject. Mrs. Cunningham said the reference to T4/T8 was a discussion on the immune system which becomes disturbed when a person has AIDS. Mrs. Cunningham said from her own memory the discussion related to AIDS because there was quite a bit of discussion at that time about these ratios.

Mr McCullough then directed Mrs. Cunningham to Mr Cann's note of the same meeting. Mr Cann notes that the factor IX and factor VIII are under discussion, and he writes "use more cryo pending intermediate concentrate". Mrs. Cunningham said, from her note and Mr Cann's note of the meeting, it would appear that the issue of AIDS and haemophilia were under discussion.

With respect to the scientific meeting of October 1983, Mr McCullough asked Mrs. Cunningham why was Hepatitis C of particular interest at that meeting? Mrs. Cunningham said she remembered that if a person had hepatitis B they might have AIDS as well and might be multi-infected. Mrs. Cunningham agreed that this was a connection between the meeting of October 13th and the previous meeting in June, when the scientific meeting was discussing AIDS. Mrs. Cunningham agreed that the discussion of AIDS and haemophilia and hepatitis B might explain Prof. Temperley's presence at the meeting.

With respect to Mrs. Cunningham's experimental heat treating of factor IX, Mr McCullough asked Mrs. Cunningham what her experiments were designed to determine. Mrs. Cunningham said the experiments would measure the loss of factor IX. She said these experiments were not conducted with respect to yield, but with respect to safety. Mrs. Cunningham said the factor IX destroyed by heat treatment could give rise to an antibody, rendering the recipient immune to treatment. Mrs. Cunningham agreed that her experiments simply indicated the loss of factor IX. Mrs Cunningham said the BTSB was not too happy about this great loss.

Mr McCullough then referred Mrs. Cunningham to her note to Dr O'Riordan concerning the heat treatment of BTSB factor IX. Firstly, at 68 degrees by 72 hours, and then by 60 degrees for 20 hours which, according to published sources, is sufficient. Mr McCullough asked Mrs. Cunningham which public sources she was referring to? Mrs. Cunningham said Dr Smith, an expert witness, had referred her to published sources but these published sources were not available to her at the time she heat treated the factor IX. Mrs. Cunningham said that the published sources to which she was referring, were those referred to by Mr Hanratty who issued her with verbal instructions concerning the heat treatment of BTSB factor IX.

Mr McCullough took Mrs Cunningham through the various heat treating protocols adopted by the BTSB. The final heat treating protocol on this document written in 1989 recorded that in February 1988 to the present day, ie. sometime in 1989, the heat treating protocol used by the BTSB was 60.6 degrees for 152 hours. This was the heat treating protocol applied to factor IX produced by the BTSB from Armour material.

Mrs Cunningham said this heat treating protocol came from Travenol via Mr Hanratty. Mrs. Cunninghamn said Travenol allowed Mr Hanratty to apply its heat treating protocol to the BTSB' product which was being made from material supplied by Armour. Mrs Cunningham applied this protocol to the Armour freeze-dried product. Mrs. Cunningham said she had sight of a written instruction from Travenol containing this protocol. Mrs. Cunningham said Mr Hanratty gave her a document where the protocol was written down. Mrs. Cunningham said she did not know if this was a Travenol document, but it was a document received by Mr Hanratty and it was addressed to him, and he gave it to Mrs. Cunningham. Mrs. Cunningham said she believed the document came from Travenol in the United States.

Mrs. Cunningham said she had not seen a copy of this document in the Discovery, but she had seen a copy of it at the time and had the original in her possession for a while. Mrs. Cunningham said this was a particularly sensitive document and she could remember the word "confidential" was written all over it. She said she did not know whether she returned the document to Mr Hanratty or kept it herself.

Mr McCullough referred Mrs. Cunningham to a inter-departmental memo from her in January 1988 where she requested full details of the patented method agreed to heat treat BTSB factor IX coming from Armour. Mrs. Cunningham agreed that the Travenol document she received from Mr Hanratty was the patent that she requested in the document of January 1988.

Mr McCullough then referred Mrs. Cunningham to a publication in *Transfusion* 1993 by Carol Kasper, where Dr Kasper records heat treatment protocols used by major companies during the period in question. The factor IX heat treatment protocol for Travenol at the time the BTSB was using the Travenol protocol, is 60 degrees for 144 hours not 60.6 for 152 hours. Mrs. Cunningham agreed that the Travenol protocol, as employed by the BTSB, is not recorded in Dr Kasper's article.

Mr McCullough then referred Mrs. Cunningham to various recall procedures which she may or may not have been involved in with the BTSB. With respect to Prof. Temperley's letter to Dr Walsh of 22nd April 1986, where Dr Walsh was told by Prof. Temperley that BTSB product may be causing seroconversions in people with haemophilia B, Mrs. Cunningham said the letter also mentioned that those who were seroconverting had also been using product from pharmaceutical companies. She assumed the letter was informing the BTSB that the seroconversions were caused by the product supplied by pharmaceutical companies, and not the BTSB. Mrs. Cunningham said she provided the information requested by Prof. Temperley through Mr Cann. She said no great sense of urgency attended this request, to her knowledge, and that as far as she was concerned she was fulfilling a routine request.

Mr McCullough drew Mrs. Cunningham's attention to the recall of BTSB anti-D, a recall in which she was involved. Mrs. Cunningham said a sense of urgency attended this recall as a very definite problem had arisen. Mr McCullough put it to Mrs. Cunningham, had a definite problem not arisen with respect to factor IX as outlined in Prof. Temperley's letter of 22nd April to Dr Walsh, Mrs. Cunningham said she had only seen a memo of these events. At this point the Chairperson and the Tribunal intervened, to say that they did not consider the issue of Anti-D strictly relevant. Mr McCullough pointed out that the relevance lay in different procedures used to recall different products.

With respect to the recall of unheat treated product in January of 1986, where Mrs. Cunningham recalled 30 vials of batch 90781, Mr McCullough asked was there any attempt to recall unheat treated product from previous batches issued by the BTSB? Mrs Cunningham said, no, these were regarded as legitimate routine batches. The only reason she recalled the 30 vial consignment was that it had been issued after the instruction had

been given to use only heat treated factor IX. She recalled the 30 vials in order to put the batch back together again and heat treat it as one lot.

Mrs. Cunningham agreed that this document was prepared in August 1989 in contemplation of litigation. Mrs. Cunningham said she was asked by Mr Keyes to prepare the information, and she did so. Mr McCullough asked Mrs. Cunningham was she not curious as to why she was being asked to prepare such information? Mrs Cunningham said she simply responded to Mr Keyes' request, and that the subject matter of the litigation was not discussed in Pelican House at the time. However, information concerning the pending litigation was contained in newspapers, and from this she learned that the litigation was in connection with possible HIV infections.

Given that she knew about HIV infections from BTSB product in 1989, or potential infections, how did Mrs. Cunningham explain that the previous day she had told Mr Durcan that she knew nothing of HIV infections until quite recently. Mrs. Cunningham said she knew nothing about specific infections until quite recently. She said she knew haemophilia patients had become infected but did not know the connection between that and BTSB products, or the possible connection.

With respect to Mrs. Cunningham's note on the meeting between the BTSB and Dr Hoppe in 1985, it was noted that screening was taking place for AIDS. It also says that there is a rumour that one seroconversion has occurred with heat treated product. and records "two patients, mostly cryo, two children". Mrs. Cunningham said that it was possible that people may get infected by cryoprecipitate. Mr McCullough asked Mrs. Cunningham did the mention of two children have any resonance with her? Mrs. Cunningham said the only resonance it had was that it was possible that someone had become infected using cryo, and that it is very possible that it did happen. However Mrs Cunningham said she was not sure whether Prof. Temperley was speaking about Ireland.

With respect to batch 9885 Mrs Cunningham agreed that this product was heated at 60.6 degrees for 152 hours, which was the protocol passed onto her by Mr Hanratty by way of communication from Travenol. Mr McCullough asked Mrs. Cunningham was she ever made party to any other heat treating protocol, specifically the super heat treatment option available from Elstree. Mrs Cunningham said the BTSB could not use this heat-treatment protocol for its factor IX as the intense heat would destroy it. Mrs. Cunningham said the BTSB's factor IX would be destroyed if heated to 80 degrees and the BTSB had conducted an experiment on this in 1984. However, the product heated at 60.6 degrees by 152 hours was not the same product heat treated to experimental levels by the BTSB in 1984. The 1988 product came from Armour. The 1984 product came from BTSB cryo supernatent. Mrs Cunningham said the BTSB did have information on the super heat treated option, but she did not think the BTSB would be able to heat treat its product to this level as it required more than simple heat treating.

PROCEEDINGS - FRIDAY 27th OCTOBER 2000 - DAY 63

Ms Bridget O'Rourke, formerly of the BTSB, was examined by Mr John Finlay S.C. for the Tribunal. Ms O'Rourke was a locum senior medical laboratory technician with the BTSB from 1981 until 1985. She was engaged initially in the production of ante natal blood products, and subsequently in the blood components laboratory.

In September or October of 1981 she was asked by Mr Hanratty to assist in a project he was involved in. This was the BTSB's factor VIII home production project. Mrs O'Rourke said she worked on the project for 10 days at the most and she had no further involvement. The technical name for the project was the Continuous Thaw Siphon Technique involving Heparin. This involved extracting cryo from plasma while it was still in a semi-frozen state. Ms O'Rourke said Mr Hanratty was engaged in the work and he did most of it himself. There was no other employee directly involved as far as Ms O'Rourke knew. She said she knew that some of the product manufactured by the project was infused at St. James' Hospital and Mr Hanratty was very excited when this occurred. Ms O'Rourke said she had no further involvement in the project and no explanation was forthcoming when the project was brought to an end, or when custom fractionation was introduced. Ms O'Rourke said the BTSB paid her salary in the form of cheques from the BTSB.

Cross-examined by Mr Martin Hayden for the I.H.S., Ms O'Rourke said as far as she was concerned, the BTSB's home production of factor VIII was successful and no difficulties were encountered with it and it appeared to be working satisfactorily. No other person was directly involved in the project. Mrs O'Rourke agreed that the project required a steady supply of factor VIII and the trials were conducted at some stage during 1982.

Cross-examined by Mr Frank Clarke for the BTSB, Ms. O'Rourke confirmed that she was in part time employment during the period of her work with the BTSB. Ms. O'Rourke said her involvement in the Tribunal commenced sometime in November 1999, when she got a phone call from the BTSB to know how much she remembered of being involved in the project with Mr Hanratty involving heparin back in 1981 and 1982. Ms O'Rourke said her memory of the whole project was very vague at this time because her involvement was so slight. It was something that had vanished from her mind.

Mrs O'Rourke said her attention was once again drawn to the matter when she read coverage of the Tribunal. She then realised that the person being referred to as a project worker on the home production of factor VIII was in fact herself. Mrs O'Rourke said she felt particularly aggrieved at an intimation in the paper that she could have been paid by a commercial company, because that certainly didn't arise. She said she took umbrage at that comment when she read it in the papers.

Ms O'Rourke agreed with Mr Clarke that at all times she was an ordinary employee of the BTSB carrying out ordinary duties.