

Susan A Murray  
Scottish Health Service Central Legal Office  
Anderson House  
Bonnington Road  
Edinburgh  
EH6 5JR

1 July 2011

Email: [REDACTED]

Copy to: [REDACTED]

Dear Susan,

**The Penrose Inquiry – C3: Heat Treatment 1985-1987**

As you will be aware, we are now in the process of gathering evidence for the above topic. In this respect, we request your clients to provide the Inquiry with the following documents:

- 1) Documents showing that on 21.11.83 (or 21.12.83?) the first experiments on dry heating were undertaken at PFC together with the results of those experiments (referred to in the SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors, prepared by Dr Foster in November 2010 (the "SNBTS November 2010 Briefing Paper"), p56).

***Two documents are supplied. The record of the experiment from Dr Cuthbertson's original laboratory notes (which are not dated) [PEN.012.1669] also with a typed version, [PEN.012.1673] and an extract from a report of Dr Foster, dated 20<sup>th</sup> December 1983, in which the preliminary result of this experiment was noted in section 4. [PEN.012.1500]***

- 2) Documents showing what was discussed at the visit to PFC by Dr JK Smith on 22.11.84 (SNBTS November 2010 Briefing Paper, p59).

***Entries in the diary of Dr Foster indicated meetings with Dr Smith on 22<sup>nd</sup> and 29<sup>th</sup> November 1984. A letter from Dr Smith of 4<sup>th</sup> December 1984 summarised the discussion of 29<sup>th</sup> November 1984. It seems unlikely that Dr Smith would have visited PFC on both the 22<sup>nd</sup> and the 29<sup>th</sup> November and it is more likely that his visit took place on the 29<sup>th</sup> instead of the 22<sup>nd</sup> November, as described in the letter from Dr Smith. [PEN.017.1365]***

- 3) The protocol produced by the ISTH in December 1984 to determine the degree to which a coagulation factor concentrate was free from transmission of NANBH (SNBTS November 2010 Briefing Paper, p54).

***We have been unable to find a copy of the protocol that was produced in December 1984. However this protocol was described in a review paper that was published in 1989 viz. Mannucci PM & Colombo M (1989). Revision of the protocol recommended for studies of safety from hepatitis of clotting factor concentrates. Thrombosis and Haemostasis, 61, 532-534. A copy of this paper is provided. [SGF.001.1758]***

- 4) Documents showing what was discussed at Dr Cash's meeting at BPL in late 1984/early 1985 (referred to in Dr Cash's letter of 7.1.85 to Dr Perry (SNB.007.4732).

***I have nothing on this. PRF***

- 5) Documents showing that in February 1985 PFL, England, prepared a trial batch of 8Y dry heated at 80°C for 72 hours for clinical evaluation (SNBTS November 2010 Briefing Paper, p65).

***This document has been provided to the Inquiry. See [PEN.012.1511]***

- 6) The memo dated 14.2.85 from Dr JK Smith to Dr Foster describing the PFL/BPL research on high-purity FVIII (8Y) (SNBTS November 2010 Briefing Paper, p59).

***A copy of the memo is provided. [PEN.017.1369]***

- 7) Documents showing what was discussed at the visit to PFC by Dr JK Smith on 19.2.85 (SNBTS November 2010 Briefing Paper, p59).

***No documents have been found other than the memo at 6). A copy of the entry in the diary of Dr Foster is supplied. [PEN.017.1372]***

- 8) Documents showing what was discussed at the visit by PFL/BPL staff to PFC on 27.3.85 (SNBTS November 2010 Briefing Paper, pp40 and 60).

***No documents concerning this meeting have been found other than a letter from Dr P A Feldman of PFL dated 17<sup>th</sup> April 1985 [SNB.007.5071] and the entry in the diary of Dr Foster. [PEN.017.1373]***

- 9) Documents showing what was discussed at the visit of Dr JK Smith to PFC on 26.4.85 (SNBTS November 2010 Briefing Paper, p60).

***No documents concerning this meeting have been found except a copy of the patent application for 8Y, [SNF.001.0091] which was most probably discussed, and the entry in the diary of Dr Foster. [PEN.017.1374]***

- 10) Documents showing that on 21.10.85 the high purity FVIII product being developed by PFC was found to not withstand heating at 80°C whereas the existing, intermediate, NY FVIII product did (referred to in the SNBTS November 2010 Briefing Paper, pp42 and 61, and the SNBTS submission 'identification of Errors, Omissions and Comments on the Preliminary Report by the SNBTS' dated January 2011 ("the SNBTS 'Errors etc' submission"), pp37-38).

***The original laboratory notes have not been found. However, results from this experiment were noted in the diary of Dr Foster [PEN.017.1375] and in a memo from Dr Foster of 22<sup>nd</sup> October 1985. [PEN.017.1376] Information concerning various related experiments is supplied. [PEN.017.1378]***

- 11) Documents showing that on 21.11.85 Dr McIntosh began experiments to examine the feasibility of applying dry heating to FVIII (ZHT) instead of

pasteurisation, together with the results of those trials (SNBTS November 2010 Briefing Paper, p61).

***The record of this experiment is supplied. It should be noted that the protocol for the preparation of pasteurised factor VIII (ZHT) has been altered to omit pasteurisation and modified to determine if the material at step 6 might form a basis for a dry heat treated concentrate. The record of a further experiment that was performed on 2<sup>nd</sup> December 1985 is also supplied. [PEN.017.1379]***

- 12) Any record of the meeting on 23.12.85 between Drs Perry, Foster, Cuthbertson and McIntosh (SNBTS "Errors etc" submission, p38 and SNBTS November 2010 Briefing Paper, p61).

***No record of this meeting has been found other than an entry in the diary of Dr Foster. [PEN.017.1383]***

- 13) Documents showing that in January 1986 Dr RV McIntosh began a programme of R&D to establish a suitable method for the rapid development of a severe dry heat treated programme (i.e. Z8) (SNBTS November 2010 Briefing Paper, p61).

***The record is supplied of an experiment performed on 31<sup>st</sup> January 1986 in which a material taken from an early stage of the ZHT process was subjected to an investigation of formulation for dry heat treatment using a process of ultrafiltration/dia-filtration. Records are also supplied of further experiments on 6<sup>th</sup>, 12<sup>th</sup>, 18<sup>th</sup>, 24<sup>th</sup>, 26<sup>th</sup> and 27<sup>th</sup> February 1986. [PEN.017.1384]***

- 14) Letter dated 18.2.86 from Dr Pepper to Dr Smith (referred to in Dr Smith's reply dated 26.2.86, SNB.007.5606).

***The letter from Dr Pepper to Dr Smith has not been found. However Dr Pepper did provide PFC with his results on samples from PFL Oxford on 27<sup>th</sup> January 1986 and this may have been the subject of his letter to Dr Smith of 18<sup>th</sup> February 1986. [PEN.017.1396]***

- 15) Any minutes or notes of the meeting on 21.2.86 between the CBLA and the Common Services Agency (the agenda for the meetings is SNB.006.5055).

***I have no record of this - PRF***

- 16) The detailed information on freeze-drying Dr Foster received from BPL on 24.3.86 (SNBTS November 2010 Briefing Paper, p62).

***A letter from Mr K Kinnarney (BPL) to Dr Foster of 19<sup>th</sup> March 1986 (received on 24<sup>th</sup> March 1986) is provided, together with the enclosures. [PEN.017.1399]***

- 17) Documents showing that on 25.4.86 Dr Cuthbertson and Dr KG Reid performed the first virus inactivation experiments on samples of Z8 prepared in the research laboratory and dry heated at 80°C (SNBTS November 2010 Briefing Paper, p62).

***A summary of experiments dated 20<sup>th</sup> November 1986 is provided in which this experiment is listed as Experiment No. 86-003 that was undertaken on 25<sup>th</sup> April 1986. [PEN.017.1407]***

- 18) Documents showing that on 23.6.86 PFC undertook the first pilot-scale batch of Z8 (Z8-6-001) (SNBTS November 2010 Briefing Paper, p62).

***The record of the trial Z8-6-001 is provided. [PEN.017.1411]***

- 19) Documents showing that on 25.7.86 the PFC management team decided that production of NY heated FVIII should cease to allow the Production Department resources to focus on the development of Z8 (SNBTS November 2010 Briefing Paper, p62).

***The minute of the meeting of the PFC Heads of Department of 25<sup>th</sup> July 1986 is provided. The decision to cease production of the established Factor VIII concentrate is noted on page 3, section 4 of the minute. [SNB.010.3298]***

- 20) Documents showing what was discussed when Dr Foster and Dr JK Smith met on 29.7.86 (SNBTS November 2010 Briefing Paper, p63).

**No record of this meeting has been found. The entry from the diary of Dr Foster is provided. [PEN.017.1421]**

- 21) Documents showing that on 4.8.86 the first trial of full-scale preparation of Z8 was carried out in the PFC production department (SNBTS November 2010 Briefing Paper, p63).

**Extracts from the Batch Record of Z8-6-003 are provided; namely, page 1 where it is recorded that 940 kg of plasma was removed from -40°C cold storage on 1<sup>st</sup> August 1986; page 3, where it is recorded that the conditioning of frozen plasma was begun at 22.00 on 3<sup>rd</sup> August 1986; page 5, where it is recorded that plasma crushing was begun at 07.50 (undated) and page 17, where it is recorded that freeze drying was begun at 19.10 on 4<sup>th</sup> August 1986 and that 990 vials of Factor VIII concentrate were freeze dried. [PEN.017.1422]**

- 22) The memo dated 7.8.86 from Dr JK Smith to Dr Foster (SNBTS November 2010 Briefing Paper, p63).

**The BPL memo dated 7<sup>th</sup> August 1986 is provided. [PEN.017.1426]**

- 23) Documents showing that on 7.8.86 Dr Cuthbertson and Dr KG Reid performed the first virus inactivation study of dry heating Z8 in which heating at 80°C and 75°C were compared, together with documents showing the results of that study (SNBTS November 2010 Briefing Paper, p63).

**A short report is provided which gives the results of virus inactivation Experiment No. FDH 86-005 which was carried out on 7<sup>th</sup> August 1986 and which concerned the dry heat treatment of Z8 at 80°C and 75°C. [PEN.017.1429]**

- 24) Documents showing that in or around September 1986 PFC found that the structure of the crystals which formed when Z8 was frozen for the purposes of freeze drying was especially critical (SNBTS "Errors etc" submission, p39).

***The minute of a meeting held on 26<sup>th</sup> September 1986 is provided in which crystal structure was discussed. [SNB.007.9092][SNB.007.9094]***

- 25) Documents showing that on 25.9.86 a study was undertaken in PFC production freeze drier of freezing FVIII solution to determine procedures for obtaining super-cooling reproducibly together with the results of that study (SNBTS November 2010 Briefing Paper, p63).

***The protocol for the super-cooling experiment of 25<sup>th</sup> September 1986 is provided. (Results of study to follow.) [PEN.017.1434]***

- 26) Documents showing what was discussed when Dr Foster and Dr JK Smith met on 9.10.86 (SNBTS November 2010 Briefing Paper, p63).

- 27) ***No record of the discussion has been found. The diary entry of Dr Foster is provided [PEN.017.1435], together with reports which are likely to have been the subject of discussion. [SNB.010.5985] and [SNF.001.1123]*** Documents showing what was discussed when J Lundblad of Bayer visited PFC on 4.12.86 (SNBTS November 2010 Briefing Paper, p63).

***No record of the discussion has been found. The entry from the diary of Dr Foster is provided. [PEN.017.1436]***

- 28) Documents showing that Z8 was issued to Edinburgh for clinical trial on 22.12.86 (SNBTS November 2010 Briefing Paper, p63).

- 29) ***The Batch Issue sheet for Z8-6-011 is provided indicating that the batch was placed at issue on 2<sup>nd</sup> December 1986; that vials were issued to Edinburgh BTS on 22<sup>nd</sup> and 24<sup>th</sup> December 1986 and that the remainder of the batch was issued to Edinburgh BTS on 25<sup>th</sup> May 1987. [PEN.017.1437]*** The report Dr Foster received from Dr JK Smith in March 1987 which described problems which arose at BPL in 1986 and which resulted in batch failures (SNBTS November 2010 Briefing Paper, p64).

***The report is provided. [PEN.017.1438]***

- 30) Documents showing that on 15.4.87 Z8 heat treated at 75°C for 72 hours was issued for routine clinical use (SNBTS November 2010 Briefing Paper, p64).

***The Batch Issue sheet for Z8-6-017 is provided indicating that the batch was placed at issue on 9<sup>th</sup> April 1987 and issued to Glasgow BTS on 15<sup>th</sup> April 1987. [PEN.017.1451]***

- 31) Documents showing what was discussed at the meeting on 22.4.87 between Dr Foster, Dr JK Smith and Dr Winkelman (SNBTS November 2010 Briefing Paper, p64).

***No record of the discussion has been found. The entry from the diary of Dr Foster is provided, together with a report on a virus inactivation study of 8Y that had been performed by PFC which is likely to have been discussed. [PEN.017.1452]***

- 32) Documents showing that on 22.5.87 Z8 heat treated at 80°C for 72 hours was issued for routine clinical use (SNBTS November 2010 Briefing Paper, p64).

- 33) ***The Batch Issue sheet for Z8-6-026 is provided, indicating that 50 vials were issued to Edinburgh BTS on 11<sup>th</sup> February 1987 with the remainder of the batch (368 vials) being issued to Glasgow BTS on 22<sup>nd</sup> May 1987. [PEN.017.1470]*** Fax dated 26.8.99 from Dr Snape to Dr Perry (SNBTS November 2010 Briefing Paper, p71, reference 55).

***This document has been provided to the Inquiry [PEN.012.1511].***

Could you also please confirm whether or not PFC produced annual reports in the period between 1980 and 1988? If they did, any such annual reports should be provided to the Inquiry.

***PFC did not produce annual reports in the period between 1980 and 1988.***

To enable the Inquiry to provide fair notice of the documents for this topic to all core participants in advance of the hearing, the documents referred to above are requested by Friday 12 August.



We hope that the documents can be provided on a voluntary basis in the first instance. If there are any difficulties in obtaining the documents within the requested timescale, however, then Lord Penrose will consider using his powers under the Inquiries Act 2005 and the Inquiries (Scotland) Rules 2007 to issue a formal notice requiring the documents to be provided by a particular date.

Please acknowledge receipt of this letter.

We are grateful to you and your clients for your assistance

Best Regards

Angus Evans