SMALLER HAEMOPHILIA CENTRES PRESENTATION

CAMBRIDGE HAEMOPHILIA CENTRE

Centre/Centre Directors

1. The Cambridge Haemophilia Centre (Centre 89, "the Centre") was based in the Department of Haematology, Addenbrooke's Hospital, Hills Road, Cambridge.

2. According to the statement of Dr Muriel Seaman [WITN3815002], Dr Chalmers was the director of the Haemophilia Centre from 1973 until his death in 1984; Dr Seaman then took over as director from 1984 to 1990. She was the only senior member of the haematology staff until 1987 when a second consultant (Dr Robert Marcus) was appointed, but he had responsibility for patients with leukaemia rather than haemophilia. Dr Trevor Baglin then became director on Dr Seaman's retirement. In 2004 Dr David Perry became consultant haematologist at, and co-director of, the Centre [WITN3173004].

Relationship with the Regional Transfusion Centre, supply arrangements, treatment policies and blood product usage

3. The documents available to the Inquiry show that the Centre received its supplies of cryoprecipitate ("cryo") and factor concentrates through the Regional Transfusion Centre ("RTC") in Cambridge: see, for example, [DHSC0100026_039] and [DHSC0100026_035] which show the supply of cryo to the Centre for 1971-2.

4. There are various letters which cast light on the supply arrangements and product usage in the 1970s:

    a. Correspondence between Dr Darnborough (director, Cambridge RTC) and Dr Maycock in March 1975 contained a discussion of targets for the production of concentrates; it was noted that *"There is, of course, going to be an awkward period when more than half the cryo used at present is diverted to producing concentrate"* [DHSC0002359_043]. It was also recorded that most of the

cryoprecipitate for the region was going to Addenbrooke's or to Norfolk and Norwich.

b. A further letter from Dr Darnborough to Dr Maycock on 9 July 1976 [CBLA0000383] asked for information about how factor VIII concentrate would be distributed from Elstree and how much was likely to be available: *"... it would be nice to know when we can start reducing cryoprecipitate. If Factor VIII concentrate were available to us now, we could very readily divert the present cryoprecipitate production into fresh frozen plasma"*.

c. On 15 July 1976 Dr Chalmers wrote to Dr Maycock, explaining that the demands which had been made by the Centre for concentrate had been extremely small *"mainly due to the excellent service we get in the form of cryoprecipitate from Dr Darnborough"* and recording that *"We now have a number of patients on home treatment using cryoprecipitate"*. He asked, however, for a supply of concentrate which patients could take on holiday to continue their therapy, as this *"presents great difficulties for my patients"*.

d. Dr Darnborough wrote again to Dr Maycock in August 1976 [CBLA0000410], expressing his and Dr Chalmers' concern about a suggestion that distribution of factor VIII might be on a supra-regional basis and that East Anglia might be tied to the metropolitan regions. Dr Chalmers was reported as stating that the East Anglian region had a *"distinct and very satisfactory system"*. Dr Darnborough also expressed his opposition to a suggestion that the RTCs could distribute commercial Factor VIII: *"I feel that it would be quite wrong for the NBTS to have anything to do with the commercial preparations"*.

e. The use of cryo for home treatment for Cambridge patients was confirmed again by Dr Chalmers in his 6 October 1976 letter to Dr Maycock (in which he requested a small regular supply of factor VIII concentrate for a new patient who had been using concentrate on a regular basis at Lewisham), observing that

"we do not have the funds to support patients on home therapy using commercial material" [CBLA0012296].[1]

f. The distribution of Elstree Factor VIII through RTCs was further discussed in a letter of 29 November 1976 from Dr Dormandy (director, Royal Free), explaining that she and Professor Ingram were to be jointly responsible for the South East Haemophilia Supraregion, which was to be split along the Thames. She would be responsible for the northern half, which contained the East Anglian Regional Health Area, including the Cambridge RTC [CBLA0000506]. Dr Darnborough responded on 3 December 1976 [CBLA0000508], reiterating his concern about the East Anglian region being linked with Thames Metropolitan regions and suggesting that it would be more sensible for East Anglia to be linked to one of the provincial regions. He explained that he, Dr Chalmers, Dr Seaman and Dr Leslie, and the Regional Scientific Officer, had recently met and had made plans for the regional distribution of cryo, NHS concentrate and commercial concentrate, which would all come through the RTC [CBLA0000508].

g. An allocation document dated 6 December 1976 suggested that the East Anglian region would receive 60 bottles per month of NHS concentrate; it was recorded that there were 44 patients treated at Addenbrooke's [CBLA00000510].

h. Dr Chalmers and Dr Darnborough do not appear to have attended the meeting held at the Royal Free on 15 December 1976 to discuss the arrangements for the distribution of factor VIII concentrates, but the minutes record, in relation to the East Anglian region (RHA 04), that the region was self-contained and the area of distribution for the RTC coincided with that of the RHA; it was also noted that there was one haemophilia centre present in the region (Cambridge), but that *"the designation of a Haemophilia Centre or Associate Centre has been proposed for the Norfolk & Norwich hospital"* [CBLA0000533]. Dr Gibson, of the BTC, reported that 40 of the 60 allocated bottles would go to Cambridge and 20 to the Norfolk & Norwich Hospital; a reserve of 50,000 units of

[1] A letter from Dr Maycock to Dr Darnborough on 19 October 1976 confirmed that there would be a monthly distribution to the Cambridge RTC of factor VIII concentrate and Dr Darnbrough was asked to make arrangements with Dr Chalmers for the treatment of this patient [CLBA0004850, CBLA0004849].

commercial concentrate was to be purchased and held by the RTC. The request by Dr Darnborough/Chalmers to change their supra-region was noted but no action was taken.

i. Dr Chalmers' unhappiness with this arrangement was expressed by him in a letter dated 7 January 1977 to Dr Biggs at Oxford [OXUH00003629], in which he emphasised that the supply of blood and blood products in East Anglia had always been extremely satisfactory. He wanted the allocation for East Anglia to go directly to the East Anglia BTS and for it to be based on the number of patients under active treatment and the amount of material supplied for fractionation in relation to the total population for the region. He also observed that *"We have to face the fact that once concentrate becomes freely available we will be committed to buying, if it is still possible to buy it, larger quantities of commercial concentrate to make up the shortfall"*.

j. Dr Chalmers attended the meeting of "Directors of Haemophilia, Associate Haemophilia and Blood Transfusion Centres from RHAs 04, 05 and 06" on 23 September 1977 [CBLA0000657], at which he reported that 50,000 units of commercial concentrate had been purchased by the RTC to be held as store and replaced as used. In relation to the Cambridge Haemophilia Centre, he reported that cryo was used in hospital and NHS and commercial concentrate for home treatment, with commercial only being used for the latter to make up for the shortfall in NHS concentrate.

5. In a letter written to Dr Aronstam in September 1980 [TREL0000317_107] Dr Chalmers reported that the Centre was normally in a position to supply *"all our haemophiliacs on self-treatment"* with NHS concentrate, with the commercial concentrate being reserved for operative procedures and cryoprecipitate for the treatment of patients attending hospital.

6. A 1983 report [CAMA0000065] entitled 'Operational Research Study of the Blood Transfusion Service' examined options for meeting regional and national demands for blood and blood products for the next decade; in relation to East Anglia, the report noted that East Anglia used about half of the national average per head of population of factor VIII and that in 1981 a total of just over 800,000 iu was used; fresh plasma

sent to BPL in 1981 was equivalent to approximately 600,000 iu: *"Thus we are not yet regionally self-sufficient"*.

7. The picture from the documents referred to above is broadly consistent with Dr Seaman's recollection, as set out in her statement, that patients were initially treated with cryoprecipitate until NHS factor VIII concentrate became available and that NHS factor VIII concentrate was obtained from the Blood Transfusion Service via the Regional Transfusion Centre. She thought that commercial heat treated products (Cutter and Armour), and later NHS heat treated product, were used from around December 1984 onwards. She could not recall the use of cryoprecipitate when she was a director (i.e. from 1984). Dr Seaman states that the Centre did not always have a choice as to what products were available and that *"Patients generally accepted what was offered to them as we could not always give them a choice"*. Home treatment was used *"wherever possible ... This was largely to treat episodes but some prophylactic therapy was used in certain circumstances"*. She could not recall a special policy for the treatment of children and recalls the Centre being largely concerned with the treatment of adult patients.

Annual returns

8. The annual returns for 1976 (completed by Dr Chalmers) [HCDO0001064] record that:

    a. 52 haemophilic patients were treated during the year and 25 Christmas disease patients;
    b. the Centre used:
        i. 472,850 units of cryo;
        ii. 3,240 units of NHS Factor VIII;
        iii. 27,025 units of Factorate, 3,000 units of Koate, 73,026 units of Hemofil and 15,000 units of Kryobulin;
    c. 140,242 units of NHS factor IX were used for the treatment of patients with Haemophilia B;
    d. 4 patients with Von Willebrand's were treated with cryo.

9. The annual returns for 1977 (completed by Dr Chalmers) [HCDO0001145] record that:

a. 33 haemophilic patients were treated during the year and 13 Christmas disease patients;
b. the Centre used:
    i. 273,490 units of cryo, of which 12,600 were used for home treatemnt;
    ii. 1,200 units of Koate and 42,211 units of Hemofil, of which 2,800 were used for home treatment;
c. 141,790 units of NHS factor VIII were supplied to patients on home treatment; the total usage of NHS factor VIII was not recorded (save for a "?");
d. 126,000 units of NHS factor IX were used for the treatment of patients with Haemophilia B;
e. 1 patient with Von Willebrand's was treated with 24 bottles of cryo.

10. The annual returns for 1978 (completed by Dr Chalmers) [HCDO0001240] show that:

a. 36 haemophilic patients were treated during the year, one with factor VIII antibodies;
b. 17 patients with Christmas disease were treated during the year;
c. the Centre used:
    i. 1926 bottles (134,820 units) of cryo;
    ii. 177,000 units of NHS factor VIII;
    iii. 46,000 units of Hemofil (Hyland);
d. 163,300 units of NHS Factor IX were used for patients with Christmas disease.

11. The annual returns for 1979 (completed by Dr Chalmers) record that:

a. 51 haemophilic patients were treated during the year, one with factor VIII antibodies;
b. 15 patients with Christmas disease were treated during the year;
c. the Centre used:
    i. 1502 bottles (105,140 units) of cryo;
    ii. 224,800 units of NHS factor VIII;
    iii. Factorate (Armour) (the return is unclear as to the precise quantity) and 20,000 units of Hemofil (Hyland);

d. 90, 400 units of NHS Factor IX were used;
e. 2 patients with von Willebrand's were treated with cryo (12 bottles; 840 units) and NHS factor VIII concentrate (3000 units)

The returns also show individual patients being treated with more than one type of concentrate [HCDO00001309]. There does not appear to be any evidence of a policy of restricting patients to only one type of concentrate or of any batch dedication policy.

12. The annual returns for 1980 [HCDO0001404] show that:

a. 39 patients with haemophilia A were treated during the year;
b. the Centre treated those patients with:
    i. 1332 bags of cryo in hospital;
    ii. 6,392 units of NHS Factor VIII in hospital and 169,545 units for home treatment;
    iii. 79,901 units of Factorate in hospital and 99,081 for home treatment, and 6,419 units of Hemofil in hospital and 13,590 for home treatment;
c. 16 patients with haemophilia B were treated using 141,958 units of NHS Factor IX in hospital and 19,030 for home treatment.

13. The annual returns for 1981 [HCDO0001502] show that:

a. 40 patients with haemophilia A were treated during the year;
b. one patient with von Willebrand's was treated during the year;
c. the Centre used:
    i. 990 units of cryo in hospital for haemophilia A treatment (12 for von Willebrand's treatment);
    ii. 5,555 units of NHS Factor VIII in hospital and 268,291 units for home treatment;
    iii. 115,709 units of Factorate in hospital and 2,276 for home treatment, and 22,396 units of Hemofil in hospital;
d. 217,595 units of NHS Factor IX were used in hospital and 47,735 for home treatment.

14. The annual returns for 1982 [HCDO0001605] record that:

a. 40 haemophilia A patients and 2 von Willebrand's patients were treated;
b. the Centre used:
    i. 515 bags of cryo in hospital (the return is unclear as tow hether cryo was also used for home treatment);
    ii. 72,940 units of NHS Factor VIII in hospital and 246,600 for home treatment;
    iii. 37,190 units of Factorate in hospital;
c. DDAVP was used for treatment for Von Willebrand's;
d. NHS Factor IX was used for both hospital and home treatment for haemophilia B patients.

15. The annual returns for 1983 [HCDO0001701] record that:

a. 34 haemophilia A patients were treated during the year;
b. the Centre used:
    i. 542 bags of cryo in hospital;
    ii. 126,965 units of NHS Factor VIII in hospital and 356,120 for home treatment;
    iii. 162,644 units of Factorate in hospital;
c. NHS Factor IX was used in hospital and home.

16. The annual returns for 1984, which record Dr Seaman as the director, report that:

a. 37 haemophilia A patients and 1 von Willebrand's patient were treated;
b. the Centre used:
    i. 18,860 units of cryo for treating patients in hospital;
    ii. 238,515 units of NHS Factor VIII concentrate in hospital and 403,305 units for home treatment;
    iii. 19,790 units of Factorate in hospital and 11,085 for home treatment, and 25,620 units of Koate for home treatment;
c. 1,680 units of cryo and 1,500 units of NHS concentrate were used for treating the von Willebrand's patient in hospital;

d. "Scottish" product was used: 22,100 units in hospital and 22,820 units for home treatment;
e. 3 patients with antibodies were treated with NHS concentrate (67,210 units) and 17,525 units of Factorate in hospital as well as 4,160 units of Scottish VIII;
f. the Centre also treated 14 haemophilia B patients and 1 carrier of haemophilia B, all which NHS Factor IX concentrate [HCDO0001797].

17. The annual returns for 1985 record that:

a. 44 haemophilia A patients and two von Willebrand's patients were treated;
b. in relation to the haemophilia A patients:
    i. 5,670 units of cryo were used for hospital treatment;
    ii. 64,130 units of NHS concentrate were used for hospital treatment and 160,060 units for home treatment;
    iii. 90,408 units of Factorate were used for hospital treatment and 183,020 units for home treatment;
    iv. 54,380 units of Koate were used for hospital treatment and 80,220 for home treatment;
c. DDAVP was used;
d. a small amount of cryo was used in hospital for von Willebrand's treatment;
e. 3 patients with antibodies were treated with NHS Factor VIII concentrate, Armour concentrate, NHS Factor IX concentrate and Alpha Factor IX concentrate;
f. 18 patients with haemophilia B were treated with NHS concentrate (43,478 units in hospital, 30,705 for home) and commercial Factor IX (40,720 units in hospital and 104,000 for home treatment) [HCDO0001889].

18. The 1986 annual returns record that 47 haemophilia A patients were treated. Some cryo was used but the returns show mostly NHS concentrate for hospital and home treatment, with some Koate (38,140 hospital; 46,570 home). DDAVP usage was also recorded. 16 haemophilia B patients and 2 carriers were treated with NHS Factor IX concentrate [HCDO0001985]

19. A letter of 10 April 1984 from Armour to the DHSS's Medicines Division added Dr Chalmers to the list of investigators carrying out work under exemption CTX 0231/0070A – Heat Treated Factorate [ARMO0000431].

20. A May 1985 UK Situation Report regarding sales of Koate reported that Cambridge had returned to buying Koate HT in May *"after having to buy from Armour because of our lack of stock"* [BAYP000024_203].

Knowledge of risk of hepatitis and HIV

21. Dr Chalmers attended a number of UKHCDO meetings including:

    a. 1 November 1974 [HCDO0001017] at which Dr Craske reported on the outbreak of hepatitis in patients in Bournemouth.
    b. 18 September 1975 [OXUH0003735] when there was a discussion about hepatitis and a proposed pilot study of hepatitis in haemophilic patients.
    c. The first day of the meeting on 20th-21st November 1979 [BPLL0007384] at which there was a discussion about the provision of data about patients who developed hepatitis or antibodies *"since those were two outstanding problems in haemophilia today"*. (He was not present for day 2, at which Dr Craske presented his report on the work of the Hepatitis Working Party or for the ensuing discussion about chronic hepatitis; the minutes of this meeting seem to have been circulated in draft form to directors in January 1980 and final form in May 1980.)
    d. October 1981 [CBLA0001464] at which Dr Craske presented a report (pre-circulated to all directors) of the Hepatitis Working Party.

22. In addition to his attendance at UKHCDO meetings, Dr Chalmers reported hepatitis (including NANBH) in patients in the late 1970s. Thus, correspondence from Dr Chalmers to Dr Maycock in March 1978 recorded a patient who was on home therapy developing jaundice in September 1977 [CBLA0008704]; the response from Dr Maycock explains that *"In view of the fact that the patient is anti-HBs positive, the*

hepatitis was presumably hepatitis A or hepatitis non A non B" [CBLA0003738][2]. A hepatitis survey form completed in 1979 recorded a patient with von Willebrand's being treated with Hemofil and developing what was probably NANBH [HCDO0000257_042].

23. There is also a report by the Regional Transfusion Centre in March 1975 to Dr Maycock of a case of post transfusion hepatitis in a haemophiliac at Addenbrooke's *"who has had many units of commercial Factor VIII concentrate as well as Cambridge "cryo""* [DHSC0100018_153].

24. As director, Dr Chalmers would have received the March 1983 and June 1983 letters from UKHCDO regarding AIDS. In June 1983 Dr Wassef (Treloar's) wrote to Dr Chalmer with an update about a Cambridge patient who had been attending Treloar's and had just left. Under the heading "AIDS RELATED INVESTIGATIONS" Dr Wassef reported that clinically the patient exhibited *"none of the stigmata of AIDS"* (apart from some weight loss) and informed Dr Chalmer that various "AIDS related tests" had been undertaken [TREL0000317_015].

25. Dr Chalmers attended the October 1983 meeting of HCDs at which Dr Chisholm raised the issue of reverting to cryoprecipitate because of the AIDS scare and Dr Craske presented a paper (pre-circulated to directors) providing information as to the current situation regarding AIDS [PRSE0004440].

26. Dr Seaman in her statement states that:

    a. She acquired any knowledge she had from colleagues and journals.
    b. She was not very conversant with the risk of hepatitis and blood transfusion but knew it did occur.
    c. She was aware of the risk of infection with untreated concentrate.

[22] The Centre completed a Hepatitis Survey form in respect of this patient which recorded that he had received both Elstree Factor VIII and Hemofil [HCDO0000255_050]. See also, by way of further example, HCDO0000255_168 which records the onset of hepatitis in another patient, this time in March 1977; and HCDO0000258_040.

d. She was aware of the risks of using unsuitable donor material.
e. She understood the nature and severity of blood borne virus infections from the literature of the time.
f. Knowledge of HIV and AIDS was gained from experience over time (her statement suggests that she thinks she probably became aware of the possible association between AIDS and the use of blood products around 1982 but cannot be certain).

27. Dr Seaman attended the September 1984 meeting of HCDs, during which Dr Craske referred directors to his report on the current situation regarding AIDS [PRSE0003659].

Patients infected/information/treatment

28. Dr Seaman's statement explains that she learnt that patients became infected (HIV) due to antibody testing by the Public Health Laboratory Service at Addenbrookes. She states that she saw all of the patients who were HIV positive and discussed the significance of the test result; the patients were seen face to face by her. All patients who had received treatment were tested. She says that *"it is likely that an explanation as to why the test was being done was given at the time the sample was taken"*. She suggests (although this seems unlikely) that hepatitis testing was undertaken by the Regional Transfusion Centre and that patients with hepatitis received care from the Regional Transfusion Centre.

29. On 8 February 1985 Dr Seaman wrote to Dr Snape at BPL regarding the protocol for the supply and use of heated Factor VIII concentrate, recording that:

> *"This Haemophilia Centre serves a rather rural practice and a large number of our haemophiliac patients live a long way away from the hospital. Over the years we have encouraged the development of home therapy for such patients and I think it is going to be difficult to revert back again to hospital treatment ...*
>
> *The other aspect which concerns me is the large amount of laboratory testing and handling that will need to be undertaken ... In the present state of our*

knowledge I do not feel that I can restrict the use of heat treated Factor VIII concentrate only to those patients who are antibody negative and I find it difficult to reconcile the restrictions recommended on one hand and the large number of tests that would need to be performed on the other. In addition we are already experiencing difficulty in getting tests performed outside our own laboratory on patients who are serologically positive for HTLV III antibody."

30. A further letter dated 19 February 1985 from Dr Seaman to Dr Snape referred to a discussion about the supply of heat treated Factor VIII. She indicated in relation to a number of children that she had not *"had all the HTLV III antibody study reports back as yet"*; in relation to other patients *"the majority are already HTLV III antibody positive"* [BPLL0010618]. She wrote again to Dr Snape in April 1985 asking when heat treated Factor VIII would be available to patients other than those already identified on a named patient basis [BPLL0010551].

31. A letter from Dr Seaman to Dr Aronstam (Treloar's) dated 6 November 1986 referred to seroconversions from heat treated products; the letter added that Dr Seaman had *"been regularly informing the GP's of all patients registered with this centre who are HIV antibody positive"*. She had told the GP of the particular patient whom she was discussing about the seroconversion but was asking Dr Aronstam if the patient's mother had been informed [TREL0000039_219]. Other correspondence relating to the patient indicates that the mother had not at that stage been informed.

32. The Inquiry has received evidence to suggest that patients were not always told of their diagnosis in person: see, for example, the evidence of Jo-Anne Cohrs [WITN1162001] – her husband, who was under care of Dr Seaman at Addenbrooke's from 1984-87 (having previously been treated at Newcastle), was told by letter in January 1985 that he had tested positive for HIV. The experience was described as very distressing. [3]

33. Provisional information received from UKHCDO suggests that 16 patients at the Centre tested positive for HIV in 1985 and 2 patients in 1986, giving a total of 18. A plaintiff in the HIV litigation (in which the East Anglian RHA was a defendant) was reported as

[3] See also the statement and oral evidence of Alan Burgess regarding the communication of the diagnosis and the lack of information provided [WITN1122001].

having sero-converted between August 1985 and August 1986, having been treated with Armour products despite his express wish to avoid such treatment [ARMO0000741].

34. Dr Seaman was a member of a Regional Working Party on AIDS [CAMA0000075], the terms of reference for which included deciding which if any functions in respect of the investigation and management of AIDS cases should be provided at a regional level [see also CAMA0000075].

35. In July 1985 Dr Seaman wrote to Dr Christie, Director of Clinical Sciences at Armour [ARMO0000798]; she referred to a particular gentleman with hepatitis who had been reported to Armour recently. In relation to a named patient, she provided information about his negative HTLV III antibody status and added *"I will try and obtain a sample of blood from him in the near future and see if we can have this tested. I will of course keep you posted with any further developments"*.

36. The Inquiry is seeking further evidence about the process of testing for HCV and for informing patients of their diagnosis. Dr Perry's statement explains that by the time he joined the Centre (in 2004) patients infected with hepatitis were managed in close collaboration with the hepatology unit; he did not know when testing for HCV began. All new patients or patients transferring from another centre would have been screened for hepatitis as part of the initial consultation [WITN1373004].

Other

37. The minutes of a meeting of the Council of the Haemophilia Society in March 1976 report a request for help for Dr Chalmers *"whose clinic for treating haemophiliacs was being hampered by the need of clerical assistance"* [HSOC0019918_010].

38. An audit of the Centre was undertaken by Dr Ludlam and Dr Hill on behalf of UKHCDO in 1994 with a recommendation that the Centre should be given Comprehensive Care Status provided that a designated haemophilia charge nurse or clinical nurse specialist was appointed [BART0002045_006]; areas that were suggested

for review included the organisation of patients' records and records of concentrate usage [BART0002045_007]. A letter from Dr Trevor Baglin (the Centre's director) dated 23 January 1995 explained that he would be developing an explicit policy for the monitoring of safe coagulation factor concentrates, with HIV testing at four monthly intervals and regular HCV and HBC testing.

39. Dr Baglin co-authored "Guidelines on the diagnosis, management and prevention of hepatitis in haemophilia" in 2001 [WITN3761021].

JENNI RICHARDS QC
RACHEL BARRETT

Inquiry Counsel Team
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