PROFESSOR JOHN CASH: PRESENTATION

Contents

Introduction

1. This note focuses on the work of the late Professor John Cash from the 1970s to the early 1990s.[1]

Professor Cash's career

At the Edinburgh and South East Scotland Blood Transfusion Service

2. Professor Cash worked at the Edinburgh and South East Scotland Blood Transfusion Service from 1971 to 1979. He was appointed as its Director in 1974.[2]

At SNBTS Headquarters

3. Professor Cash became the National Medical Director of the Scottish National Blood Transfusion Service ("SNBTS") in 1979. In 1988 his role changed to National Medical and Scientific Director.[3]

4. The operation of SNBTS was summarised as follows in its 1988-9 Annual Report:

> "*There are 7 operational units which make up the SNBTS: 5 Regional Transfusion Centres (based in Aberdeen, Dundee, Edinburgh, Glasgow and Inverness), the Protein Fractionation Centre and the Headquarters Unit (both located in Edinburgh). The total population served is approximately 5.2 million. Each Regional Centre is responsible for the collection of blood donations from its own local panel of voluntary blood donors and the provision of blood and blood products as well as a wide variety of diagnostic and clinical consultation services for all the health services within its regional boundaries. The Regional Centres also provide all the plasma required by the*

[1] For some of this period his title was "Dr" but for simplicity this note refers to him as "Professor" Cash throughout.
[2] PRSE0003376
[3] PRSE0003376

Protein Fractionation Centre which returns the products prepared from this plasma to the Regional Centres for use in health service establishments, including, when appropriate, primary care (general practice) establishments. The Protein Fractionation Centre also processes plasma collected in Northern Ireland and returns the products to the Blood Transfusion Centre in Belfast. The Headquarters Unit is responsible for the overall co-ordination of the national service."[4]

5. While this presentation touches briefly on some of the work Professor Cash did as a result of his responsibility for the Protein Fractionation Centre ("PFC"), more evidence in respect of this part of his work will be adduced by the Inquiry in due course.

Committees and memberships

6. In 1970, Professor Cash was appointed to the Medical Research Council ("MRC") subcommittee on hepatitis,[5] the European Society for Clinical Investigation and the British Society for Haematology.[6]

7. From 1980 to 1982, Professor Cash was a member of the MRC Research Committee on Blood Transfusion.[7] He told the Penrose Inquiry he was *"dismayed, astonished and alarmed"* when this Committee was disbanded, in his view without any consultation of the UKBTS.[8]

8. In 1981, he was a founding member of the British Blood Transfusion Society.[9]

9. He was a member of the Department for Health and Social Security ("DHSS") Expert Advisory Group on AIDS from 1985 to 1987.[10]

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[4] NHBT0002934
[5] PRSE0003376
[6] LOTH0000127
[7] PRSE0003376
[8] PRSE0002836
[9] PRSE0003376
[10] PRSE0003376

10. In 1989, the UK Advisory Committee on Transfusion Transmitted Diseases ("ACTTD") was set up by Dr Harold Gunson to consider the implications of transfusion-transmitted infections on the transfusion services in the UK and to provide advice to the DHSS. On 24 February 1989, Professor Cash attended the first ACTTD meeting, at which he gave a verbal report on a study in Scotland on non-A non B hepatitis.[11] He continued to attend ACTTD meetings throughout the relevant period.

11. Dr Gunson noted in correspondence that Professor Cash's efforts to establish a ministerial group to control the introduction of additional donor testing led to the formation of the Advisory Committee on the Virological Safety of Blood ("ACVSB") in 1989.[12]

12. In his C4 Witness Statement to the Penrose Inquiry, Professor Cash stated that the establishment of the ACVSB was *"welcomed but proved not to be entirely satisfactory"*. There was no mechanism for the SNBTS management team to have input on the construction of the ACVSB agendas, submit briefing papers, or have access to meeting minutes. The ACVSB operated a strict code of secrecy, which on many occasions resulted in senior SNBTS management being unaware of important issues.[13]

13. For example, Professor Cash wrote to SNBTS General Manager, Mr David McIntosh, in August 1991 in terms which suggested that the SNBTS only became aware of the UK Health Ministers' endorsement of a uniform starting date for routine HCV antibody screening when he was granted access to the relevant ACVSB minute.[14] Mr McIntosh's response outlined serious concerns with the lack of clarity around the status of the ACVSB's advice and how that advice was communicated and promulgated into actual policy.[15]

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[11] NHBT0000043_002
[12] NHBT0000192_058
[13] PRSE0002529
[14] PRSE0000615
[15] NHBT0000077_071

14. Professor Cash stated to the Penrose Inquiry that senior officials from the DHSS took action to prevent attempts to establish formal links between the ACVSB and the ACTTD.[16]

15. Professor Cash was also a member of the SNBTS/NBTS Liaison Committee, which held its first meeting on 27 June 1990.[17]

16. In addition Professor Cash:

- Was a member of the Co-ordinating Group of the SNBTS.
- Attended the meetings of the Scottish Regional Transfusion Directors ("RTDs").
- Was a member of the SNBTS Medical and Scientific Committee which held its first meeting on 10 November 1990.[18]
- Was a member of the SNBTS Ethics Committee (Clinical Research Investigations) set up in March 1984.[19]
- Attended many of the meetings of the English and Welsh RTDs as the SNBTS representative.
- Attended some of the meetings between Haemophilia Centre Directors and English and Welsh Regional Transfusion Directors,[20] as well as those in Scotland.[21]
- Was a member of the Working Group on Trends in the Demand for Blood Products formed in 1977.[22]

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[16] PRSE0002529
[17] NHBT0000189_173
[18] PRSE0000348
[19] SBTS0000138_037
[20] CBLA0000473 and CBLA0001446
[21] PRSE0001556
[22] DHSC0002189_014

- Was a member of the Medicines Inspectorate's Ad Hoc Project Steering Group set up in May 1982 to advise the Blood Transfusion sub-committee on the proposed work to PFC and to co-ordinate matters relating to the Medicines Inspectorate.[23]

- Attended many of the meetings of the Advisory Committee on the National Blood Transfusion Service (NBTS) as an observer.[24]

- Attended some meetings of the Scottish and Northern Ireland Coagulation Factor VIII Working Party.[25]

- Attended the NIBSC/UKBTS Liaison Committee which had its first meeting on 18 March 1987.[26]

Interactions with the Scottish Home and Health Department

17. Professor Cash was appointed as Consultant Advisor on Blood Transfusion to the Scottish Home and Health Department ("SHHD") from 1979 to 1986.[27]

18. On 18 January 1986, Professor Cash wrote a critical letter to Dr McIntyre at SHHD:

> *"I write to express my grave concern at the way colleagues in SHHD have been put in a position (and appear to have accepted this position) in which they are prepared to challenge the professional competence of my senior scientific and medical staff. I refer to the matter of our plans to validate the safety of our heat treatment processes with respect to AIDS viruses. The good professional relationships we have enjoyed over many years with colleagues in SHHD are too precious a commodity to the SNBTS for me to do anything that would cause unnecessary harm. On the issue in question therefore I would*

[23] PRSE0001439
[24] See for example CBLA0001207 and CBLA0001208
[25] SBTS0000300_043
[26] NHBT0108865_010
[27] PRSE0001514

wish only to conclude that we have agreed that the plan is not an overkill reaction, that it never was our intention to validate spiking experiments in patients nor undertake spiking activity within the production facility at PFC. Whilst I acknowledge that those of us who work within the public sector must accept the ultimate dominance of 'political' considerations, I would, at this time, make a plea that those of your colleagues who continue to express concern at "spiking" procedures being done in PFC come to PFC, look at the relevant facilities and discuss the problems with Dr Perry and his staff'. Should you wish to have any senior virology consultant join your party then we would have no objection: indeed Dr Cuthbertson, our QA Manager, who is himself a virologist would welcome this. I was most grateful for your clearance that we could press on with making arrangements to send a senior scientist down to the Chester Beatty Institute. Dr Perry and I have now been to the Institute and arrangements have been made to expedite matters. In the meantime we have just learnt that the Medicines Commission not only approve of what we have proposed but are making this a mandatory activity for all plasma fractionators and require the preliminary validation data by the end of 1986. I am about to go off to the Far East and would suggest that you take up these matters with Dr Perry direct."[28]

19. On 24 March 1986, he resigned from his role as Consultant Advisor to the SSHD, stating:

    "*It has been my privilege to act as Consultant Adviser in Blood Transfusion to the Scottish Home and Health Department since 1979.*

    I take the view that it is no longer appropriate for me to hold this formal position, which has attached to it a modest honorarium, I would therefore wish to resign."[29]

20. In his response to David McIntosh's C4 Witness Statement to the Penrose Inquiry, Professor Cash commented that whilst in theory the SHHD could, at any time, have "*gone its own way*," Scottish Ministers often invited the DHSS to take the lead on

[28] PRSE0002563
[29] PRSE0001514

policy development, and the SHHD considered UK solidarity to be a "*substantial policy commitment*" with regard to donation screening. He sought to persuade Scottish Ministers to develop a separate Scottish policy approach.[30]

21. In a letter to the SHHD in 1990, Professor Cash stated that there were "*serious defects in the operational liaison between SHHD and DHSS with regard to Blood Transfusion matters*" throughout the 1970s and 1980s.[31]

Relationship between Scottish blood services and the rest of the UK

22. On 14 March 1969, Professor Cash attended a meeting at the Edinburgh Regional Transfusion Centre ("RTC") with representatives from the Scottish (Cumming, Watt) and English (Pendreigh, Maycock, Vallet) blood services, at which the building of new fractionation centres at Liberton (PFC) and Elstree (BPL) was discussed. The minutes record:

> "*The need for standing arrangements for co-ordinating policy matters at departmental level which affected both B.P.L. Edinburgh and B.P.L. Elstree was discussed. It was suggested that, in the first instance a co-ordinating committee might be formed of officers from D.H.S.S. and S.H.H.D. On such a committee representation of the medical, administrative and financial sides would probably be necessary, together with representatives of the two units concerned. It was agreed that S.H.H.D, should be asked to put a proposal on these lines to D.H.S.S.*"[32]

23. The same group met again on 27 June 1969, and jointly discussed matters including projected revenues, equipment and processes, transportation, range of products, and record-keeping.[33]

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[30] PRSE0004020
[31] SBTS0000187_047
[32] PRSE0002199
[33] SBTS0000470_090

24. In his B3 witness statement to the Penrose Inquiry, Professor Cash commented that upon taking up his position as National Medical Director of SNBTS he found the relationship between the directors of the PFC and BPL to be "*greatly strained*". He describes in 1980 trying to arrange a meeting between the PFC and BPL management teams with a view to exploring ways of developing factor VIII concentrate production and associated research on a joint UK basis. However, *"BPL management refused to agree to such a meeting – I was later to learn this had the support of DHSS."*[34]

25. The minutes of a meeting of SNBTS directors held on 23 June 1981 record that Professor Cash and Dr Mitchell had been invited to attend meetings of English and Welsh directors. In return, SNBTS directors agreed to Professor Cash's suggestion to invite Dr Wagstaff as well as Dr Tovey to the meetings of SNBTS directors as observers.[35]

26. In his B3 Penrose statement, Professor Cash described a "*difficult"* meeting with BPL on 15 December 1982, at which he expressed his opposition to SNBTS supporting clinical trials on UK haemophilia patients of US sourced commercial factor VIII concentrates that had been subject to some form of viral inactivation. His reasoning was that the small group of patients who had never been exposed to commercial concentrates (the highest percent of whom were in Scotland) should be kept in reserve for UK (NHS) fractionators to validate their own viral inactivated products, not *"given away"* to commercial interests. Subsequently SNBTS contacted Haemophilia Centre Directors in Oxford, Edinburgh and Glasgow to stake an SNBTS 'claim' on access to their patients.[36]

27. Following his resignation as Consultant Advisor to the SHHD, Professor Cash wrote an article, published in the BMJ on 12 September 1987, which was heavily critical of the NBTS, labelling it a "*fragmented and disorganised shambles*".[37] The article made the following points:

[34] PRSE0002836
[35] PRSE0003924
[36] PRSE0002836
[37] PRSE0000598

a. In 1985, Scotland had identical annual per patient usage of factor VIII as in England, but no commercial purchases whereas in England a third of the material used was commercial product. He says, "*The consequences of these figures in terms of infection with the human immunodeficiency virus in this group of patients is self evident*."

b. There was a failure by the NBTS to meet demand for blood and blood products: "*The sustained failure of the transfusion services in England and Wales, known as the National Blood Transfusion Service, over the past two decades to meet the needs of the National Health Service extends far beyond the provision of factor VIII concentrates. In London and the home counties there are chronic and occasionally serious shortages of blood, which have an appreciable impact on both the NHS and a large uncontrolled private sector. There are many areas of the country in which the supply of platelet concentrates from regional blood transfusion centres is restricted for operational reasons, and there are severe shortages throughout England and Wales of specific immunoglobulin preparations and albuminoid products*."

c. Inappropriate supervision by hospital blood banks meant "*there is both overprescribing and underprescribing and thus unnecessary exposure of patients to iatrogenic hazards and waste of precious, often irreplaceable, and costly resources".*

d. There was a lack of standardised regulation: "*These centres continue to produce therapeutic products against no nationally agreed specifications, yet are within nine months of new legislation on product liability*."

e. He criticised the "*infrequency with which the DHSS convenes its Blood Transfusion Service Advisory Committee and the indifferent quality of its business*" and the lack of regional consultation on important policy decisions.

f. He concluded, "*Undoubtedly over the past 25 years there has been a remarkable failure of senior civil servants and therefore politicians of all political colours to recognise the unique and strategic importance of the*

nation's blood donors, their donations, and the associated work of the blood transfusion services. It has not been simply a matter of budgetary restrictions but primarily a lack of interest, vision, and commitment."

g. He recommended, "*Above all, the overriding operational priority must be a commitment to provide blood and blood products to the NHS that is based on patient need in a cost effective manner. Current trends which view the voluntary blood donor as a source of marketable commodities need to be challenged and debated.*"

28. Professor Cash later reflected on the relationship between the services in a letter dated 11 January 1990 written in the context of the HIV litigation:

> "*… during the anticipated litigation efforts will be made to demonstrate that there were serious defects in the operational liaison between SHHD and DHSS with regard to Blood Transfusion matters. I have to tell you that in my view this is a correct interpretation and is no better today than in late 1970 and throughout the 1980s. I attempted to persuade, on numerous occasions, both the CSA and SHHD that there was an urgent need for policy harmonisation and joint programmes of work: I even went and saw Mr David Smart (previous Chairman of CBLA) and pled with him to no avail. I persuaded Sir Simpson Stevenson (Chairman of CSA) to go down to visit Mr Smart and he subsequently declined to brief me on what transpired. In all these exercises I had kept the relevant SHHD Undersecretary fully briefed and on every occasion I was advised that the problem was in DHSS.*
>
> *I sense the ineptitudes of the past (1970s - 1980s) are about to catch up with us and am of the opinion that this anticipated litigation should be settled out-of-court, if possible.*"[38]

[38] SBTS0000187_047

29. In a statement to the Penrose Inquiry, he wrote that he felt the SNBTS was "*increasingly being caught up in the politically controlled management chaos of the NBTS*".[39]

30. At the final English Regional Transfusion Directors Meeting on 19 January 1989, it was noted that:

> "*With reference to Scotland, it was recognised that the only remaining formal contact across Hadrian's Wall, would be between Dr. Gunson and Prof. Cash, as the National Medical Directors*."[40]

31. This changed on 27 June 1990 when the first meeting of the NBTS/SNBTS Liaison Committee took place.[41] These meetings were alternately chaired by Dr Gunson and Mr MacIntosh (General Manager of SNBTS). Professor Cash was one of the attendees. The meetings covered a wide variety of topics including the date for HCV screening, quality assurance, register of research and staffing and training issues. The minutes of the first meeting record that SNBTS had provided NBTS with units of blood (4,000 since 1st April 1990 – said to have been necessitated by QA failures in three RTCs).

Professor Cash's views on licensing and product liability

32. Professor Cash attended his first Regional Transfusion Directors' Meeting as Medical Director of SNBTS on 27 June 1979. At the meeting, he expressed concern about product liability:

> *"DRAFT CONSULTATIVE PAPER ON PRODUCT LIABILITY - RTD(79)6*
> *Directors were worried that they, as producers of blood products at the RTCs, could be held personally responsible if the product was eventually found to be defective…. Dr Cash thought that it was difficult to discuss product liability*

[39] PRSE0002223
[40] SBTS0000628_011
[41] NHBT0000189_173

until the Department decided whether the NBTS should be covered by Crown privilege, and if there was to be no Crown privilege then the Government would have to provide financial support in the event of a mishap leading to liability. ...'[42]

33. His concern about Crown immunity was in sharper focus following the AIDS crisis of the 1980s. On 5 February 1987, he wrote to Mr J T Donald, General Manager of the Common Services Agency[43] in Edinburgh:

> "*Blood/Blood Products: product licences*
>
> *Bob Perry and I attended an informal meeting in SHHD on the 3rd February l987 (Dr MacIntyre, Dr Forrester and Mr Calder (Chief Pharmacist) were present).*
>
> *Mr Calder made it very clear that Boards (and presumably the CSA) had been advised several years ago that there was no requirement for SHS manufacturers of pharmaceuticals to obtain product licences. The reason for this was the privilege of Crown Immunity. Mr Calder went further and indicated that if SHS had ignored this circular and gone ahead with licensing products then Crown Immunity would no longer apply and if any legal action arose from products so licensed then the Agency would be liable and possibly the Director of PFC (who has no medical defence cover) and myself.*
>
> *Mr Calder further advised that product licenses were required if products were to be sold and he conceded that this would appear to be the case who the CSA supplied products to Private Hospitals.*
>
> *I do not at this time wish to enter into any unnecessary wrangles in terms of who didn't tell what to whom or why previous SHHD colleagues collaborated with us in getting product licences but I do most strongly advise that you arrange an urgent meeting with Mr Hugh Morison with a view to getting the matter clarified.*
>
> *In the meantime I will make four points:-*

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[42] DHSC0002367_003 p.7

[43] The Common Services Agency of the Scottish Health Service was responsible for SNBTS - NHBT0002934

1. There are 15 haemophilia A patients in Edinburgh who have been unequivocally infected with HIV from PFC product which we believe is licensed (thus we presume no Crown Immunity). You will be aware of the pending legal actions with regard to the Glasgow patients.

2. We have several products we believe are fully licensed. Is it the Agency desire that we immediately seek to revoke these licences?

3. Is it the Agency desire that all work currently going on licence PFC products should stop - we plan to amend our Factor VIII licence (for 28) early in April?

4. You may wish to consider, after appropriate consultation, reissuing the Private Sector Agreement with an additional clause containing a disclaimer of liability."[44]

34. Professor Cash's belief that applying for a product licence could affect Crown immunity was erroneous according to a letter from a Legal Advisor to the Common Services Agency, who wrote on 11 May 1987:

"I refer to your memo of 22 April enclosing a copy of a letter of 5 February received from John Cash.

As far as I am aware the relevant circulars issued by SHHD are 1975 (GEN) 40 dated 13 May 1975 and 1975 (GEN) 73 dated 24 September 1975. These circulars provide that, since in Scotland it was considered that Health Boards (and the Agency) were not entitled to Crown exemption by virtue of their status as occupiers of hospital premises, they would have to apply for and hold licences as required by the Medicines Act 1968. I am not aware of these instructions having been altered by SHHD, although a stronger view has emerged in the interim from Lord Advocate Mackay that Health Boards (and the Agency) are Crown bodies and entitled in appropriate cases to Crown immunity (SHHD/DS(81)1). In fact, there is currently before the Inner House of the Court of Session an appeal from a decision by Lord Prosser in an interim interdict petition against Greater Glasgow Health Board that the

[44] PRSE0003850

Board does not enjoy Crown status. This point, therefore, has not yet been judicially determined in Scotland, so that it might be premature to alter the advice tendered in the 1975 circulars.

I cannot understand the reference to Crown immunity not applying in the event of product licences being obtained- Crown immunity can be pleaded at any time, and the fact of having done something which the immunity made unnecessary does not preclude immunity subsequently being claimed- The only effect of such immunity in the present context would relate to offences and prosecutions under sections 123 to 125 of the 1968 Act and, if appropriate, a plea of Crown immunity could be taken by the Agency and/or its employees regardless of the existence of product licences. The matter of raising and pursuing claims for damages on the grounds of negligence in respect of product manufacture is one which is in no way affected by Crown immunity especially in the light of the two 1975 SHHD circulars. The point is that the policy in the matter is that pharmaceutical manufacture in the NHS is controlled under the licensing provisions of the 1968 Act in broadly the same way as applies to commercial pharmaceutical manufacture - regardless of whether or not Crown immunity can be argued.

Finally, I cannot understand why it should have been suggested that product licences were required if products were to be sold - regardless of whether or not Crown immunity arose. Section 8 of the 1968 Act provides for both the "manufacturers' licence" and the "wholesale dealers' licence. Any Crown immunity from the 1968 Act would apply to the entire Act, so that in this context the two licences are indistinguishable."[45]

35. The issue of product licences was revisited at an informal meeting between SNBTS and SHHD representatives on 26 October 1987. It was suggested that PFC products did not require licensing but there was a presentational advantage in doing so, whereas the RTCs were not making *"medicinal products"* so the position was complicated. Notes of the meeting record Professor Cash's contribution as follows:

[45] PRSE0002909

"*Professor Cash suggested that a specification should be drawn up for the production of the RTCs' medicinal products, which could, if appropriate, be agreed with the Medicines Inspectorate. However if a product or a process did not fall within the conditions imposed by the Act (or was exempt) then the Medicines Inspector would have no role in inspecting, monitoring or advisory on these products/processes*."[46] (sic)

36. Concerns regarding product liability were raised again in 1987. Dr Perry, Director of PFC, wrote to Mr Donald, General Manager of the Common Services Agency, on 21 December 1987, copying in Professor Cash:

"*… I must conclude that in the face of existing laws of negligence and the new consumer protection laws, I (and my senior colleagues) remain exposed and vulnerable in an area of product manufacture which attracts considerable public attention. Perhaps my sustained anxieties stem mainly from the fact that the manufacturing activities of the Centre are at a level substantially above that for which the Centre was designed and there exist major breaches of GMP in our day to day activities as a consequence which can only be resolved by the provision of additional buildings. One might argue therefore that I am professionally negligent in allowing such activities to continue. However, I continue to do so in the interests of self-sufficiency and, in my opinion, in the public interest. The Agency is aware of this position but to my knowledge, has never explicitly instructed me to continue with a policy of growth. I am therefore knowingly operating the Centre above its capacity and I am ever conscious of recent disasters elsewhere whereby the corporate body and individuals are subject to criminal proceedings. As the captain of this particular ship, I find the analogy too close for comfort.*

Clearly, I am not implying an imminent disaster at PFC since we continually make strident efforts to compensate for deficiencies at the Centre but I believe it is appropriate and reassuring for myself and senior staff) that we clarify unequivocally that the Agency is aware of the deficiencies at the Centre and

[46] PRSE0004722

has authorised the continuation of activity at the present level. I recognise that this amounts to an instruction to carry out our professional duties outwith minimum standards required of the pharmaceutical industry but in the circumstances, such an instruction will at least relieve some of the anxiety felt by myself and senior colleagues."[47]

37. Mr Donald replied sometime later on 13 June 1988:

> *"...Regarding the Consumer Protection Act it is clear that the view of Duncan Macniven and Jim McCubbin that this is a red herring in this particular context. It neither increases nor decreases the personal liability of the staff at the PFC.*
>
> *... Now setting the strict legal position aside, it is Duncan's view that the arrangements which have been agreed for the licensing of PFC and certain of its products in accordance with the Medicines Act should give substantial reassurance to you and your colleagues on the points which you have raised. In fact that is indeed one of the reasons why he thought that licensing was desirable. He does not accept PFC is operating outwith the standards required of the pharmaceutical industry. The products are of the required standard and are clinically safe. He adds that there is no evidence that the products from PFC are otherwise and, where product licences (or their equivalent) have been applied for, they have been granted."*[48]

38. This sparked a strongly worded response from Professor Cash, on 20 July 1988:

> *"... I am bound to put on record my concern at the comments you have attributed to Duncan Macniven, for it is my professional view that PFC has and is operating outwith the standards of the pharmaceutical industry. The evidence for this can be summarised as follows:-*

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[47] PRSE0000712

[48] SBTS0000187_012; see also earlier correspondence between them at PRSE0000640 and PRSE0000712

1. PFC has manufactured product which has unequivocally endangered the lives of patients. The two recorded occasions since it was commissioned in 1975 (the second one just months ago) were of course investigated and it is my view that breaches of GMP could not be ruled out.

2. There have been a number of occasions when I have been called upon to authorise the issue of products which failed to meet specification. I have on many occasions since 1979 with Bob Perry's support, given authorisation, over the head of the QA Manager, in order to keep supplies in place for the SHS.

3. Unlike our sister commercial organisation we have received no instruction to clear all batches of PFC products with the National Institute of Biological Standards and Control — before we issue for clinical use.

4. Notwithstanding the awaited formal report of HM Medicines Inspectors both Bob Perry and myself were party to a conversation which clearly indicated that on the basis of breaches of GMP PFC's continued function rested on the provision of crown immunity.

5. It is important for us to remember that the provision of a product licence in the pharmaceutical industry will only take place if the manufacture has a manufacturing licence. This does not seem to have applied to PFC and for Duncan Macniven to equate the acquisition of a product licence by PFC with good (safe) manufacturing practice is inappropriate.

It is with my earnest hope that in the months ahead our current collective public interest stance will be vindicated, but more important for the future, particularly as we approach the time for new legislation ... ... that we enhance the quality of the management of the SNBTS to a point where clear policy objectives are available ..."[49]

39. On 6 July 1989, Mr McNiven advised Mr Donald:

[49] PRSE0000462

"*As regards the import of blood products, John Cash suggested when we met on 1 March that the Directive would not be effective unless the Scottish Health Service "bought" its blood products from the SNBTS (as distinct: from the reality of the present situation, where the Scottish Health Service uses the SNBTS as its "in-house" source of blood products, with no money changing hands). That is a possible interpretation of this Directive, read on its own. But, not surprisingly, the other Directives to which it refers: (and of which I enclose key sections) require Member States to conduct the operations of their Health Services in a fashion which makes explicit the costs of supply (in-house or not). So the fact that SNBTS does not at present charge Boards for blood and blood products does not exempt us from the Directive.*"[50]

Guidelines and standards

40. On 18 March 1987 Professor Cash attended the first meeting of the NIBSC/UKBTS Liaison Group where it was agreed that there should be collaboration in formulating scientific guidelines for the standardisation and safety of blood and blood products provided by the UKBTS. The meeting minutes provide as follows:[51]

> *"The aims of the Liaison Group included: the formulation of Guidelines for the Manufacture of Biologicals for use in Transfusion Medicine; guidance on in-process control; final specifications for products made at the Blood Products laboratories in Elstree and Edinburgh for national use, and those made at Transfusion Centres for local use; the setting up of biological standard needed for production control or for diagnosis; and identification of topics arising from such work that required research. The proposal for the formation of this Liaison Group and its work, outlined in a letter (24.2.87) from Dr Schild, had been accepted and agreed enthusiastically by the membership listed.*"

[50] PRSE0000039
[51] NHBT0108865_010

41. On 8 August 1990, Professor Cash wrote to the National Institute for Biological Standards and Control ("NIBSC"), regarding the development of NIBSC National Standards for HIV and HCV:

> *"NIBSC: UK BTS: MICROBIOLOGY*
>
> *As many of us become increasingly involved in the fine details of the impending litigations associated with HIV, it is becoming increasingly evident to me that there is an urgent need, particularly also against the background of the impending legislation associated with the EC Directive 89/381, that NIBSC becomes pro-active in the general area of the transmission of microbial diseases by blood and blood products. There will, of course, be an involvement in the context of the Institute's responsibilities to monitoring large pool fractionated products but I am particularly concerned that your microbiology team begin to develop a commitment to the whole question of donation testing.*
>
> *We desperately need to address many things but I believe just at the moment the highest priority ought to be given to the preparation of National Standards, particularly for HIV and HCV.*
>
> *NIBSC has made, in its support of the development of the UK Guidelines for Blood Transfusion Services, quite profound contributions to the future development of UK BTS. It is time to press on and the area of those aspects of microbiology which are relevant to Regional Transfusion Centres is now desperately needing your attention."*

42. The collaboration between the UKBTS and NIBSC resulted in publication of the Guidelines for the Blood Transfusion Service in the UK (commonly known as the Red Book). The first edition came out in 1989[52] with the revised second edition being published in 1992.[53] These included guidelines on the selection of donors.

[52] NHBT0000027_030
[53] NHBT0054484_003

Self-sufficiency

43. In an interview on 30 May 1990, Professor Cash commented:

> "*It was always assumed in Scotland, ever since I joined the service in 1962/3, that our job was to provide all blood and blood products required for Scotland. The concept of self sufficiency more clearly emerged in 1975, against the background of the WHO report. My (personal) interpretation of self sufficiency from the WHO recommendations was that we must develop a programme which led us to advise the commercial providers of plasma products that they were no longer required. Such sentiments, of course, had political connotations and, in those days, one sensed we didn't have overt Scottish Office support for the concept of "Commercial companies go home" but we did sense strong Scottish Office support for the idea that we should get going and make as much as the Scottish Health Service patients needed*".[54]

44. At a meeting of Haemophilia Centre Directors on 18 September 1975, Professor Cash was recorded as contributing as follows:

> *"the target of 375,000 donations was quite inadequate. The MRC Working Party estimate of 500,000 donations was a minimum estimate and the need was likely to exceed this amount. Dr. Cash said that there was a difficult lag phase between the collection of plasma and its issue as concentrate."*[55]

45. Professor Cash also attended a Directors' Meeting of the SNBTS held at the PFC on 30 September 1975. The minutes record a discussion of the fact that intake of FFP to PFC was declining. Directors were asked to reduce their production of cryoprecipitate as stocks of intermediate factor were building up and to send the equivalent in FFP to the PFC.[56]

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[54] SBTS0000053_055
[55] OXUH0003735
[56] PRSE0001612

46. On 17 December 1979, Professor Cash attended the first meeting of the Blood Transfusion Research Committee. The minutes record:

> *"Dr Cash thought that there was a need for further studies of the use of PPF and other albumin solutions. He considered that there was little difference in the content of prekallikrein activator between different PPF's, but PPF occasionally caused renal failure or changes in the noradrenaline status of patients, particularly those in shock. Since 1975 the Edinburgh policy had been automatically to provide red cell concentrates for the first two units of blood requested but thereafter bleeding patients automatically received whole blood. Only about 20% of patients needed more than 2 units during any one 'transfusion'. Professor Stratton agreed that a British trial was probably still necessary to convince surgeons to use plasma reduced red cells. Dr Cash thought that the major increasing need for plasma in the future was to supply factor VIII but Professor Stratton felt that this need was limitless and could never be satisfied with available technology. Dr Cash noted that the target in the United States for factor VIII production was 1.8 m Units per million of the population. Though much factor VIII was now imported into the UK, he thought that eventually the UK should aim to be self-supporting. Dr Jenkins commented that the transmission of non-A, non-B hepatitis was still a problem with factor VIII concentrates."*[57]

47. On 1 December 1980, Professor Cash attended a meeting to discuss UK self-sufficiency in blood and blood products with representatives from the SHHD, the DHSS, the DHSS Northern Ireland and the Welsh Office. The minutes of the meeting record that:

    a. *"Scotland was almost self—sufficient (e.g. 5 million ius of Factor VIII were currently produced and one million ius purchased commercially)."*

[57] CBLA0001040

b. "*Although at the moment England, Wales and Northern Ireland were being supplied by BPL it was agreed that the Protein Fractionation Centre Edinburgh could play a role in helping to meet total UK needs.*"

c. "*Dr Cash's view was that in order to meet the rising UK demand for blood products the target for plasma collection would have to be in the region of 1 million litres per annum. Experience in Belgium, which also had a voluntary donor system, had shown that this could be possible if a major plasmapheresis programme were set up.*"

d. "*Meanwhile, in the short term, Dr Cash and Mr MacPherson explained that PFC could fractionate an extra 500 litres of fresh frozen plasma (ffp) per week to produce Factor VIII and albumin, provided the Medicines Inspectors saw no difficulties… In the longer term it was considered that PFC could cope with up to 1500 litres per week, and perhaps more provided funds were made available and provided agreement could be reached on shift working… There was a possibility that ultimately PFC might be able to meet up to half the UK's requirements for blood products.*"

e. "*It was agreed that the question of how future UK fractionation might be divided between BPL and PFC would have to be discussed in detail once total requirements had been defined. One possibility might be that PFC would fractionate plasma from the 4 Northern English Regions and from Northern Ireland.*"[58]

48. On 30 January 1981, Professor Cash attended a meeting of SNBTS Directors and Haemophilia Centre Directors. The group had not met since 1977. Dr Cash presented a paper "Trends in Plasma Procurement and Production of Factors VIII and IX Concentrate" which set out details of production over the period 1975-1980. The data presented showed for 1970 and 1980 *"a significant and apparently increasing quantity of commercially produced factor VIII was being used".*[59] The reasons for this were discussed, with Haemophilia Centre Directors reporting that sometimes only

[58] DHSC0000064
[59] PRSE0000144

commercial product was available or for clinical reasons a high purity product was required. PFC intermediate factor VIII was said to have slower solubility and some patients experienced more side effects with it. The minutes record that "*Dr Cash emphasised the important part cryoprecipitate could play in haemophilia treatment*" and he suggested considering whether cryoprecipitate could be used for home therapy; however, the Haemophilia Centre Directors were not in favour of this suggestion.[60]

49. On 4 March 1981, Professor Cash attended a meeting of the Haemophilia and Blood Transfusion Working Group.[61] At that meeting Professor Cash expressed concern at the level of commercial material being purchased and it was agreed the aim was for Scotland to be self-sufficient. Professor Cash suggested that self-sufficiency included the provision of a reserve stock capable of meeting unexpected demands such as a temporary failure at PFC.

50. On 22 June 1981, Professor Cash attended the third Meeting of the Advisory Committee on the National Blood Transfusion Service.[62] At that time, an issue impeding increased production at BPL was sufficiency of plasma donations. The idea of buying plasma from abroad was rejected as risky and impractical. The minutes record that "*Dr Cash suggested that any temporary surplus capacity might be utilised by fractionating, on an agency basis, plasma from other voluntary donor systems.*"

51. At a meeting of SNBTS and Haemophilia Centre Directors on 21 January 1983, the commitment to Scottish self-sufficiency was re-affirmed, and a specific concern regarding distribution to Edinburgh raised:

> "*The Chairman* [Dr Bell] *stressed that the SNBTS had been set up to have the capability to cope with all Scottish requirements, other than those few therapeutic agents the production of which might not be justified on a very small scale, and that in terms of national policy the purchase of commercial products should be avoided so far as possible. Dr Ludlam also expressed some*

[60] PRSE0000144
[61] SBTS0000382_008
[62] CBLA0001388

misgiving that Edinburgh perhaps did not receive as much PFC factor VIII concentrate as it should pro rata. It was remitted to Dr Cash, Dr McClelland and Dr Ludlam to resolve any problems which had arisen in relation to supplies to Edinburgh."[63]

52. At a meeting of the SNBTS Co-ordinating Group on 24 May 1983, it was noted that "*the PFC had received a record input of 61,000 kg of plasma in the year to 31 March, 1983*" but that the existing staff levels and technology meant only 50,000kg could be processed. Professor Cash explained a proposal had been made to introduce shift working to boost productive capacity.[64] In a later letter writing in the context of the HIV litigation, he explained that, "*PFC undertook a Shift Experiment (worked day and night for 3 weeks) in 1980/81 and demonstrated in this mode they had very substantial spare fractionation capacity and that the products produced were of higher quality than the existing (day work) arrangements... It was assumed by those of us on the shop floor that this experiment would expedite arrangements to give England and Wales assistance - but nothing materialised… Aside from the E/W connection PFC management are on record over many years of repeated requests for shift working facilities. It is my understanding - and that of PFC management - that SHHD consistently rejected these proposals. It is also the opinion of those of us involved in this succession of requests that the SHHD response on this issue was dictated by London and that this in turn was influenced by the Union ASTMS which had a closed shop at BPL and was opposed to shift working.*"[65]

53. On 2 February 1984, at a meeting of SNBTS Directors and Haemophilia Centre Directors, Professor Cash "*asked members to consider whether, given the present SNBTS production level of factor VIII concentrates, it was necessary to purchase commercially unless exceptionally a superior product was available.*" He also recommended reducing the number of batch exposures per patient per year.[66]

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[63] PRSE0001736 p.3
[64] PRSE0003620
[65] SBTS0000187_047
[66] PRSE0001556

54. At a meeting on AIDS held on 9 February 1984 at the National Institute for Biological Standards and Control, Professor Cash "*noted that Scotland is now totally self-sufficient and thought there might be an opportunity to study these patients who have not been exposed to commercial blood products...*"[67]

55. Professor Cash emphasised the goal of self-sufficiency in a letter to Dr Bell at the SHHD dated 25 June 1984:

> "*I came across the following in a Minute of the Central Consultative Committee on Blood Transfusion (held 4th July, 1974):-*
> *"Two meetings had been held between DHSS and SHHD and there had been agreement on broad matters of policy.*
> *DHSS were totally committed to the voluntary donor principle and would be prepared to consider the introduction of legislation if it was in danger. The aim of the two Departments was to achieve self sufficiency and this would involve DHSS in raising the level of blood donations from the present level of 1,500,000 per year to 1,800,000 per year and in educating clinicians to use more red cells. The first objective was to ensure that existing production was fully utilised.*"[68]

56. In the interview on 30 May 1990, Professor Cash commented that PFC was able to meet all of Scotland's needs sometime in 1983/4, and "*It wasn't the Fractionation Centre that was rate limiting. It was the availability of plasma.*"[69]

57. The minutes of the meeting of the SNBTS Directors and Haemophilia Directors on 5 March 1986 show that Professor Cash anticipated that demand for factor VIII would outstrip supply that year. The target for factor VIII production was 2.75 m.i.u./m.pop./year, which required additional funding. The current clinical uptake was then in the region of 1.7-1.8 m.i.u./m.pop./year but it was "*becoming clear that heat*

[67] CGRA0000610
[68] SBTS0000145_012
[69] SBTS0000053_055

treatment reduces yield to the extent that the current plasma supply is all committed".[70]

58. At an informal meeting between SNBTS and SHHD representatives on 26 October 1987, Professor Cash was confident that sufficient blood donation levels could be maintained to meet Scottish needs:

> "*Mr Macniven explained that the Department was keen for appropriate action to be taken if the SNBTS directors deemed it to be necessary, to maintain blood donations at the level necessary to meet Scottish needs. Professor Cash explained that the Directors were indeed considering this. They would not be slow to advocate action if they felt that it was justified. At first sight, however, he did not think that extra publicity was at present needed: it would indeed risk a large flood of donations which would substantially outstrip demand. It was possible that fine tuning (for instance by reviewing the AIDS guidance) was all that was required. The SNBTs Directors would consider the issue further and Professor Cash would be in touch with the Department.*"[71]

59. Professor Cash's SNBTS National Medical Director's Report for 1988-9 stated that in the previous year there had been a decline in blood donations, but now,

> "*the decline has been checked and certainly in some parts of Scotland it appears to have been reversed. We cannot be content to rest on our laurels for we believe we need to increase our blood collection programme by a further 40,000 donations per annum to meet the many and varied needs of patients in the 1990s… the effort required to stand still seems to be greater than it was in the 1960s and 1970s.*"[72]

60. In the same report, Dr Cash stated that plasmapheresis was being "*increasingly undertaken*" in Scotland.[73]

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[70] PRSE0001081
[71] PRSE0004722
[72] NHBT0002934
[73] NHBT0002934

61. In a discussion paper 'Self-Sufficiency in Blood and Blood Products' written in 1989 for SNBTS Directors, Professor Cash's assessment of Scottish self-sufficiency was notably pessimistic compared with earlier documents. In particular:

a. "*The lack of policy on this issue of self sufficiency in blood and blood products and appropriate and timely policies associated with the loss of Crown immunity have proved to be major factors in the deteriorating operational position of the SNBTS in the latter half of the 1980s.*"[74]

b. *"Current evidence (derived from discussions associated with the HIV/haemophilia litigation) would suggest that both SHHD and DoH are keen to pursue in the courts what, on matters of evidence, seems a lost cause, because they wish to secure the position that such Government departments have no legal duty of care."* [75]

c. He criticised the SHHD for failing to comment on proposed product targets and their "*sustained negative managerial approach*". [76]

d. He suggested that self-sufficiency ought to entail completely meeting the national need for blood products, and not simply being able to satisfy demand while services chose to also purchase products privately. In his view, "*It would appear that England and Wales have rejected the concept of national self sufficiency and espoused the emerging philosophy of European (EC) self sufficiency… Recent developments, the accruing of unwanted stockpiles of factor VIII and albumin and [at] BPL, may suggest that this hybridised and extended version of self sufficiency is inherently destabilising, almost impossible to control and manage and potentially really quite dangerous – to blood donor attitudes.*" [77]

[74] PRSE0004541 p.1
[75] PRSE0004541 p.2-3
[76] PRSE0004541 p.4
[77] PRSE0004541 p.4-5

e. That in Scotland, "*We had an all too brief macho period of self sufficiency for factor VIII*". [78] He explained further, "*Self sufficiency was made our operational policy by the SNBTS Directors, in isolation, in 1980. We achieved our objective in 1984 without any targeted additional resources, particularly staff resources. In this period total plasma input to PFC rose 114%. Total HIV-1 donation testing was introduced throughout the SNBTS in October 1985 without (with the exception of Aberdeen) any additional staffing resources (c.f. NBTS). The same applies to CMV donation testing. Since 1980 the production of platelet concentrates has increased by 46%, again with no increase in staff resources. Much the same applies to PFC, and all the time HQ has demanded increased facts and figures from hard pressed technical and A&C staff! And now SHHD demand efficiency savings.*" [79]

f. He suggested that factor and albumin production could all move to BPL and all immunoglobulin products be made at PFC. [80]

62. In 1992, Professor Cash gave a presentation on 'Donor Plasmapheresis: A View from Scotland', in which he stated at the present time the factor VIII concentrate made available from the recovered plasma source in Scotland totally covered the clinical demand. Donor plasmapheresis was a relatively small and specialised contributor to the plasma procurement programme in Scotland. He explained:

> "*The opportunity to achieve self-sufficiency has been much enhanced by the blood transfusion service having its own plasma fractionation centre. Thus a single organisation has managerial control over both plasma acquisition and its fractionation, the former represented by 5 regional centres and the latter by the protein fractionation centre. Control is manifest in the context of the acquisition of market intelligence and using this in planning, the selection of appropriate options for plasma procurement, fractionation and the associated research in both these areas. In all these matters we have sought to make*

[78] PRSE0004541 p.5
[79] PRSE0004541 p.10
[80] PRSE0004541 p.5

freely available to patients in Scotland blood and blood products of high quality and in a quantity which matches legitimate clinical demand."[81]

63. It is worth noting Professor Cash's views on the use of red cell concentrates (RCC). as part of the strategy to achieve self-sufficiency:

- In February 1972, Professor Cash published a report entitled "The Principles of Effective and Safe Transfusion", in which he urged clinicians to use RCCs whenever patients did not require whole blood.[82] He argued that the practice of giving whole blood had led to the wastage of several thousand litres of plasma and billions of platelets, and the alternative of using RCCs was simpler and safer. In his opinion, the practice of using whole blood had become entrenched because the Blood Transfusion Service had, up to this point, seen no reason to conserve plasma and so had not made RCCs available. This was not helped by the isolation of Scottish Regional Centres 'from the bedside', which meant it was difficult to effectively encourage the use of RCCs. Professor Cash argued, clinicians and the BTS ought to see routine whole blood transfusion as a *"thoughtless habit"*, and should not shy away from the realities of efficiency, in terms of optimal use of raw material.
- In August 1980 Professor Cash published an article 'Factor VIII supply and demand' in the BMJ criticising doctors who treated patients with whole blood rather than RCCs, which he claimed resulted in thousands of litres of fresh plasma a year being diverted away from producing Factor VIII in the UK.[83]

  "Although there are several outstanding exceptions, there is little doubt that unless those in charge of hospital blood banks are more successful in persuading their clinical colleagues to use red-cell concentrates rather than whole blood in the management of the majority of routine hospital transfusions, the creation of major new plasma fractionations facilities will not be the salvation Dr Aronstam seeks."

[81] SBTS0000603_027
[82] PRSE0002637
[83] PRSE0000110

64. In Scotland, approximately 80% of all donations were given as whole blood in 1971.[84] By 1976, 45.5% of donations were issued as RCCs.[85] By 1982 60% of donations were being processed into RCCs by having 220ml plasma removed.[86]

Knowledge of risk

Knowledge of risk of hepatitis

65. A Hepatitis Report was published by the Royal Infirmary of Edinburgh ("RIE") on 20 February 1970.[87] Professor Cash was involved in the work and the recommendations of the report, which were:

> "*1. That the Scottish Home and Health Department be asked to provide guidance as to the procedure to be followed by persons exposed to the risk of infection.*
>
> *2. That the S.E.R.H.B. be asked to provide facilities for the treatment of major hepatic failure in Edinburgh as soon as possible.*
>
> *3. That all close contacts in the treatment of [a patient who had died] be given gammaglobulin, and at the same time 5 ml. blood be taken off and sent to the Blood Transfusion Centre.*
>
> *4. That the City Hospital be informed of the above.*
>
> *5. That all cases of hepatitis occurring in the R.I.E. group be notified to the Medical Superintendent.*"

[84] PRSE0002637
[85] PRSE0002133
[86] SBTS0000231_024
[87] LOTH0000111_018

66. The Report further recommended the purchase of equipment for carrying out Hepatitis Antigen Tests.

67. That year, Professor Cash received a WHO Travelling Fellowship to visit the United States, where he "*investigated problems of Australia Antigen testing (hepatitis Associated Antigen), systems for the long term storage of cells by freezing, platelet therapy and tissue typing*".[88]

68. He was in correspondence with a Dr Charles Huggins of the Massachusetts General Hospital, who wrote to Professor Cash on 10 June 1970:

> *"The Department of Public Health in the State of Massachusetts is in process of establishing regulations that would require the use of Australia antigen negative washed frozen blood in the dialysis patients (see enclosed). We are in the process of (1 major equipment redesign to simplify the processing requirements for the frozen blood cells. A major objective in this effort will be to reduce the cost of the plasticware. Hopefully, this equipment could be made in the United Kingdom to eliminate the additional expense of shipment and duty."*[89]

69. On 24 January 1976, the BMJ published a letter from Professor Cash titled 'Commercial and NHS Factor VIII Concentrates', in which he gave his opinion that the need for purchase of commercial factor VIII would not be eliminated, "*not least because the present NHS production target for concentrates is too low*". He stated:

> *"There is no doubt that the import into the United Kingdom of factor VIII concentrates derived from external sources, however well screened for hepatitis viruses, represents an unequivocal pathway by which the level of a potentially lethal virus into the whole community is being deliberately increased."*[90]

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[88] LOTH0000127
[89] SCGV0000279_100
[90] PRSE0004064

70. Professor Cash was a member of the Reconvened Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody. At the first meeting of the reconvened group on 7 December 1978, one of the aims agreed was to "*To advise the Department [of Health] on measures which should be introduced to offer greater safety to recipients of blood and blood products and to protect the interests of blood donors*."[91] At the group's second meeting on 2 April 1979, it was agreed that blood donors should not be screened for raised transaminases as a potential indicator of hepatitis.[92] The group published a report in 1981.[93]

71. On 25 June 1981, Professor Cash attended the second meeting of the reconstituted Blood Transfusion Research Committee. During a discussion of post-transfusion hepatitis, it was noted that, *"the Working Party had been considering... the detection of non-A non-B carriers. Difficulties had been encountered as most carriers were anicteric and evidence of liver damage obtained from biopsies had had to be relied upon. Serum levels of alanine transaminase were used in America to indicate liver damage but would reduce greatly the number of possible donors. Dr Cash thought a prospective of alanine transaminase would nevertheless be valuable."* However, the Committee decided there was "*at present no need to screen potential blood donors for non-A non-B Hepatitis*".[94]

72. On 8 December 1981, Professor Cash chaired a SNBTS Directors' Meeting.[95] A summary of the meeting recorded that:

> "*Dr Cash recalled that the SNBTS had proposed to the NBTS Directors that a UK Working Party should be established on the subject of microbial contamination of blood products. It had been noted at the previous meeting that the proposal would be considered at the NBTS Directors' meeting in February. In the event the item had been deferred from lack of time and Dr Wagstaff had written on 25 February to all the Directors asking for their views*

[91] DHSC0002191_099
[92] CBLA0000931
[93] DHSC0002211_007
[94] CBLA0001396
[95] PRSE0003364

on a proposal to study post-transfusion hepatitis. Dr Cash agreed to draw Dr Wagstaff's attention to the fact that the SNBTS proposal had not been confined to hepatitis. Dr Cash reported that the MRC's Blood Transfusion Research Committee had decided recently to disband their Hepatitis Working Group, because a number of groups in the UK were studying hepatitis."[96]

73. Professor Cash was present at meeting on AIDS held on 9 February 1984 at the National Institute for Biological Standards and Control, where it was reported that 100% of haemophiliacs could be expected to contract non-A, non-B hepatitis and *"There seems to be some indication that the 100% incidence of non-A, non-B hepatitis is recent and is related to increased pool size since 1978."*[97]

74. In November 1989, Professor Cash was involved in discussions leading up to a product recall from PFC due to routine testing identifying a plasma pool that had been used to make factor VIII as positive for HBsAg. A *"major administrative error"* was suspected.[98] A further similar product recall took place in February 1991.[99]

Knowledge of risk of HIV

75. Professor Cash is reported as having drawn members' attention to articles concerning AIDS in the United States, and in the Observer and the Lancet, at a meeting of SNBTS and Haemophilia Centre Directors on 21 January 1983.[100]

76. On 22 March 1983, Professor Cash attended a meeting of the Haemophilia and Blood Transfusion Working Group. The minutes record that members were reminded of recent articles at home and abroad about AIDS. Dr Ludlam reported that in the UK a letter and questionnaire had been sent out to haemophilia directors. It was noted that:

"*AIDS was an emotive issue in the USA and Canada, and was causing a move away from factor VIII concentrate to the use of cryoprecipitate, with resultant*

[96] MDUN0000004_024
[97] CGRA0000610
[98] SBTS0000352_017
[99] SBTS0000010_061
[100] PRSE0001736 p.7

supply problems. There was concern that AIDS might appear in the UK, and the Haemophilia Society was attempting to reassure its members and put fears of infection from blood products into perspective. The Transfusion Directors were loathe to ask questions to which exception could be taken by potential donors but it was hoped that homosexuals and others at risk might be discouraged from being blood donors."[101]

77. On 15 February 1984, Professor Cash wrote to Dr Bell at the SHHD that the SNBTS Directors took the group view:

> "*That there should be formed a single UK group responsible to the Departments of Health for co-ordinating research in the area covering the interface between blood transfusion and AIDS. This group should have representatives of existing smaller groups already in existence - haematologists and haemophilia centre directors and of the SNBTS Directors.*"[102]

78. Professor Cash was copied into a letter dated 1 October 1984 from Dr Perry of the SNBTS to Dr Lane at BPL, regarding 2,000 vials of factor VIII produced at PFC which had failed their usual product specification:

> "*In our present supply situation it is not considered appropriate to issue this product for use in Scotland although in the past this would have been considered as one option for the disposal of this product when there was a shortfall in NHS supply. Bearing in mind the tentative evidence which is emerging in relation to the infectivity (AIDS) status of commercial product, Haemophilia Directors in England and Wales may well consider that the use of this "sub-specification" product is preferable to the use of commercial concentrates in some situations…* "[103]

[101] PRSE0000728
[102] PRSE0003911
[103] CBLA0001900

79. On 15 November 1984, Dr McClelland wrote to Professor Cash regarding "*the discovery that some recipients of PFC Factor VIII have developed antibodies to HTLVIII during 1984, which must, at present, be attributed to infusions of PFC product*". He reported that, "*it appeared that there are, so far 16 patients in whom seroconversion is known to have occurred during 1984 and who have received exclusively PFC factor VIII, or (in one case only) commercial factor VIII several years ago which can be discounted from the present problem*". A highly suspect batch of product which had been given to all but one of those patients had been withdrawn. [104]

80. Further details of this product recall were provided in Dr McClelland's email of 20 November 1984. He stated that on 27 October 1984, the day after six seroconversions were reported, and again on 30 October 1984, Dr Cash took the view that the data did not justify a product recall. The product recall decision was subsequently taken on 3 November 1984.[105]

81. The batch recall was discussed at the SNBTS Directors' Meeting on 11 December 1984. Further steps had by then been taken:

> "*Dr Cash recalled the decision taken at the Co-ordinating Group meeting on 20 November to quarantine the plasma from subsequent donations by donors who had contributed to the suspect pool and to discard the red cells, platelets etc. It had transpired that discarding cells would cause considerable shortage in some Regions, particularly over Christmas and the New Year and it had therefore been relaxed: the final decision on the matter would lie with individual Directors. All the plasma had been identified and notified to the Transfusion Centres who would continue to keep the donor samples. Dr Mitchell explained that a donor had been identified in his region who was presumed to be a homosexual and had given one donation which was weakly positive for VD. He hoped to have the actual donation tested for HTLV-III by Dr Tedder of the Middlesex Hospital: there was no possibility of testing the*

[104] LOTH0000005_052
[105] PRSE0000828

4,000 other donations in the suspect pool. After discussion it was agreed that the Directors should continue to hold the plasma of donors who had contributed to the pool, releasing the red cells and platelets for clinical use, until the result of Dr Tedder's test of the donor sample mentioned earlier. Dr Mitchell and Dr McClelland would notify the result of the test to other Directors."[106]

82. Professor Cash contributed to the UKHCDO AIDS Advisory Document published on 14 December 1984. This noted:

> "*Antibody positivity probably correlates with exposure to imported concentrates but there have been two notable recent episodes concerning U.K. concentrates…*
>
> *It seems probable that HTLV III has been incorporated into at least one BPL and one Scottish batch of factor VIII. Recipients are being followed up.*"[107]

83. This AIDS Advisory Document further advised that "*From now on all Scottish factor VIII will be dry heated to supply Scotland and N. Ireland.*"

84. On 24 January 1985, Professor Cash wrote to Dr Bell at the SHHD criticising the lack of strategy in relation to the unfolding AIDS situation:

> *"I have been seriously concerned by reports I have received from those who attended the meeting of the Working Group on AIDS "to consider the implications for the National Blood Transfusion Service of testing blood donations for antibody to HTLV-III" This meeting, from the stand-point of those left with the actual responsibility of running the UK Transfusion Services, was wholly inadequate. None of the really important matters which will affect policy were appropriately discussed and more importantly no arrangements were made for the creation of sub-groups to examine some of the many major problems, nor even was a date set for any further meeting.*

[106] PRSE0001767
[107] HCDO0000270_007

The SNBTS (Director) representative, the Chairman of the NBTS Directors' meeting and the DHSS Adviser on Blood Transfusion have all reported to me that they remain "completely in the dark".

...

The biggest anxiety of the NBTS Directors with regard to this problem is the Scots: that they will unilaterally move to come in line with the American proposals. They're right; we are in detailed discussion with commercial (kit) companies, our technical staff are already looking at ways of introducing the technology within existing staff establishments, we have the Western Blot technique (HQ and SE Labs), we are already liaising with local (Communicable Disease) physicians with a view to securing care for our positive donors and we are currently arranging our financial planning accordingly. I advised the NBTS Directors that we would do everything possible to avoid such a development. They were not impressed and cited our unilateral introduction of RIA HBs-Ag testing; the issue of heat treated factor VIII and our new AIDS donor leaflet. I had much sympathy with them for I am bound to reflect that "everything possible" isn't much when we're dealing with a non-existent management structure of a fragmented organisation led by the Department of Health which, as far as I can see, in terms of this aspect of the NHS, is lost and floundering in an increasingly high profile.

I write therefore once again to request that the SSHD pursues this matter into the UK arena."[108]

85. It could be said from this letter, that there was a perceived difference in the way the Scottish RTC Directors were approaching the HIV risk and that a desire on the part of the NBTS to maintain a united front may have been a factor holding the Scottish back.

86. On 29 January 1985 Professor Cash attended the Expert Advisory Group on AIDS meeting at which there was discussion about whether AIDS should become a

[108] PRSE0004386

statutorily notifiable disease.[109] Dr Galbraith presented two papers at that meeting, one on notification, [110] and one on surveillance.[111] It was agreed unanimously that statutory notification was not required and that an informal approach was to be preferred.

87. On 5 February 1987, Professor Cash wrote to Dr Perry at PFC:

> *"P.T. HIV*
> *I've just been reminded of some figures (Oct. 1986 CDC USA) which appeared and which maybe of value (assuming more media interest over the months ahead) to you:—*
> *Risk of death general anaesthesia 63/ 10,000*
> *Risk of death car accident 22/ 100,000*
> *Risk of death transfusion reactions 2/ 100,000*
> *Risk of AIDS from transfusion 1/1,000,000*
> *Also, "the risk of acquiring HIV from transfusion is three times less than death from tonsillectomy under general anaesthesia".*"[112]

88. At a RTC Directors' Meeting on 13 February 1990, Professor Cash warned that "*HTLV-I might be moving into the Scottish drug user population and that some form of surveillance should be mounted*".[113]

89. In his evidence to the Penrose Inquiry, Professor Cash identified his key concerns about the UKBTS' response to HIV/AIDS were:

> *"(a) a lack of effort to ascertain whether there were some safer options with regard to the purchase of commercial coagulation factor concentrates (b) delays in the generation of new guidelines on donor selection (c) delays in assessments of HIV donation screening kits (d) insufficient effort to examine*

[109] PRSE0002734
[110] DHSC0002257_027
[111] DHSC0002257_028
[112] SBTS0000034_026
[113] PRSE0000205

the efficacy of HIV confirmatory tests and (e) insufficient effort to develop alternative donation testing sites for non blood donors."[114]

Responding to and/or reducing the risk of infected blood / blood products

Alternatives to factor VIII

90. On 18th September 1976 the BMJ published an article by Professor Cash titled "Haemophilia A and the Blood Transfusion Service: A Scottish Study".[115] This provided that cryoprecipitate was suitable for home treatment.

91. Professor Cash was part of a working group on 'Trends in the Demand for Blood Products', appointed by the DHSS in January 1977.[116] They produced a report in December 1977 in which it was stated that *'We believe the long term aim should be the complete transfer of cryoprecipitate to a fractionated freeze dried concentrate.'*

92. Professor Cash attended a meeting on 4 March 1981 of the Haemophilia and Blood Transfusion Working Group.[117] At that meeting there was a discussion about the introduction of freeze dried cryoprecipitate. Professor Cash was asked to comment on the proposal that free dried cryoprecipitate should be produced with a view to studying, on a multicentre basis, its role in home therapy. Professor Cash put forward two factors in favour of this product - first the increased yield and secondly the increased pool size - going on to say

"although there was a school of thought in the UK that the larger pool size may increase the risk of hepatitis."

[114] PRSE0003395
[115] PRSE0003425
[116] CBLA0000672
[117] SBTS0000382_008

93. He urged members to think carefully before embarking on a full-scale programme noting that the majority of home therapy patients had no problems when using cryoprecipitate and in Belgium it was used extensively

94. At a meeting of SNBTS and Haemophilia Centre Directors on 21 January 1983, freeze dried cryoprecipitate (FDC) was discussed:

> *"Dr Cash expressed SNBTS thanks to those who undertook the successful clinical trial of this product in the west. Notwithstanding this work, it had been decided to abandon production of FDC meantime, having regard to the closure of the plasma freeze drying plant at Law and the cost of meeting the standards demanded by the Medicines Inspectorate. The prospective availability of a hepatitis risk reduced factor VIII concentrate also cast uncertainty over the future of FDC at the present time."*[118]

95. Dr Cash sent his apologies to the meeting that took place between a large number of Haemophilia Centre Directors (including some from Scotland) and others including Dr Perry of PFC, Dr Brookes of Dundee RTC, and Dr Boulton who was deputising for Professor Cash, on 17 October 1983.[119] At that meeting, Dr Chisholm, the director of the Southampton Haemophilia Centre, raised an issue at the end of the meeting under AOB:

> *"Dr Chisholm raised the problem of patients refusing to take up commercial factor VIII concentrates because of the AIDS scare. She wondered in view of the worry of the patients whether the Directors could revert to using cryoprecipitate for home therapy. Professor Bloom replied that he felt that there was no need for patients to stop using the commercial concentrates because at present there was no proof that the commercial concentrates were the cause of AIDS. Dr Chisholm pointed out that there was a further problem in her region because of problems getting large amounts of commercial concentrates whereas she could get unlimited supplies of cryoprecipitate. Other Directors reported that they had the same problems. After discussion it*

[118] PRSE0001736 p.3
[119] PRSE0004440

was agreed that patients should not be encouraged to go over to cryoprecipitate for home therapy but should continue to receive the NHS or commercial concentrates in their usual way."

96. In an interview on 30 May 1990, Professor Cash was asked about cryoprecipitate and commented, "*Cryoprecipitate was very unpopular with some patients: for some of the reasons you have given but also the higher incidence of allergic reactions when compared to AHF*" but that minimising exposure to commercial factor VIII was a paramount concern.[120]

Donor selection, information and counselling

97. At a SNBTS Directors' meeting on 29 March 1983, blood collection in prisons and borstals was discussed:

> "*Dr Cash reported that the Medicines Inspector had commented adversely on the practice of collecting blood in prisons and borstal institutions, and he invited Directors to comment on the practices in each region and to give their view on the Medicines Inspector's criticism.*
>
> *It was reported by all Directors present that sessions were held in penal institutions in all regions, although Dr Brookes and Dr Urbaniak intended to review the situation in their regions.*
>
> *It was not possibly for the Directors to agree on future policy, but it was agreed that Dr Brookes, as the Scottish representative, should ask the Working party on the Selection and Care of Blood Donors to consider this issue. In the meantime, Dr Cash agreed to inform the Medicines Inspectorate of these SNBTS discussions and conclusions*."[121]

[120] SBTS0000053_055
[121] PRSE0000193 p.5

98. At a meeting of the SNBTS Co-Ordinating Group on 24 May 1983, the issue of donor selection was discussed in light of the risk of AIDS. Different directors reported taking different approaches. The minutes record that:

> "*Dr Cash sought his colleagues' agreement to the issue of a general statement to the media to the effect that until appropriate markers had been developed the SNBTS would not wish to have blood donations from certain individuals. It was reported that the Directors of England and Wales had discussed the problem at their most recent regular meeting and had decided that publicity should be both local and national, the latter in the form of a press release plus nomination of a Press Officer from DHSS to maintain contact with the media. They had decided also to ask Dr John Barbara to draft a leaflet for the information of donors to be made available in Transfusion Centres. This leaflet was to be ready by 30 June.*
>
> *It was agreed, after discussion, that Dr Cash should contact Dr Barbara for information about the proposed leaflet after which he would arrange a meeting with colleagues from SHHD to discuss the possibility of a press statement for Scotland and the provision of information which the Transfusion Directors could use if they wished.*"[122]

99. Following that discussion, Dr McClelland wrote to Professor Cash enclosing a copy of a draft leaflet to brief donors on AIDS.[123]

100. Professor Cash attended a meeting of SNBTS Directors and Haemophilia Centre Directors on 2 February 1984 where "*Members discussed the reports from abroad which suggested that recipients of blood could also be at risk. The effectiveness of the leaflet addressed to blood donors was discussed. It was felt that some modifications might be made and stressed that the leaflet must in the absence of a test to screen out donors be given to all prospective donors.*"[124]

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[122] PRSE0003620
[123] PRSE0003679
[124] PRSE0001556

101. The SNBTS produced a leaflet for donors regarding AIDS by 14 August 1984 entitled an *"Important Message to Blood Donors"*.[125] In a meeting of the SNBTS Co-ordinating Group held on 20 November 1984 and chaired by Professor Cash[126] it was agreed that this leaflet (or the information in on it in another printed form) should be provided:

(i) with call-up letters;

(ii) at sessions to every donor who attends;

(iii) to the organisers of workplace and college/university sessions;

(iv) with the registrations book to new donors;

(v) and to the home address of donors, who, not having been called to a session, attend nevertheless. This would be after donation.

102. On 8 October 1986, Professor Cash attended a RTC Directors' Meeting at the DHSS at which the 'AIDS Donor Leaflet' was discussed. His contributions were as follow:

> "*Dr. Cash… expressed concern that the AIDS leaflet was not being taken seriously and supported this with evidence of his own experience as a donor recently. He said that Directors in Scotland were considering sending a health check letter with every call-up which would incorporate the details in the AIDS leaflet…*
>
> *Dr. Cash appealed for cross border co-operation in the preparation of future literature and asked the Chairman to approach the DHSS regarding his proposals for a study into the effectiveness of the literature in self-excluding donors in high risk groups. One proposal was that closer attention to the exclusion of donors from malarious areas would assist with excluding those who had visited countries where HIV was endemic*."[127]

[125] PRSE0000286
[126] SBTS0002210
[127] CBLA0002345

103. At a meeting of the SNBTS Directors chaired by Professor Cash and held on 3 March 1987, Professor Cash reported that it had been hoped that a joint SNBTS/NBTS group could be formed "*to advise the DHSS on the content of future messages to donors, with the aim of achieving uniformity between the NBTS and the SNBTS"* but that this proposal did not have the support of the DHSS.[128]

104. On 7 December 1989, Dr Mhairi Thornton, SNBTS, wrote to Dr Cash suggesting that the SNBTS donor health questionnaire needed improvement.[129] He replied on 14 December 1989:

> "*Your letter of dismay came as no surprise to me. I have passed it on to the Directors. I share your view and that of the IRD0s, that there is an urgent need to produce a harmonised standard (SNBTS) health questionnaire. I make this point as the person who has the awesome task of enhancing quality assurance at a national level. I would also wish to persuade my colleagues, in the light of my knowledge of details of the impending HIV litigation - that some, if not all, are at high risk in any future litigation. Lawyers are already requesting copies of donor session documents and if the data presented in your table is accurate then we need to move as fast as is reasonably possible. I will raise this topic with the Directors as soon as possible."*[130]

105. At a RTC Directors Meeting on 13 February 1990, there was a difference of opinion on donor counselling between the Scottish and English services:

> "*There was a further brief discussion about the appropriate method of counselling and it was noted that the Scottish directors had already agreed in principle that the service should undertake full counselling and a referral to specialist care, with the proviso that this would be very difficult in North Scotland. Dr Gunson advised that NBTS Directors were split (50/50) on this issue. Dr Watt explained that the SHHD would have to await a formal*

[128] PRSE0004163
[129] SBTS0000144_003
[130] SBTS0000189_081

recommendation from the DoH Advisory Committee on the Safety of Blood before offering advice to Ministers."[131]

106. In August 1990, Professor Cash prepared a paper containing 'Proposals for Future Maintenance of Medical Standards for the Care and Selection of Blood Donors'. His stated aim was to create "*a more broadly based UKBTS approach*" with a new standing committee.[132] He further wrote to Dr Gunson on 6 August 1990 to suggest that a standing UKBTS group be established to maintain a *"close watching brief"* for the NBTS and SNBTS on the care and selection of donors,[133] to which Dr Gunson agreed.[134]

107. Professor Cash wrote again to Dr Gunson on 3 October 1990 regarding donor counselling:

> "*I fully appreciate that you may feel that this is one area, because of differences in opinions with regard to the involvement of BTS medics in donor follow-up, in which it isn't appropriate to pursue harmonisation between NBTS and SNBTS. Should that be so, then 1 think we should simply recognise and record it. We will press on and I will keep you fully briefed on the outcome of our deliberations and evolved strategies. On the other hand, you might feel it helpful if we dialogued with those NBTS colleagues that shared our philosophical approach*."[135]

108. On 14 December 1990, Professor Cash wrote to Dr Kenneth Calman, Chief Medical Officer, that in Scotland the approval of SHHD was not required for the production of new blood donor self-exclusion leaflets. This allowed SNBTS to introduce change far more quickly, often as soon as WHO or FDA guidance on blood safety changed - many months before NBTS. Professor Cash was firmly in support of the "*Scottish system*" and encouraged the UK to adopt it.[136]

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[131] PRSE0000205
[132] SBTS0000443_053
[133] NHBT0006940_003
[134] SBTS0000630_017
[135] NHBT0000073_007
[136] NHBT0000190_063; see also SBTS0000633_061

109. On 18 September 1991, Professor Cash wrote to Dr Gunson expressing concern:

> "*that North London RTC intend to remove all donors from their panel who are HCV screen +ve (without any reference to confirmatory tests). It follows that they would therefore not send plasma which was screen +ve to BPL. It also follows that, notwithstanding all previous discussion at the ACTTD, Marcella Contreras would appear to have reversed completely her view, which we share, — that the Blood Transfusion Services have a major moral obligation to (a) ensure that donors found to be carrying an infectious disease were appropriately counselled and offered referral and (b) limit the process by which donors were inappropriately labelled as carriers of infectious disease in view of the possible adverse social and psychological effects on their lives.*"[137]

110. In 1993, Professor Cash commented on donor selection policies:

> *"While the consensus view would be that most of the enhanced donor selection procedures developed in the early and mid-1980's have been unequivocally successful, there has been increasing evidence that further improvement is both desirable and possible. These concerns have emerged during the counselling of 111V positive and HCV positive donors in recent years, when it has become clear that, notwithstanding all the information and education, high risk donors have passed through the selection process and have been bled."*[138]

Viral inactivation

111. According to the statement given by Dr Peter Foster to the Penrose Inquiry, Professor Cash attended the conference in Bohn in October 1980 at which Behring presented their work pasteurising Factor VIII. This was said to be the first time it had

[137] NHBT0000193_034
[138] SHPL0001070_003

been suggested that Factor VIII could withstand heat treatment which may destroy hepatitis.[139]

112. On 30 March 1982, Dr Cash chaired a meeting of the SNBTS' Factor VIII Study Group. He spoke against including plasmapheresis in a "process validation" study to evaluate the handling of plasma from donation to delivery to PFC.[140] At the same meeting, it was recognised that "*Hepatitis B is still a risk although reducing now that screening was available*." Further, *"Available data indicated that the properties of NANB were similar to those of hepatitis B although this was by no means certain."*[141] The practicalities of proposed research into viral inactivation were discussed.

113. On 6 January 1983, Professor Cash wrote to Dr Forbes in Glasgow:

> "*New SNBTS Factor VIII Concentrates*
>
> *I thought I ought to let you know, in advance, that we (PFC) hope to have a new factor VIII concentrate available by the late Spring of 1983 for preliminary studies (in vivo yield and half-life). The new product will be one which is of a higher potency than the existing intermediate preparation, and will have a much lower fibrinogen content that the latter. The production methods have to remain a secret at the moment until patenting formalities have been finalised. However, prior to the initiation of the clinical studies the basis of the methods will be discussed with you. It is our intention, once this new product has been shown to have an in vivo yield and J* [sic] *life comparable to the intermediate VIII concentrate, to come to you soon thereafter with the same preparation, but which has now been heat-treated. Once again we would wish to examine the in vivo yield and i* [sic] *life of the heat-treated product. I therefore write to enquire, in advance, whether you would be prepared to collaborate with us and undertake the necessary studies.*"[142]

[139] PRSE0003349
[140] PRSE0000752 p.3
[141] PRSE0000752 p.5
[142] PRSE0004875 p.1-2

114. Professor Cash wrote further to Dr Ludlam on 13 June 1983 regarding his progress in developing a heat-treated product and requesting he test it:

> "*Heat Treatment of Factor VIII Concentrate*
>
> *I promised to follow up our telephone conversation with a note which would include a proposed protocol and information which may be of interest to you and the Infirmary Ethics Committee…*
>
> *Perhaps I should first emphasise that the plan I proposed at the last Scottish Haemophilia/BTS Directors' WP still stands - we intend to come back to you and Charles Forbes with a matched pair (heated/unheated) of factor VIII concentrates. We had, in fact, hoped to be able to move forward at this time but unfortunately the unheated part of the pair proved to be unacceptably pyrogenic in the rabbit test. Thus we have at the moment a small amount of heat treated material only.*
>
> *John Watt and I feel that it would be most unfortunate not to use this first heat treated batch on its own. If you were able to show in 2 or 3 patients that its behaviour was broadly similar to previous data you, Chris and Frank have collected on cryoppt. and intermediate VIII then it would considerably boost the confidence of the PFC team and, I should hasten to add, the Licensing Authority within Medicines Division who are being kept fully briefed on the work up here (thus no Clinical Trial Certificate or Exemption required).*
>
> *Finally, in this preamble, I would turn your attention to the point you rightly raised with regard to the possibility of molecular damage during the heat treatment process. John and I would be delighted if you wished to take a couple of the available vials and test them in your own laboratory against your known antibodies. You will be interested in the enclosed information produced I;>yDr Dawes. Her data suggest, using immunoassays, that there does not appear to be damage following heat treatment with respect of VIII:CAg, VIII:RAg, thrombospondin, BTG and PF4.*
>
> *I enclose a suggested protocol and the profile of batch NY.761. The only comment with regard to the profile is that the osmolality is higher than existing products (it will be suitably adjusted in future batches). We suggest*

that you make each vial of this batch (NY.761) up with a volume of 25 ml. distilled water. I've suggested a dose of 20 i.u./Kg. which for a 70 Kg. patient will require 10 vials of this particular batch. Thus you will have more than enough to do 3 patients."[143]

115. He added a postscript, *"We would much appreciate it if, after you've done the 3 severe haemophiliacs and if there was a sufficient number of vials from batch NY.761 left over, you would consider giving an infusion into a Von Willebrand's Syndrome patient. We would all like to know whether it is efficacious."*

116. Dr Ludlam replied on 11 January 1984. The test batch had been given to a single patient with severe haemophilia on three separate occasions. Dr Ludlam reported that "*the recoveries and survival times were reasonable*" but that the patient had felt ill with "*significant and unacceptably adverse*" side-effects on each occasion.[144] Dr Cash replied thanking him and promising to send a further batch by April 1984 "*with further improvements on heat treatment and low sorbitol content*" which he hoped would address the side-effects. [145] On 15 March 1984, Dr Forbes reported that patients in Glasgow had not reported such side-effects. [146]

117. On 2 February 1984, at a meeting of SNBTS Directors and Haemophilia Centre Directors, Professor Cash reported that "*trends over the last 5 years indicated that the SNBTS production of factor VIII concentrates may be exceeding clinical demand in that current stocks at RTCs appear to be increasing*". The minutes record that he "*asked for views about the phasing in of heat treated factor VIII for routine clinical use and how this could be achieved and quantified.*"[147] (Dr Ludlam raised the side-effects experienced by his patient using the test batch.)

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[143] PRSE0004875 pp.2-3
[144] PRSE0004875 p.6
[145] PRSE0004875 p.7
[146] PRSE0004875 p.10
[147] PRSE0001556

118. It was put to Professor Cash during the Penrose Inquiry that the infection of the group of people known as the Edinburgh Cohort would have been prevented if PFC had moved to dry heat treated product at the beginning of 1984. His response was:

> "*That the first experimental dry heating of PFC VIII took place in November 1983 and that within 12 months the manufacture of the first batch of PFC VIII destined for clinical use was commenced. In the context of the pharmaceutical industry I would judge this 12 month period would be regarded as very short.*
>
> *The batch we believe caused the HIV Edinburgh cohort HIV infection was processed in the first week of November 1983 - almost certainly before the first experimental dry heated batch- It follows that if mv recollections are correct your proposition is a non starter.*
>
> *There was great concern among many of the clinicians that any form of heating might be associated with protein denaturation which could have serious consequences for the patients. Much laboratory effort was put into this perceived problem and the move to put products in to patients had hitherto been very cautious. Faced with the reality that HIV had got into the Scottish donor population the move to put dry heat treated PFC VIII in to patients was pushed forward in late 1984 with much less caution. I and mv clinical colleagues found December 1984 a very anxious time. We found ourselves alone, without active support from SHHD or the MCA. Thus, to our surprise, we found ourselves pleased with the comfort that we were operating under the cover of Crown Immunity - though it has to be said we were never sure to what extent this feeling of comfort was justified.*"[148]

119. Professor Cash also had an interest in the development of recombinant factor VIII. On 25 June 1984 he wrote to Mr Robert A Swanson, President and Chief Executive of Genentech Inc, California:

> "*The Scottish National Blood Transfusion Service is an organisation which is part of the UX Government's Health Service for Scotland. Its responsibility is*

[148] PRSE0002836

to service all aspects of transfusion practice for all hospitals in Scotland (population 5.2 million). To this end our blood donation collection programmes are totally adequate for all our needs and we have our own modern plasma fractionation centre with, for instance, a unique and successful computer controlled continuous small volume mixing fractionation system for albuminoid products. In addition we have a relatively substantial research capacity (more than 12 post-doctoral personnel).

I write to enquire whether your company would be interested in some sort of joint venture in the area of genetically engineered coagulation factor VIII. We believe we may be able to offer significant contributions in the areas of assays, downstream technology and clinical evaluation (under the aegis of the UK licensing authority). Currently we supply all the factor VIII used in Scotland and our production is in excess of demand. We have an interesting range of monoclonal-antibodies to factor VIII antigens and are currently evaluating (clinically) a heat treated factor VIII concentrate derived from human plasma."[149]

120. Mr James M Goweer of Genentech replied on 14 August 1984 explaining that the exclusive UK rights to his company's recombinant factor VIII were owned by Speywood Laboratories Ltd and so a commercial collaboration was not possible.[150]

121. In October 1985, PFC discovered that their intermediate NY factor VIII product withstood heating at 80°C. Asked during the Penrose Inquiry why such heating of the existing product was not introduced immediately but only in May 1987, Professor Cash explained:

> "*I recall there were a number of formidable technical challenges to be addressed before a satisfactory (reproducible) process was obtained. Most notable, I recall, was freeze drying, there was also time required for preliminary clinical studies, with regard to product tolerability and efficacy. In this regard, I recall that I found that operating outside the comfort of the*

[149] SBTS0000322_011
[150] PRSE0003638

Medicines Act (1968) gave rise to enhanced causation with regard to my involvement in developing new products and this may have contributed in some measure to my any delay."[151]

122. At the meeting of the SNBTS Directors and Haemophilia Directors on 5 March 1986, Professor Cash reported that, "*even material dry heated at 68°C for 24 hours may not be non-infective with regard to HTLV Ill and Non A/Non B hepatitis"*. His colleague Dr Perry explained that the PFC had recalled all residual stock of material heated at 68°C for 2 hours for testing. He said that difficulties had arisen in relation to the heat treatment of the new high purity product and it had been decided to introduce an intermediate stage: a product that was only 2-3 times purer than the existing intermediate factor VIII but could be dry heated at 80°C for 72 hours.[152]

123. On 5 January 1987, Dr Ludlam wrote to Professor Cash that he was no longer willing to test new NHS blood products on his patients unless there was a guarantee of financial compensation should something go wrong, reminding him: "*You will recall that one of my patients had symptoms of a potentially lethal condition during an infusion to test a new PFC product and such an occurrence clearly raised my level of concern.*"[153] He told the Penrose Inquiry that the issue of compensation / indemnity may have been a material cause of up to 3 months' delay in commencing clinical trials of Z8, between autumn 1986 and late February 1987.[154] At an informal meeting between SNBTS and SHHD representatives on 26 October 1987, Professor Cash emphasised the need to have compensation arrangements in place for clinical trials, including urgently for "*the clinical trial of RF/HBs/1 which it was proposed to trial in Belgium (because there were too few British patients who required the product, to allow a valid study to be mounted in this country)*".[155]

124. Professor Cash further told the Penrose Inquiry, regarding product development:

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[151] PRSE0000651
[152] PRSE0001081
[153] PRSE0003282
[154] PRSE0000651
[155] PRSE0004722

"*I would advise that consideration is given to the difficulties which arose in the development of in vitro virus inactivation validation studies at PFC and how these might have contributed to any delay. These developments were intended to provide preclinical data on efficacy of different heat treatment programmes. The delay in the introduction of this important development arose following an intervention by SHHD.*

Finally, it is worth re-emphasising the complex problems PFC had with regard to its plasma supply during product development and implementing product change-over. As I recall, when the first heat treated VIII was issued, the unheated material was returned to PFC, heated and re-issued. It followed that the net demand on additional plasma sourcing of this transfer was marginal. However, in a situation where product cannot be recycled, and there is no permitted facility to boost a matching plasma intake, to cover the gap, then the logistics of Introducing a new product (such as Z8 which was heated at 80 degrees centigrade for 72 hours) are much more challenging."[156]

125. In a further statement, he added:

"*It cannot be overemphasized that for a small public service plasma fractionators such as the SNBTS which exclusively relied on a fixed indigenous voluntary unpaid donor base for its plasma source, and which in 1983 had achieved self sufficiency but was expecting major new and escalating clinical demands, we were reluctant to encourage our PFC colleagues to pursue a heat treatment programme which led to high production losses. This would have led to increased exposure of haemophilia patients in Scotland to higher risk commercial products - unless we had an assurance of funding to commence a programme of plasmapheresis which would generate source plasma to further augment our plasma intake. This difficulty must have put considerable pressure on our PFC team. Moreover, even the quantities of plasma required simply to support these heat treatment*

[156] PRSE0000651

production experiments were a cause of considerable concern and tension at that time."[157]

Pool Sizes

126. On 21 September 2010 Professor Cash made an enquiry into the average pool sizes (i.e. number of donations) for Factor VIII production at SNBTS. The response was as follows:[158]

1975 – 1979: 160 litres (batch thaw)

1979 – 1981: 300 litres (continuous thaw)

1981 – 1991: 600 – 1000 litres

1992 onwards: 3000 – 4000 litres.

Testing for HIV

127. In his B4 statement to the Penrose Inquiry, Professor Cash described in early 1984 learning about the nascent development of HIV testing, including work undertaken by Professor Robin Weiss at the Chester Beatty Institute to develop a RIA to anti-HIV and the developing commercial ELISA programme in the US. He stated that SNBTS had been excluded from discussions between Dr Gunson and DHSS in a proposed evaluation programme, and he later learned that time had been wasted on *"internal civil service wrangles"*. This resulted in the company that in December 1984 took over the UK research, Wellcome Diagnostics, having to play catch up.[159]

[157] PRSE0002836
[158] RCPE0000289_013
[159] PRSE0003395

128. Professor Cash attended the Tenth Meeting of the Advisory Committee on the National Blood Transfusion Service on 8 November 1984. The minutes record under "*AIDS - HTLV III Testing*" that:

> "*Dr Smithies advised that the Middlesex Hospital and the Chester Beatty Laboratory were testing for HTLV III antibody using a radioimmunoassay method. A survey of 1,000 NBTS donors had revealed no infection, but it was hoped to undertake a larger survey to confirm findings. Pilot screening at an RTC was one of the points to be considered by the Working Group on 27 November. Dr Cash advised that in the USA the individual's permission was necessary before screening could be carried out; there were many implications for donor morale."*[160]
>
> *"...It has always been mv belief that had the two organisations (BPL and PFC) been able to pool their limited R&D resources, and perhaps some manufacturing resources, it may have made a significant difference, throughout the 1980s, to the availability of desirable plasma products in the UK. The most certain example of this was IVIG. It is mv understanding that the availability of IVIG from BPL was some years after PFC had a licensed product. It follows that in this period IVIG was purchased at considerable cost to Regional Health Authority pharmacy budgets."*[161]

129. Professor Cash told the Penrose Inquiry that in January 1985, SNBTS gave up the idea of a joint UK approach and decided to undertake an evaluation of the commercial HIV donation screening kits as soon as possible. The manufacturers were willing to supply these free of charge in exchange for research data. However, due to a hostile reaction from the DHSS, this SNBTS initiative was stood down. The DHSS did subsequently conduct a screening test evaluation programme, which Professor Cash considered to be unsatisfactory.[162]

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[160] PRSE0004783
[161] PRSE0000651
[162] PRSE0003395

130. Professor Cash was one of a number of authors of a letter to the Lancet published on 2 March 1985. They wrote:

> "*We believe that current commercial kits for HTLV-III antibody tests are likely to give a high rate of false-positive results. We would therefore recommend that careful consideration be given before they are introduced for the screening of all voluntary blood donors, for the amount and degree of unnecessary stress and hardship that a fair number of our donors and their families would thus have to undergo is unacceptable. This in turn could lead to a sizeable drop in the supply of blood and blood products. Of no less importance, for the safety of transfused patients, is the need to ensure that the first priority for the introduction of any HTLV-III antibody tests into a community is given to patients attending special (venereal disease) clinics and other members of the general public who wish to have access to these tests. If this is not done, many high-risk people, from a blood-transfusion point of view, may present themselves at blood-donation sessions simply to find out their HTLV-III antibody status. We do support, strongly, the screening of all blood donors for HTLV-III antibody testing, but we would advise that this is delayed until test systems have been appropriately evaluated and efforts have been made to give all members of the public access to HTLV- III antibody testing*."[163]

131. Professor Cash also wrote to Dr Abrams of the DHSS on 14 March 1985 suggesting that HTLV-III antibody testing should be introduced simultaneously in the UK and supporting a counselling requirement for those who were found to be anti-HTLV-III positive.[164] Dr Gunson wrote a follow up letter to Dr Abrams on 19 March 1985, criticising Professor Cash's *"rather aggressive letter"* and advocating a more gradual approach.[165]

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[163] PRSE0004824
[164] NHBT0007985
[165] NHBT0007984

132. On 24 June 1985, Dr McClelland wrote to Dr Gunson and Professor Cash regarding "*AIDS Diagnostic Test Using Recombinant DNA Antigen*":

> *"I've just seen a note that Centocor is planning to launch an AIDS diagnostic test using recombinant DNA antigen in June 1985. Apparently the test is currently in clinical evaluation.*
> *It may be worth considering whether the second phase of the BTS trial (once we have the first four kits evaluated) should wait for a month or two in hope that it can look at one or more second generation test systems."*[166]

133. Professor Cash attended the fifth meeting of the Expert Advisory Group on AIDS on 30 July 1985. The minutes do not record his contribution to the meeting, but there was a discussion about "*AIDS screening tests*". The tests under evaluation were Vironostika anti-HTLV-III (Organon Teknika Lid), Wellcozyme anti-HTLV-III (Wellcome Diagnostics) and HTLV-III BioEnza Bead (Ortho Diagnostic Systems Lid). Further:

> "*The question of patient consent to HTLVIII testing was discussed. A positive test result could be serious for an individual patient and the implications of tests taken as an infection control measure for staff and not for the benefit of the individual's diagnosis and treatment should be carefully considered. The BTS would be informing blood donors, who were volunteers, that the test was being done on their blood donation. However, in the context of the diagnosis and treatment of a patient it was agreed that a general clinical approach should be adopted. Patient's permission for hepatitis B testing was not always sought and, with a variety of tests being taken, it should not be necessary to inform the patient in all cases that these included a test for HTLVIII antibody. It was also agreed that the result of the HTLVIII antibody test should not be awaited before undertaking other tests which might be critical in the treatment of a patient. Professor Zuckerman said that with hepatitis B it was now accepted that other tests should be done while the result of the hepatitis B test*

[166] NHBT0004262

was awaited. These tests should be handled in a high risk laboratory and no additional precautions were required."[167]

134. HIV-1 donation testing was implemented across SNBTS in October 1985. [168] Professor Cash later commented that SNBTS had been excluded from key discussions which resulted in a delay to the commencement of testing, saying "*You will recall that mass HIV-1 donation testing was commenced in the USA in March 1985 and not until October 1985 in the UK*".[169]

135. By 8 October 1986, Professor Cash reported to a meeting of the RTC Directors regarding "HIV Antibody/ELISA Conversion" that:

> "*where a donor was repeatedly positive in the screening tests, but where positivity was not confirmed by the reference laboratory, it had been agreed that such donors should be withdrawn from the panel on the basis that their results were not fully understood. However, the observation to which Dr. Cash was referring was made where a considerable number of samples had been tested from donors giving false positives and some of these did indeed become negative. Opinion appeared to favour the reinstatement of such donors and Dr. Cash reported that opinion in America was moving similarly but that FDA approval had not yet been given*".[170]

136. HIV-2 screening was introduced in 1988. On 19 May 1988, Professor Cash wrote to Dr Hilary Pickles at the DHSS querying an instruction (described as *"wholly inappropriate"*) from Dr Gunson at the NBTS that blood from donors who had visited listed West African countries could not be used until cleared with an HIV-2 test. For some reason, which is not entirely clear, Professor Cash thought a problem with this might arise from the Consumer Protection Act 1987.[171] Dr Gunson responded that this was unreasonable as the procedure had been implemented by several European countries, did not require major resources, and *"the implications of an HIV2 infection*

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[167] PRSE0002628
[168] PRSE0004541 p.10
[169] SBTS0000061_033
[170] CBLA0002345
[171] NHBT0003677

in a patient would cause repercussions which would be intolerable to the BTS."[172] By 21 June 1988, Professor Cash appears to have come to the same view as he wrote to SNBTS directors regarding an interim policy for HIV-2 testing.[173]

137. Professor Cash told the Penrose Inquiry that:

> "*Unlike their English counterparts, SHHD recognised that there was a need to invest in specialist confirmatory testing and donor care services. This proved to be a most significant policy decision and in due course led to the establishment of the SNBTS Microbiological Reference Centre in 1989. This development gave much value to our contract (to do no harm) to Scottish blood donors. This did not take place south of the border and became a particularly embarrassing issue when HCV donation testing emerged.*"[174]

138. He also commented in the same statement that: "*It is still my view that HIV donation screening was introduced in the UK without the most appropriate consideration of the welfare of blood donors*".

Testing for HCV – surrogate testing

139. The SNBTS Directors' meeting minutes for 25 June 1986 show that factor VIII concentrate then being issued was derived from unscreened plasma but *"it was anticipated that the position would change fairly soon"*. It was further noted that *"There was increasing evidence that the USA and several European countries were introducing anti-HBc and/or ALT testing of blood donors in an effort to minimise the risks of NANB transmission through blood and blood products. Dr Cash believed that the SNBTS would soon come under pressure from clinicians to introduce testing. "*[175]

[172] NHBT0003680
[173] NHBT0003673
[174] PRSE0003395
[175] PRSE0002641

140. On 23 July 1986, Professor Cash wrote to Dr McClelland regarding a research proposal on surrogate testing by Dr Jack Gillon:

> "*I am in receipt of a copy of a letter from Jack Gillon to Professor Bouchier (dated 18th July, 1986).*[176]
>
> *In the second para of this letter Jack indicates in a very positive way his intention to follow-up patients receiving blood which has been "surrogate tested".*
>
> *I'm delighted to learn of this but would point out that my understanding is that SEBTS did not intend to pursue this topic. If the position has changed then I feel Jack should make contact with Ian Fraser (Bristol) sooner rather than later.*"[177]

141. At a meeting of the Advisory Committee on the National Blood Transfusion Service on 17 June 1987, ALT testing for transfusion-associated (NANB) hepatitis was discussed. The minutes record that Professor Cash was in favour of introducing surrogate testing:

> "*30. The Chairman asked whether the Committee agreed with the Lancet article concluding surrogate tests for hepatitis could not be justified.*[178]
>
> *31. Dr Cash said that Scottish Directors were proposing to establish such tests in view of impending product liability legislation in 1988; there was also clear indication that the private sector would test and they did not wish to fall behind.*"[179]

142. However, others in the group considered the introduction of surrogate testing would be premature, had not been sufficiently researched, and would result in the loss of donations; the conclusion was the Committee would continue to monitor the situation.

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[176] Dr Gillon's letter is at SBTS0000177_018
[177] SBTS0000177_017; the Gillon letter referred to is at SBTS0000177_018
[178] This is a reference to the letters to the Lancet of 18 April 1987 NHBT0000025_010 and 13 June 1987 PRSE0002104.
[179] BPLL0007202

143. On 4 July 1987, the Lancet published a letter from Dr Cash and other SNBTS directors advocating for the introduction of surrogate testing using alanine aminotransferase (ALT) and hepatitis B core antibody (anti-HBc) as surrogate markers to reduce transfusion- transmitted non-A, non-B hepatitis. They argued that the time for exploratory research studies was passed and that the introduction of surrogate testing was *"virtually inescapable"* for three reasons: "*producer's liability, competition, and value for money*". They noted that,

> "*Although we all hope that pooled plasma fractions will soon be made safe by heating or other antiviral treatment, these processes remain to be validated in large-scale trials. Meantime, even if surrogate marker screening would only modestly reduce the level of infectivity in these products, many would argue that some improvement is better than none*".[180]

144. The letter caused consternation amongst RTDs in England and Wales. In a letter written by Dr Fraser to Professor Cash in relation to the letter, dated 2 July 1987, Dr Fraser thought that they would not be 'very pleased' at reading the letter because they had understood that it was agreed that there was a need for 'synchrony' between the services.[181]

145. Professor Cash's response on 8 July 1987 provides:

> *"The SNBTS Directors do not wish, and currently have no intention, of introducing NANB surrogate testing unilaterally.*
>
> *…….*
>
> *I really don't believe you should view the Lancet letter as any more than part of a debate which was initiated in this journal's columns by our friends and colleagues at Edgeware. It can also be viewed as yet another attempt to persuade central management (DHSS) to give renewed thought to the way the transfusion services interface with the Medicines Act and forthcoming*

[180] PRSE0001444
[181] PRSE0004482

legislation on product liability and perhaps even to ways for improving the co-ordinated management of the transfusion services on a UK basis."

146. This controversy is described by Dr McIntyre in a note of 21 July 1987:

> "*Professor Cash has assured Dr Fraser of Bristol NBTS, in a letter dated 8 July, that he will not institute testing 'unilaterally' We have however no assurance that he will not do so in the near future without specific funding and without necessarily reporting what he has done to CSA or SHHD. DHSS have expressed their concern and dismay at the letter by Professor Cash and colleagues and have interpreted this as being SHHD policy; we have attempted to reassure them that it is not so. Their concern is that if we should commence testing unilaterally they will feel obliged to follow. Professor Cash and his colleagues have been given the opportunity to engage in a research programme to evaluate the need for this testing but have withdrawn as they feel 'the time for this study has already past'*."[182]

147. On 1 September 1987, Dr Perry, Director of PFC, wrote to RTC Directors including Professor Cash to suggest a review of the SNBTS criteria for possible viral contamination, "*bearing in mind our now stringent heating conditions for coagulation factors*". He wrote:

> "*We (SNBTS) are not ALT testing although it seems likely that such testing will be in place in the near future and we need to address ourselves to the relevance of such test results to PFC product recall and release in readiness for this testing.*"

148. He suggested that donations with abnormal elevated ALTs would not be sent to PFC but that donations which were retrospectively identified as having elevated ALTs would not be traced to batching and accordingly no PFC action would be taken.[183]

149. In December 1987, Professor Cash discussed with colleagues that the DHSS was allowing commercial plasma fractionators to note on product literature where they

[182] PRSE0004562
[183] SBTS0000250_122

had tested donors for ALT; this caused consternation at BPL.[184] Dr Rotblat, DHSS Senior Medical Officer, responded that "*this decision has been made by most of the major fractionation companies… it seems that so far no suggestion that ALT testing should be carried out in the UK has been made despite the fact that the commercial fractionators have been doing this for some time and it has been in their data sheets probably for more than a year*".[185]

150. Professor Cash's objection was that he had been unsuccessful in obtaining funding for surrogate testing to be conducted in the RTCs, which he wished to implement. His position is described in a note by Dr John Forrester dated 17 December 1987:

> *"For some time he* [Professor Cash] *has sought funds to screen all donations by both ALT testing and another test, as a way to exclude some donations likely to transmit non-A, non-B hepatitis. He has not received funds, for reasons previously explained, and so far as I know, no research is being mounted in Scotland or England into the cost and value of the screening.*
> *The recipients of SNBTS unscreened blood have no choice: they cannot get any other blood. But the recipients of blood products do have a choice, usually no doubt made for them by the clinicians treating them. They can have SNBTS products, apparently gratis, made from unscreened donations. Or they can have commercial products, at the cost of the Health Boards, made from partially screened donations; partial, because ALT screening is only one of the two tests proposed together to reduce transmission of non-A, non-B hepatitis."*
> [186]

151. In May 1988, Chiron announced the identification of HCV. Professor Cash recalled to the Penrose Inquiry that *"thereafter, the controversy surrounding surrogate testing gradually faded as attention turned to HCV screening."*[187]

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[184] PRSE0001194
[185] NHBT0000187_009
[186] PRSE0001159
[187] PRSE0003232

152. However, there is some subsequent discussion of surrogate testing in the contemporaneous documents. On 12 January 1990, Professor Cash wrote to Dr Gunson, having learned that NBTS was implementing a new policy decision requiring all NBTS RTCs to commence routine ALT donation testing of plasmapheresis donations on 1 April 1990. The letter reflects a sense of betrayal on Professor Cash's part. He reminded Dr Gunson of

> "*our (SNBTS) professional views on the matter and the subsequent assurance we gave to you that Scotland would not introduce any form of routine surrogate NANB donation testing, unless it was a joint UK exercise and one which, like HIV-1 donation testing, had Ministerial approval.*
> *... I wonder where that leaves us all? 1 suggest, with the deepest and most profound regret, that it looks as though the NBTS and SNBTS must go their separate ways in regard to quality assurance. I would have thought that with all the emerging litigation associated with blood and blood products, particularly against the background of the new product liability laws, this must surely have~ signalled the beginning of something so desperately needed for the last 30 years - a coming together on policy and operational matters of the NBTS and SNBTS.*"[188]

153. Dr Gunson replied on 16 January 1990 to the effect that the testing was necessary for product licensing, and suggested that it was the SNBTS that had failed to engage in joint policy-making on quality assurance.[189] Professor Cash's next letter on 30 January 1990 in response was more conciliatory, but he reiterated, "*The point I was trying to make in my "cris de coeur" was that we had previously agreed (at Department level) that whatever happened on ALT testing we would run together and at the very least would be in close consultation.*"[190]

154. On 2 February 1990, Dr Gunson replied that:

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[188] NHBT0000027_011
[189] NHBT0000027_012
[190] PRSE0001347

"*The first request I received from CBLA was for all the plasma to be tested. This I refused because of the implications for the cellular products and eventually settled on the apheresed plasma. The quantity of plasma from this source will not be anywhere near enough for BPL to provide i.v. Ig in quantities to make England and Wales self-sufficient for this product, but it will allow them to have a product available from about 60-70. tonnes plasma per year.*

I will not agree to total ALT testing of donations until, and if there is a uniform policy for the UK and who knows at this time what line this will take."[191]

155. At the next SNBTS RTC Directors' Meeting on 13 February 1990, "*It was noted there would be a problem if ALT testing commenced in England and Wales and not in Scotland. Mr McIntosh reported that Dr Mcintyre (SHHD) had reported to him by telephone the reasons why ALT testing should not be commenced in Scotland.*"[192]

156. Professor Cash later commented to the Penrose Inquiry:

"*Documents which reveal that the position of the SNBTS Directors on surrogate testing, finally declared in July 1987, whilst at the time subject to much English (and SHHD) ridicule, was, less than 3 years later, espoused by DHSS, CBLA and some former vociferous NBTS Directors. Of interest is that SHHD claimed it had not been briefed by DHSS on much of this radical change in policy. Thus former expressions of righteous indignation and strident calls from SHHD for research before change (which was never supported), rapidly gave way, as predicted by SNBTS Directors, to the inevitable pressures of the market place (3-13). Even more remarkable is the evidence that the introduction of large scale surrogate testing in England and Wales was commenced after the introduction of HCV donation screening - again for market reasons! The morality of this latter development must surely*

[191] NHBT0000027_015
[192] PRSE0000205

be addressed in this Inquiry despite the fact that they arose in the period beyond the limits set by the Inquiry Team."[193]

Testing for HCV – antibody testing

157. On 5 July 1988, Professor Cash wrote to Mr Allan Follett, Marketing Director of Ortho Diagnostic Systems Ltd, requesting details of Chiron NANB antibody testing kit for full donation testing in UK:

> *"I would be most grateful if you would confirm that Ortho will be marketing the recently announced development of Chiron Inc - a kit to detect NANB antibody. Subject to you confirming this then I would also be most grateful if you would let me know some idea of the current time schedule to the point of full marketing in the UK for full donation testing."*[194]

158. Mr Follett replied on 19 July 1988, explaining that the tests were not yet available:

> "*Thank you for your letter dated 5th July requested information on the Non A Non B Hepatitis Antibody detection kit. Ortho Diagnostic Systems do have an agreement with Chiron to develop and market the product but I do not know precisely when this product will be available. The best information I have been able to obtain is that the product may be available towards the end of 1989. However, I am sure you will appreciate that there is a great deal of work to do regarding manufacturing and trials between now and then. I am sorry that I cannot be more precise with this information but please let me know if you feel there is any further information which we can supply.*"[195]

159. At a meeting of the National Directorate of the NBTS UK Advisory Committee on Transfusion Transmitted Diseases held on 19 May 1989, anti-HCV testing of donations from Scotland was discussed as follows:

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[193] PRSE0003232
[194] PRSE0002363
[195] PRSE0002112

"*Professor Cash reported that the SNBTS would be interested in taking part in evaluative trials of the Ortho Pharmaceutical Company's Chiron test and said he would be grateful if Dr. Gunson would contact him about this matter. In particular the West of Scotland Centre has a bank of frozen donor samples already tested for ALT, from which further samples are available of i.v. IgG known to have produced raised ALT levels in recipients.*"[196]

160. On 5 July 1989, Professor Cash wrote to Mr Peter Savage at Ortho Diagnostic System Limited to order 11 testing kits at a cost of £5,000 which would enable SNBTS to undertake 5,000 tests.[197]

161. On 26 July 1989, Dr Gunson wrote to Professor Cash:

"*CHIRON TEST*

I am pleased that you are carrying out 5000 tests for anti-HCV. John Barbara has now almost completed the tests on the 9000 from England and when the results are to hand I will send them to you.

I am having some difficulties with Ortho who are wanting to know when (not if) we are going to introduce routine testing and how many tests we wish to order...

My view is that we should not move until we know what our European colleagues are doing. For the U.K. it is important that the SNBTS and the NBTS act in close collaboration since I can foresee difficulties if one of us introduced the test unilaterally.

I hope we can discuss this matter soon."[198]

162. On 4 August 1989, Professor Cash wrote to Dr McIntyre at the DHSS regarding the introduction of Chiron testing. He had met with Mr Peter Savage of Ortho Diagnostic Systems Ltd but had not discussed start dates for routine testing because, as he emphasised, "*the decision to introduce this testing would be made on a UK*

[196] NHBT0000088_001
[197] SBTS0000365_019; the previous month he had also requested HCV tests for colleagues in Poland - SBTS0000365_017
[198] NHBT0000076_003

basis". An informal meeting for BTS representatives with Ortho had been arranged for 23 August 1989 in the Strand Palace Hotel, London. One crucial issue was confirmation testing:

> "*I pursued Mr Savage on confirmation testing which I believe is a crucial issue, both with 'regard to its absolute scientific/medical value but also a means whereby we can regain some initiative over Ortho. In brief they have a confirmation test (RIA) but it uses the same antigen as the screening test (scientifically weak but at present better than nothing) . The main problem is that Ortho currently do not wish/plan to market it. Mr Savage indicated that Ortho (UK) would make arrangements to send screen repeat positives to Ortho (USA) to be confirmation tested (probably at least 1500/annum from SNBTS alone) I indicated to Mr Savage, that in my view this proposal was wholly unacceptable. We would wish/insist that the confirmation testing, which has a profound influence on the lives of many donors, was in our hands.*"[199]

163. The Strand Palace Hotel meeting took place as arranged on 23 August 1989. Professor Cash did not attend but Dr Mitchell and Dr Follett from SNBTS were there, and reported the meeting to him by letter on the same day. He was told that the introduction of routine testing had been discussed in the following terms:

> "*Has any decision about blood testing been made? If not, how is it to be made and if any other information is required from Ortho Laboratories? The answer was given that no decision had been made. That the decision would be subject to the advice of the National Advisory Committee on the Virological Safety of Blood. If the Advisory Committee were to make a recommendation, then this would go to Ministers in England and Scotland for a final decision. It was made clear by us that no decision was possible before the October 17 meeting which was to follow the Rome meeting which some Transfusion Directors were arranging to attend with their Senior Technical staff. Mr Davis then moved to the position of 'What if a decision were to be made in favour of doing the test?*

[199] NHBT0000188_016; Mr Savage also noted his conversation with Professor Cash, in a letter to Dr Gunson dated 11 August 1989 - NHBT0000188_023

What would be the time and events schedule? Would there be a simultaneous announcement or a phasing and would any preparation be needed?'. We explained that if such a decision were to be made, then the UK would move in unity and that there would be a simultaneous announcement as happened with the HIV antibody testing. We explained that there would be other events and preparations not connected with the introduction of the tests, such as the arrangements for counselling of donors, the staffing and other matters which you have raised with the Management Committee of the CSA on the PES submission this year."[200]

164. On 26 August 1989, the Lancet published two letters on HCV antibody screening, one from Drs Contreras and Barbara at the North London Blood Transfusion Centre (who said that *"precipitate action should be avoided"*) and another from SNBTS doctors including Professor Cash. The SNBTS letter read:

> *"The apparent absence of a confirmatory test will cause serious problems for blood transfusion services, which are likely to bear the brunt of sensitive donor counselling. A repeatably reactive ELISA test is suggestive but not definitive evidence for antibody. We accept that the existing difficulty (use of the same antigen) is scientifically less than satisfactory, but it is better than nothing. Ortho Diagnostic Systems should make available, as a matter of urgency, appropriate reagents and/or tests so that even when an identical antigen is used, assay systems that are fundamentally different from the marketed ELISA screening tests can be used for confirmation testing. Of no less importance for blood donors, as you have indicated in your editorial, is the need for Ortho and/or Chiron to deposit the sequence of the viral genome in the GenBank database. These matters are so important that they should be taken up by Government health departments. In view of the impending European Legislation of blood transfusion, European governments are especially well placed to coordinate such actions."*[201]

[200] PRSE0000815
[201] NHBT0083819

165. On 3 October 1989, Professor Cash wrote to Mr Savage at Ortho:

> "… *I write to raise with you, formally, the issue of the confirmation test. I more than appreciate the difficulties both Ortho and Chiron have with regard to the availability of confirmation test kits. Nonetheless, I must pursue you and request that supplies of antigen are made available for reagent purposes. This type of exercise was done for HIV-I by DuPont some years ago, prior to this company licensing its own confirmation test kit. It would be our intention to set up in house confirmation assays using the Chiron antigen.*"[202]

166. On 27 November 1989, Mr Savage wrote to tell Professor Cash that the export permit for the Ortho HCV antibody ELISA test had been approved by the FDA, USA. This meant the screening test was available for export to the UK for routine use and not just research purposes.[203]

167. On 27 November 1989, Mr Jack Goldstein of Ortho wrote to Professor Cash:

> "*Your letter to Peter Savage regarding Hepatitis C confirmation was referred back to me. In this regard. We have just completed production of a small number of prototype confirmatory tests in our RIBA (Immunoblot) format. This test has three separate bands of antigen in a strip approach with several control Immunoglobulin bands. The three antigen bands are the C-100 HCV protein we utilize in our screening test which is produced in yeast, a protein called 5-1-1 which is a portion of the C-100 protein but this is produced in F. coil and an SOD band since C-I00 is produced in yeast as a fusion protein with SOD for efficient yeast production. We hope to take these kits out to the field this month and obtain feedback from several labs throughout the world that participated in our original clinical trials so that we can use this information to introduce our confirmatory test during the first quarter of next year. As to your question regarding availability of the C-100 antigen for*

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[202] NHBT0027482; he wrote again on 12 October 1989 saying that, "*the SNBTS programme will be co-ordinated from this office. Thus in due course you will hear of the SNBTS regional requirements*" - SBTS0000365_038

[203] NHBT0000188_123

testing we are unable to make it available to investigators at this time. If you have any further questions, please do not hesitate to contact me directly."[204]

168. Professor Cash replied,

"*We're delighted with your news of a confirmatory (HCV) test. Please advise whether it would be possible for our National Reference Laboratory to participate in the forthcoming field trails of your confirmatory test. We are very keen to do this.*" [205]

169. The Inquiry has not been able to trace a response to this letter.

170. On 5 December 1989, Dr Ludlam of the Edinburgh RTC wrote to Professor Cash urging him to support the implementation of routing anti-HCV screening:

"*Anti HCV Testing of Blood Donors*

I write to ask about the current SNBTS view of the possibility of routine anti-HCV screening of blood donors. I realise that the present antibody test is not ideal and that confirmatory tests as well as a more "sensitive" antibody test would be advantageous. The present test may well not identify all NANB infectious units and furthermore there may be false positive results. On balance, however, it seems to me that a case can be made for using the present anti-HCV assay to screen all donations and discarding all positive units.

I appreciate some of the drawbacks of introducing a screening test for "infectious" donations of blood but I wonder whether we should not be considering the recipients. I am mindful of the debate about, and enormous effort that went into the setting up of anti-HTLVIII screening in 1985. I well remember the view being put forward in early 1985 that anti-HTLVIII testing should be introduced and that positive units should be discarded (without informing the donor). If this policy had been adopted, one possible outcome would have been fewer transfusion cases of HTLVIII infection in recipients of a low number of products e.g. red cells. It could be argued that we are in a

[204] NHBT0000188_122
[205] NHBT0000188_127

similar position now with anti-HCV testing. You will be as familiar as I am with the long term complications of NANB hepatitis. I fear that if there is delay in the introduction of anti-HCV testing we will be exposing patients to preventable viral infection.

I do appreciate that the decision to introduce an imperfect test is difficult but on balance I would encourage SNBTS to do so at an early date.

You may have many cogent arguments against what I am suggesting and if so I should be most interested to learn of them."[206]

171. On 21 February 1990, Dr Boulton wrote to Professor Cash, strongly advocating for the introduction of HCV antibody testing as soon as possible:

> *"Please find enclosed a rather hasty transcription of my notes of the HCV Symposium early this month. Could I just add that in spite of obvious difficulties with the current Ortho Elisa assay (susceptibility to "stickiness", unreliability of predictive value with heat treated samples, etc) I have developed a very strong feeling that the screening of donors for HCV antibodies should be introduced at the earliest possible opportunity. This is not because of the "science", but because there appears to be little doubt that people have contracted HCV as a result of transfusions which they would not have received had those transfusions been screened for HCV antibody. Furthermore there are apparently five known cases of HCC due to PTH. The reason, therefore, from my proposing this view is actually one based on future litigation. I am pretty convinced that the NBTS and SNBTS will find legal action taken against them in about 10 years' time from persons who have sustained post-transfusion hepatitis as a result of receiving HCV antibody containing blood which was presumably infectious for HCV at the time."*[207]

172. A memorandum from Dr Gunson to RTC Directors on 22 January 1991 announced:

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[206] SBTS0000155_102
[207] PRSE0001562

"*ANTI-HCV TESTING OF BLOOD DONATIONS*

1. The Department of Health have agreed that routine testing of all blood donations for anti-HCV can be put into operation.

2. I have been asked to try and ensure that testing starts simultaneously in RTCs in England and Wales and that it is co-ordinated with commencement of testing in Scotland.

3. Will you please advise me what you consider to be the earliest date that you could commence testing. It would be helpful if I could have this response by Tuesday 29th January.

4. Financial arrangements to cover routine screening and supplementary tests have still to be concluded and I will advise of these at a later date.

5. The U.K. Advisory Committee on Transfusion Transmitted Diseases has met and have put forward proposals for protocol for carrying out the tests. These will have to be put to the at a meeting scheduled for 25th February. When the minutes of our mooting have been agreed by the members I will circulate them for comments.

6. I will inform Ortho and Abbott that routine screening for anti-HCV has been approved and that we will inform them of the starting date in due course."[208]

173. Professor Cash felt that the time was not right for the introduction of anti-HCV testing to be implemented routinely, as he explained in a letter to Dr Gunson dated 24 January 1991:

"*ANTI—HCV : DONATION TESTING*

Many thanks for your memo of 22nd January. I have liaised with SNBTS RTDs and we are unanimous in advising, with the greatest respect but in the

[208] NHBT0000076_006

strongest possible terms, that anti—HCV donation testing should not be commenced in the UK BTS until after the Gulf conflict is over or at least until such time as we are confident our blood collection and microbiology testing teams can cope with what will be quite substantial changes and increased workloads. Just at the moment there are a lot of exhausted staff in our RTCs and I would judge that when the troops go in, our current frenetic activity will be sustained. We would be most grateful if you would see Ministers are appropriately advised. We would wish you to emphasise that we do not intend to be obstructive in any way but believe this increased load (HCV donation tests) in the present circumstances could lead to GMP failures in existing overstretched programmes. We remain firmly committed to starting on the same day as our NBTS colleagues and if pressed by Ministers I would suggest, in the circumstances, a May/June date should be considered. However, I would much prefer to wait another month and then respond to your letter."[209]

174. Dr Gunson replied on 28 January 1991, agreeing that starting testing in the immediate future was *"entirely impractical."*[210] Professor Cash reiterated his concerns in a letter of 15 February 1991:

> *"HCV DONATION TESTING: START DATE*
>
> *Thinking ahead to the end of June 1991 and checking over previous correspondence I think we need to do one more thing in the not too distant future. I refer to defining what "start date" will mean - it's a re-run of the HIV-1 programme.*
>
> *Whatever the "start date" will be, do we mean that by 9 a.m. on that day all RTC products and those in associated hospital blood banks will be HCV (screen) negative? The definition of RTC products will, of course, be those not from BPL or PFC. If we adopt this definition, then clearly testing will have to commence well in advance of the "start date".*
>
> *Next we will need, as on previous occasions, to obtain a policy decision with regard to plasma already in bond at both fractionation centres and awaiting*

[209] NHBT0000073_033
[210] PRSE0004144

uplift (at RTCs) for the fractionation centres. If a decision is made to test aliquots from these donations, the task is doable but formidable.

Sorry to pester but I suspect you will have to pursue Dr Metters' Committee on these topics. Once again we would very much like the SNBTS to stay in line with NBTS/BPL."[211]

175. The start date was discussed at a meeting of the UK Advisory Committee on Transfusion Transmitted Diseases which Professor Cash attended on 25 March 1991. At that meeting, "*It was agreed that testing of blood and plasma donations would commence on a specified date. There would not be retrospective tests carried [out] on donations collected prior to that date.*"[212]

176. On 27 March 1991, Professor Cash wrote to Dr McIntosh:

"*UK BTS HCV DONATION TESTING: START DATE*

You will want to know that our NBTS colleagues are struggling, on a number of accounts, to meet the 1st July deadline, as previously discussed and I thought agreed. We believe the fundamental problem is one of financial resourcing.

At a meeting of the UK BTS Advisory Committee on Transfusion Transmitted Diseases in Manchester on Monday last, the following was agreed:

(a) Harold Gunson would advise DOH that the 1st July start date should be delayed until such time as an evaluation of the new generation of HCV screening tests had been completed. If this is accepted it could push a start date to September. Both Ruthven and I supported this proposal.

(b) The definition of a start date now proposed will be exactly as stated - the date when routine HCV donation testing will commence. NBTS colleagues do not wish to accept the original proposal (which applied to HIV-1 testing) that the definition of a start date would be that on that date all RTC products issued would have been HCV tested.

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[211] PRSE0002763

[212] NHBT0000073_063

More anon when things are clearer!"[213]

177. On 3 April 1991, Dr Gunson sent a further letter to RTC Directors revising the proposed start date for anti-HCV testing from 1 July to 1 September 1991, to allow for a "second-round" comparative evaluation of anti-HCV test kits at the Newcastle, North London and Glasgow RTCs.[214]

178. Professor Cash replied on 5 April 1991: "*My colleagues would wish you to know that this most recent development leading to a start date in September 1991, has the SNBTS Directors' fullest support*".[215]

179. A controversy was sparked when Dr Huw Lloyd at the Newcastle RTC decided to commence anti-HCV testing in advance of the planned national roll-out. He explained his reasoning in a letter of 2 May 1991:

> *"Re: Hepatitis C Testing*
>
> *As you know there was a date of 1st July set for Hepatitis C Antibody testing • Fairly recently this was changed with a provisional date set for September 1991.*
>
> *In view of the fact that we were already set up for testing, I have decided to keep to the July date. By 1st July, all units of blood for transfusion in the Northern Region will be negative for Hepatitis C antibody.*
>
> *My personal view is that not to test now that we have the ability to test would be indefensible under the current Product Liability Legislation. I appreciate that individual Directors may take a different view on the potential liability under the Consumer Protection Act, but the fact that this Centre is testing, should not materially alter that judgement.*
>
> *I would be interested to know if any Centre is currently carrying out any additional tests such as Hepatitis B core testing or ALT testing and if so, what criteria are being used to select donors/samples for testing."*[216]

[213] SCGV0000163_053
[214] NHBT0000073_065
[215] NHBT0000191_133
[216] NHBT0000074_014

180. Professor Cash responded to Dr Lloyd on 7 May 1991 that he had received the news of his decision with "*quite profound dismay*" and stated that "*this unilateral action is both disgraceful and mischievous*", showing "*the NBTS descending into a position now more accurately described as chaos*". He concluded, "*I beg of you to reconsider the matter. Collective responsibility and security has much to commend it and if you can spare the time to study the HIV/haemophilia litigation papers, you should confirm this conclusion.*"[217] Several other RTC Directors were also critical of Dr Lloyd.[218]

181. Dr Lloyd replied to Professor Cash on 9 May 1991:

> "*I too have spent many hours looking at material relating to HIV litigation, but my conclusion is different to the one you appear to be drawing. The situation is now quite different to that which existed when HIV 1 testing commenced, and I personally believe that to start HCV testing to the original schedule is the correct decision, even if it appears unpalatable to some.*"[219]

182. On 8 May 1991, Professor Cash wrote to Dr Gunson proposing a national large scale validation study of the Abbott and Ortho anti-HCV testing kits involving some, but not all, RTCs. This was proposed to be conducted over two phases, the second running to 31 August 1991. He explained:

> "*The "public" reason for this phase will be (using only participating trial RTCs) to collect more screen test positives to allow more extensive studies in the confirmatory laboratories. This period could be extremely valuable scientifically, but, operationally, it will allow all participating Centres (particularly Newcastle!) the option of not stopping and then starting on 1 September 1991.*

[217] NHBT0000074_019
[218] NHBT0000192_009, NHBT0000074_017, NHBT0000074_020, NHBT0000074_021, NHBT0000074_031, NHBT0000074_030
[219] NHBT0000192_031

It will also ensure that non-participating Centres don't get jittery (product liability) in the month of August 1991!"[220]

183. On 9 May 1991, Dr Gunson advised the RTC Directors that the DH had reviewed their policy in light of Dr Lloyd's decision to commence testing early, and that they concluded the 1 September decision should remain. In particular, they were awaiting the second generation anti-HCV tests receiving FDA licences.[221]

184. On 13 May 1991, Professor Cash responded to Dr Gunson linking the Newcastle RTC's decision with his wider concerns to establish a ministerial advisory group to provide oversight of and give approval to blood donation policy decisions. He wrote:

> "*It has always been the view in Scotland, both in the Scottish Office and throughout the SNBTS, that the introduction of additional microbiology donation screening tests would be subject to Ministerial approval. Our understanding of this issue goes back many years to when SHHD directly intervened to stop one SNBTS Centre unilaterally starting HBsAg donation testing. In recent times, evidence that Ministers wished to acquire a firmer grip on this activity came with the establishment of the Advisory Committee on the Virological Safety of Blood. This development, in principle, was warmly welcomed in Scotland.*
>
> *In the past months we have witnessed two happenings in the NBTS which unequivocally indicate that our interpretation of the policy referred to above may be seriously flawed. I refer to the unilateral action of BPL demanding ALT donation testing and the most recent HCV episode in Newcastle. It is difficult not to conclude, particularly having witnessed the passivity of the DOH on both occasions, that Ministers no longer wish to be involved in this exercise and that their current intention is to leave such matters to respective Health Authorities. Should my conclusions be confirmed, then I would wish to emphasise that I deplore this development. It will lead to chaos which will become evident in the courts. To the best of my knowledge, this is a*

[220] NHBT0000074_024
[221] NHBT0000192_024

development in the management of blood transfusion services which is unique in Europe. There can be little doubt that the impact of the White Paper concepts of the marketplace are contributing to the development of this chaos. You will recall that I proposed several years ago that there be established an authoritative ministerial advisory group which concerned itself with all policy issues relating to the safety of blood donations. I do believe this matter now requires urgent consideration. Such a group should not be restricted to virus transmission and must, above all, be authoritative."[222]

185. On 14 May 1991, Professor Cash circulated a memo to SNBTS board members, in which he stressed the need for patience in evaluating anti-HCV test kits to ensure maximum sensitivity and specificity. He described the decision to change the implementation date from July to September to allow evaluation of second generation testing kits *"prudent and responsible."* He also stated: *"Beyond this, representations are being made, in the light of the developments at Newcastle RTC, as to whether, in future, the SNBTS is bound to a UK BTS approach with regard to donation testing, against a background of Ministerial involvement."*[223] On the same day, he also wrote to Dr Gunson to confirm that SNBTS would contribute to the UKBTS second generation testing study and looked forward to receiving the protocol in due course.[224]

186. On 20 May 1991, Dr Gunson replied regarding Professor Cash's proposal to form a ministerial advisory group. He was in broad agreement with Professor Cash's position:

"I agree that something needs to be done to ensure that all RTCs act in concordance in these important matters. Both the ALT affair, as a result of which my actions were criticised and are still causing repercussions, and the most recent incident, have presented me with considerable difficulties. Also, I can tell you that whilst these two instances are ones which have come to your notice because of their magnitude there have been many other occasions

[222] NHBT0000192_039
[223] NHBT0000192_144
[224] NHBT0000078_030; see also NHBT0000074_050

where RTCs have "gone it alone" which I have had to try and resolve and the whole business is becoming very frustrating."[225]

187. On 5 June 1991, Professor Cash wrote to the Director of Aberdeen and North East Scotland BTS to propose the commencement of an HCV antibody (anti-HCV) screening programme for all donors involved in the 'boosting cells in anti-Rh(D) programme".[226] On 3 July 1991, Dr Urbaniak wrote to Professor Cash:

> "*HCV TESTING RED CELL DONATIONS FOR SNBTS ANTI-D IMMUNISATION/BOOSTING PROGRAMME*
>
> *Thank you for your note indicating it would be now acceptable to "go official" on anti-HCV testing of red cell donors used for boosting. In actual practice, we had anticipated this likelihood and our last SNBTS Guidelines (February 1990) includes a provision for anti-HCV testing as and when available. There is therefore no need for the Guidelines themselves to be revised and I understand that retrospective accreditation of current red cell donors has been undertaken in the West. Subject to confirmation that this is actually being done and documented, everything regarding anti-HCV testing is in place.*"[227]

At a meeting of the UK Advisory Committee on Transfusion Transmitted Diseases on 10 June 1991, the possibility of routinely performing confirmatory tests on all donations with repeated positive anti-HCV tests was discussed. At that time the best available confirmatory test was thought to be RIBA-2, but that needed further study. Best practice would entail donors confirmed to test positive receiving counselling before being referred to a consultant physician. However, this was considered not to be practicable due to resource implications, save that "*The situation in Scotland is different from that in England and Wales and it was considered that SNBTS could implement the proposals*".[228]

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[225] NHBT0000192_058
[226] NHBT0000074_046
[227] SBTS0000021_042
[228] NHBT0000044_003; Dr Follett later noted that Professor Cash had opposed the use of the RIBA-2 test and pushed for independent confirmatory laboratory testing - NHBT0000192_087

188. It appears that Professor Cash and Dr Lloyd later resolved their differences to some extent, and on 4 July 1991, Dr Lloyd wrote to thank him for "*burying the hatchet*". However, he also reiterated that:

> *"I am concerned that the U.K. seems to be dragging it's [sic] feet over testing. I appreciate that many questions are not answered and for some Transfusion Centres, their organisation will find it difficult to introduce another test. By waiting until everyone's problems etc. are sorted out, we run the risk of accepting the lowest common denominator. I somehow doubt that you would be happy to accept the lowest common denominator approach. The attitude of UK Transfusion Centres has often not been very positive and when we look back at the plasma procurement situation (South of the border) over the years, it presents a very dismal picture. A little more fire and enthusiasm for Transfusion is required and a little less local protectionist activity and negative thinking."*[229]

189. On 5 July 1991, Professor Cash wrote to the SNBTS Directors regarding a proposed protocol for disposal of plasma which screened positive for anti-HCV. His proposal was:

> "*(a) All repeatable screen test +ves will be handled as follows: (i) Samples sent to Reference Laboratory. Index donation (all components) labelled "biohazard" and discarded. Donor Record flagged "Medical Hold" equivalent.*
>
> *(b) All donors who are confirmed positive by Reference Laboratory (RIBA 2+ve or RIBA 2 Indeterminate but PCR +ve) (i) Donor Record flagged "Permanently Off Service" (Local and National Register). Donor counselled and if appropriate referred to specialist physician.*"[230]

[229] PRSE0001183
[230] NHBT0000044_035

190. On 8 August 1991, in advance of a UKACTTD meeting on 13 August 1991, Professor Cash informed Dr Gunson that the SNBTS was not happy with Dr John Craske's proposals regarding confirmatory testing:

> "*A wee note in advance of the meeting: intended to prevent any possible disharmony. We (Scots team) are not happy with John Craske's proposals. As you know, we have always had much concern about the internal setting of cut-offs. Looking at some of the variations between Centres using the same test (same company) on the same samples, and also batch variations (IR and RR), leave us feeling that John's proposals are fraught with problems that could have future legal consequences. We were not happy with the conclusions Richard and his team came to in their Lancet paper. The admitted absence of questioning on drug abuse is a critical flaw in this paper. The technology used is also a little dated - though we wouldn't wish to pursue that. But the underlying conclusion for us is that at the present time we still don't feel there is sufficient evidence of sexual transmission to lead us to modify our counselling stance to donors. Hope these comments are helpful.*"[231]

191. On 20 May 1992, Professor Cash wrote to Dr Gunson regarding an anti-HCV testing post introduction study. He expressed disappointment that the NBTS laboratories did not deliver on agreed targets: *"It's difficult not to conclude that as a consequence the science of this study is weak and certainly not now novel. Moreover, a significant part of the data are of a quality which could lead to confrontation - possibly of a legal nature - with some commercial kit manufacturers."*[232] In a further letter on the same day he told Dr Gunson that he had advised his team to publish their data independently of NBTS colleagues.[233]

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[231] NHBT0006389
[232] NHBT0000193_122
[233] NHBT0009797

192. In various communications around the possibility of litigation regarding HCV, Professor Cash maintained that the decisions concerning the testing implementation date had been appropriate.[234]

Look Back

193. Professor Cash told the Penrose Inquiry that he was not directly involved in the look back exercise, but did promote it.[235]

194. On 9 July 1990 Professor Cash wrote to all RTC directors stating that both he and Dr Gunson had agreed that it would not be appropriate to introduce a systematic look-back programme after the start of HCV testing. [236]

195. By 3 October 1990 however, Professor Cash had written to Dr Gunson saying:

'I would much appreciate your thoughts on the issue of "look-back". You will have noted that our team have indicated the need for a policy statement and in their view "look-back" should be attempted.'[237]

196. Dr Gunson's reply informed him that it would be considered by the UK Blood Transfusion Service Advisory Committee on Transfusion Transmitted Diseases on 8 January 1991.[238] It was indeed agreed at that meeting that there may be an ethical obligation to inform patients who had received transfusions from anti-HCV positive donors but that this would require a lot of additional extra work and funding.[239] No decision was made to undertake this work.

197. In addition, on 6 November 1990, the SNBTS Medical and Scientific Committee agreed that Professor Cash should write to the Chair of the DOH ACVSB asking that careful consideration be given to a lookback programme.[240]

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[234] NHBT0000077_061, NHBT0000193_001, PRSE0000615, NHBT0000077_071
[235] PRSE0001273
[236] PRSE0001133
[237] NHBT0000073_007
[238] PRSE0002167
[239] NHBT0000073_028
[240] PRSE0000348

198. On 22 November 1990 Professor Cash wrote to Dr Metters, Deputy Chief Medical Officer, suggesting that the Department of Health Advisory Committee on the Virological Safety of Blood consider whether a policy of look-back should be implemented.[241]

199. On 19 February 1991, the SNBTS Medical and Scientific Committee met and it was recorded that "In the light of national events, it was agreed no 'look back' should be introduced at present".[242]

200. Professor Cash again raised the issue of look back with Dr Gunson on 18 November 1993, suggesting that the issue might be discussed by the Advisory Committee on the Microbiological Safety of Blood and Tissue for Transplantation ("MSBT").[243]

201. Professor Cash continued to press for a lookback exercise to be undertaken. The SNBTS Medical and Scientific Committee on 18 May 1994 agreed that where a donor was identified as HCV positive, archive samples should be tested to identify a seroconversion date and information about the components would be sent to clinicians including the recommended action they should take. Where components were provided to a named patient, it was agreed the SNBTS would identify the recipients and provide relevant information to the relevant medical officer. However, Dr Keel requested that nothing be pursued until there had been communication with SHHD.[244]

202. Professor Cash's view that a lookback should be undertaken was known to his colleagues, and it may be that he was one of the key advocates behind the pressure that was felt by Dr Ala, as Chair of the NBS Advisory Committee on Transfusion-Transmitted Infection, to promote a lookback.[245] Professor Cash participated in the Birmingham ad-hoc meeting of experts for SACTTI, that took place on 5 August 1994.[246] This meeting accepted that there was a duty of care to

[241] PRSE0001573
[242] PRSE0003568
[243] PRSE0003928
[244] PRSE0003685
[245] NHBT0095526_0026
[246] NHBT0009383 and PRSE0001386

recipients requiring a lookback exercise.[247] A paper was produced by Professor Cash setting out the recommendations of the SACTTI, that there was a serious case for Hepatitis Advisory Group and the MSBT to consider a lookback exercise.[248]

203. At the meeting of the SNBTS Medical and Scientific Committee of 10 November 1994, he had secured Scottish support for a lookback to be completed and liaised with Dr Robinson to seek a recommendation from the MSBT that it should take place. It was agreed that SNBTS RTCs would commence the lookback programme, but only to the point of gathering data ready to subsequently inform patients.[249] A recommendation that a lookback should be conducted across the UK was made by the MSBT on 15 December 1994.[250]

204. On 20 February 1995 Professor Cash wrote again to Dr Metters making a number of suggestions about the proposed UK guidelines for HCV lookback.[251] The final guidance was issued on 3 April 1995.[252] It appears from this letter that the SNBTS RTCs provided a 'substantial direct/hospital blood banking service' and so would be able to adequately track donations/recipients from their own records. By 14 March 1995, the SNBTS were ready to initiate procedures to inform patients that they had received implicated transfusions but were waiting for other nations to catch up.[253]

205. The SNBTS Medical and Scientific Committee took the decision on 10 October 1995 that general testing of those who had received a transfusion should not be offered until the lookback exercise was complete. Professor Cash was asked to communicate that position to Dr Metters of the Department of Health.[254]

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[247] PRSE0001386
[248] PRSE0001236
[249] STHB0000684
[250] NHBT0009714_004
[251] NHBT0005835
[252] NHBT0002796_002
[253] DHSC0003595_030
[254] STHB0000687

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