DRAFT

Dr Brian McClelland Witness statement 3

Schedule headed "AIDS and HIV"

Historical view

The questions raised in the Schedule are mainly about the early part of 1983. The use of the heading "AIDS and HIV" could be taken to imply knowledge that was either extremely new in early 1983, or that did not arise till later. The term AIDS arose first at a meeting of leaders from the blood industry, haemophilia groups, gay community organisations, and representatives from the NIH and the FDA on July 27 1982.[1] 10152.tif

The virus that was shown to be the causative agent was first reported in mid 1983 as LAV (lymphodenopathy associated virus)[2] 10153.tif and in mid 1984 as HTLVIII (Human T Lymphotropic virus type III)[3] 10154.tif

The term HIV was not assigned by the International Committee on Taxonomy of Viruses until May 1986.

Personal background relevant to the matters in the Schedule

As a first year junior house officer in 1969, I was privileged to work for the late Dr Howard Davies, an Edinburgh Royal Infirmary consultant physician who cared for patients with haemophilia. Dr Davies was a strong proponent of cryoprecipitate rather than factor VIII concentrate. I remember clearly that his rationale for this struck me as being eminently sensible. It was that by avoiding the use of products made from the blood of thousands of donors, especially those from other corners of the world, one was almost bound to reduce the risks of passing on infections, known or unknown to the patients.

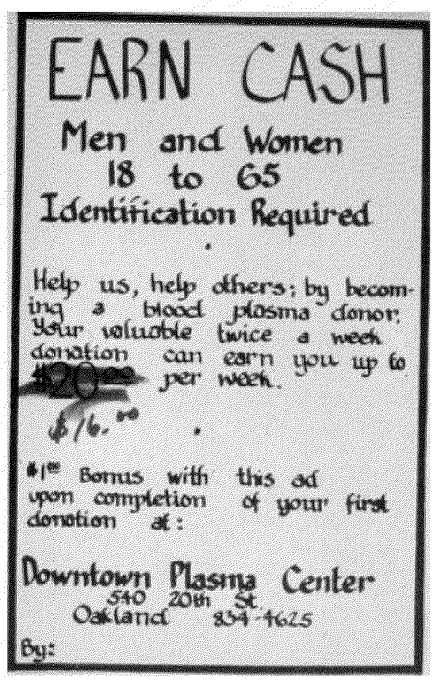
I did not undertake specialist training as a haematologist and my job as regional

transfusion director in Edinburgh did not include clinical responsibility for the care of patients with haemophilia. The selection and use of blood products for patients with haemophilia is not an area in which I have ever been clinically involved. It is also the case that during my whole tenure as regional director, those medical consultants in the BTS in Edinburgh, whose specialist qualifications were in haematology, were not involved in the clinical management of haemophilia patients in Edinburgh.

I also remember very clearly an experience that has coloured my thinking about the use of blood from commercial donors throughout my career, and I cannot think of any reason why this would not have influenced my own views about commercial Factor VIII during the early 1980s. Shortly after my appointment to the SNBTS in 1977 (I do not have a record of the dates) I visited the Cutter Company in San Francisco. During this trip I visited their Oakland plasma centre. I have a very clear recollection of being amazed to find that there were no donors in the centre and that I asked one of the two staff in evidence why the centre was empty. I recall her response, which was that this was typical for that day of the week, because it was the day for collection of social security cheques. I also recall that I took away a copy of a notice displayed in the centre (Figure 1). This stated the fees for a plasma collection - $US 16

Figure 1

Scan of a poster obtained during visit to the Downtown Plasma Centre, Oakland Ca about 1982



This visit left me in no doubt that even in this relatively favoured part of the USA, the company depended very heavily on the provision of plasma by people of low income. One implication of this that was clear to me at that time was that plasma was being collected from individuals who might be dependent on the payments from the plasma centre and who would therefore have an incentive to conceal any aspects of their health that might make them unsuitable as donors.

Structure of this Statement

I have dealt with the points in the order of the Schedule. I have numbered each of the individual questions raised under headings 1, 2, 3 and 4 of the Schedule as 1.1, 1.2 etc. I have also attached a copy of the Schedule into which I have inserted the numbering used in this statement.

Response to the questions raised in the Schedule

1.1 By the beginning of 1983 was there any recognition that the arrival of AIDS and its possible connection with commercial blood products required a re- assessment of the risks/benefits associated with the use of commercial rather than NHS products?

In August 1982, Dr Peter Foster and I attended the Budapest Joint meeting of the ISBT and ISH and Dr Foster noted in his report of the meeting that Dr Lou Aledort, who was a doyen of haemophilia treatment in the USA, had referred to cases of AIDS in patients with haemophilia. There had already been a report of 3 such cases by the CDC in July. I do not have any recollection of my own reaction to this information at that time.

On 18th January 1983 I attended a meeting of the regional transfusion directors transfusion associated hepatitis working party (WP TAH). Dr John Craske reported that

he "will be studying the effects of American factor VIII in UK recipients…examining immunological markers..."[4]10155.tif

I do not remember the context of this statement but it appears to indicate that there was concern among this group about the safety of American products.

There is evidence (in the form of a letter dated May 23rd 1983 from Dr Arthur Bloom replying to Dr Frank Boulton in Edinburgh) that Dr Boulton had written to Professor Arthur Bloom, chairman of the haemophilia reference centre directors expressing concerns about the safety of Factor VIII from the USA. I have been unable to obtain a copy of Dr Boulton's original letter, nor do I have a clear recollection of having seen it at the time, but I think it is most unlikely that we did not speak together about this subject, as we had adjoining offices and had frequent informal discussions.

1.2 Why was there no discussion about the possible connection between AIDS and commercial blood products?

I do not believe that it is the case that there was "no discussion". I think it is evident from Professor Bloom's letter to Dr Boulton, that there was discussion about risks of commercial Factor VIII, both between Bloom and Boulton, and at the meetings of the haemophilia reference centre directors. The minute of the WP TAH on January 18th 1983 also indicates that there were concerns about factor VIII from the USA and these were beginning to be investigated. I am sure that there would have been discussion in other places about this matter.

2.1 Should Scottish representatives have been invited (to the UK HCDO meeting on 13th May 1983)?

I am surprised if no Scottish haemophilia clinician was at this meeting as it was a UK

group and I would have expected that an invitation would have been sent.

2.2 Was there reluctance to involve them?

I have no knowledge of this but I would be surprised if there had been reluctance to involve haemophilia clinicians from Scotland in a meeting of the UK group. I was not aware of the distinction that appears to be made in reference DHF.001.7665 between "centre of excellence" and "reference centre" and I do not see why this should have had a bearing on the invitations to this meeting

2.3 Was their any thinking along the lines of Dr Spence Galbraith's letter to the DHSS in Scotland?

I have already referred to the letter from Professor Arthur Bloom to Dr Frank Boulton. This seems to show that Dr Boulton had made a number of proposals that were intended to address the risks of commercial factor VIII. Without a copy of Dr Boulton's letter I cannot say if his proposals included banning or restricting the use of factor VIII from the USA, but Prof Bloom's reference to "deferring of home treatment" might suggest this.

The Schedule states that "there must have been knowledge in Scotland of this recommendation by Dr Galbraith", and I would be surprised if Dr Galbraith's concerns had not been transmitted by DHSS to the SHHD, since this matter was important to the regulation of blood products and this was a UK matter.

I am sure, however, that I was not aware of the existence of Dr Galbraith's letter before I started to work on preparation for the Inquiry. I believe that I was informed of it about one year ago by Dr Peter Foster who had found reference to this letter during research in the DHSS website. It could be this letter that is referred to in Dr Mitchell's note of the English Directors minute of 18th May 1983, although if this is the subject of the

comment, the reference is cryptic "The reported banning of USA material for haemophilia treatment was not confirmed by DHSS". I have read the redacted minutes of this meeting (113) 10278.tif and could find no reference to commercial factor VIII.

2.4 (Was there) recognition that cessation of use of products from the USA would eliminate risk from that source?

The fact that there is so much contemporary evidence of resistance to reduction in the availability of commercial concentrates is itself an indication that the idea of reducing supplies of these products must have been a matter of concern in many quarters. I do not believe that the risks of imported factor VIII were unrecognised and by implication, it must have been evident that if these products were not used there would be no risk from them. In retrospect it became obvious that many or most clinicians underestimated the risk. The initial belief by many clinicians and the Haemophilia Society that the benefits of continued use of commercial factor VIII outweighed the risk of AIDS was ill founded. I think that in the UK the risks began to be recognised soon after the publication in July 1982 of the MMWR report on AIDS in haemophilia patients [LIT.001.0559]. Although the source of the products that the reported patients had received is not given, it is likely that they had received predominantly commercial factor VIII. I was certainly aware of the first report in 1983 of AIDS transmission by platelets[5] 10156.tif and around this time we had invited one of the authors (Dr Diane Wara) to Edinburgh BTS to speak at a seminar on possibilities for surrogate testing to detect individuals at increased risk of transmitting the putative agent of AIDS. This is referred to in the accompanying paper [6]

2.5 Was the advice from Professor Arthur Bloom disseminated?

I cannot answer this question but I would be most surprised if Dr Ludlam had not shared this information with his colleagues.

2.6 Was there a gathering of Scottish haemophilia clinicians to discuss?

This would have to be answered by those clinicians who would have been involved.

2.7 Was any different advice issued in Scotland?

I do not know, but it seems most unlikely that the substance of this guidance would not have been reflected in any advice issued in Scotland

2.8 Practice in relation to the treatment of children in Scotland

Individual clinicians treating patients with haemophilia would have made their own clinical decisions about the choice of product. My recollection is that the view of the haemophilia doctors who I talked to around this time was that the choice of treatment for young children should aim to keep the risk of infection as low as possible. I am however aware that some clinicians believed in starting concentrate treatment in quite young children (See Appendix 1)

2.9 Large quantities of Commercial factor VIII used at Yorkhill?

I have no direct knowledge of this but I do recall that for many years I have had the impression, from whatever sources, that the late Dr Michael Willoughby was a believer in the use of relatively large amounts of factor VIII concentrate for his patients. His early interest in prophylactic therapy using concentrates is evident in his 1976 textbook[7] 10157.tif

I also have had the impression that he favoured the use of some commercial products. I assume that choices of product were made on the basis of selecting the product judged to be most suitable for individual patients.

2.10 Was any attempt made to formulate strategies for reducing the amount of concentrate…used. .?

From the view point of the SERTC, there is no doubt that a substantial amount of effort was put into improving the yield of cryoprecipitate by use of the thaw siphon technique.[8] 10158.tif Dr John Cash had a very active research interest in DDAVP and I am sure that he would have made efforts to encourage its use.[9] 10159.tif.

2.11 Use of DDAVP in Scotland

I do not have information about the extent of use of DDAVP in Scotland but I am aware that it was recommended for the treatment and management of suitable patients. I do not remember exactly when the use of DDAVP began but it was quite early in my time in SNBTS.

2.12 Attendance at WFH/ISTH meeting on June 27 – 29 1983

I do not know which of the Scottish haemophilia clinicians attended this meeting, nor about the distribution of Dr Peter Foster's report.

2.13 Scottish participation in the CSM Biologicals Subcommittee meeting on 13th July 1983

I do not know if there was a Scottish representative present or whether its proceedings were notified to anyone in Scotland. I was under the impression that all meetings of the CSM were confidential as the business involved information that was commercially confidential

3.1 The Aarhus Conference in 1983

Dr Peter Foster attended the Aarhus conference. I do not know if others from Scotland

attended.

3.2 The WHO Geneva Conference in 1983

This was attended by Dr John Watt and myself. Dr Watt presented a paper entitled 'Acquired immune deficiency; implications for blood and blood products'[10] 10160.tifI submitted my report and recommendations from the Geneva Conference to both the SNBTS and to Dr AE Bell of the SHHD (21, 77, 78, 111). 10213.tif 10242.tif 10243.tif 10276.tif I do not have records detailing further dissemination, but it would have been consistent with my usual practice to have given copies to colleagues who shared an interest in the topic

3.3 *In relation to the UKHCDO meeting and various communications from or relating to the Haemophilia Society around this time the emphasis appears to have been strongly on maintaining the use of commercial concentrates. Is this an accurate impression?*

That is certainly my understanding of the general view among haemophilia clinicians at that time.

3.4 *Did haemophilia clinicians from Scotland agree that patients should not be encouraged to revert to cryoprecipitate for home therapy?*

I have no personal experience of the information communicated to patients on this mater

3.5 Did haemophilia clinicians in Scotland follow the advice from the Geneva conference?

The report of the WHO meeting (Acquired Immune Deficiency Syndrome Emergencies, Report of a WHO Meeting, Geneva 22-25 November 1983,WHO/STD/84.1) (112)

10277.tif includes the following recommendations relevant to the use of blood and blood products:

Informing persons with hemophilia and their physicians of the potential health hazards of factor VIII or factor IX products, including risks related to AIDS

Considering the use of auto transfusion using frozen or conventionally stored blood for suitable patients

A predeposit autologous transfusion service was provided by the SERTC during the years 1987 to the early 2000's and was eventually ended due to lack of clinical requests. . I cannot say from personal knowledge whether or not specific note was taken of these WHO recommendations by the haemophilia clinicians in Scotland. There is little doubt that the Haemophilia Society and some haemophilia clinicians felt that the benefits of treatment with factor VIII outweighed the risks of infection, and gave advice accordingly.

3.6 Was there an awareness of Scottish patients with AIDS?

It is now quite simple to understand the sequence of events that leads from infection with the virus through a period without any symptoms or clinical signs to the first clinical features that may suggest weakness of the immune system and on to the fully developed syndrome of AIDS. This can be monitored by laboratory tests that detect and quantitate the virus and measure the progressive deterioration of lymphocytes that are central to the immune system.

To answer this question I have to try to reconstruct my own understanding during 1982-1983 of what was a new, or newly perceived disease during the early stages after it had been recognised. I have also included as Appendix 2 an extract from a paper by Dr Bruce Evatt who was at the CDC in Atlanta during the early years of the AIDS epidemic.

I think that soon after the initial CDC reports of the new syndrome, some clinicians, especially those working in genito-urinary medicine (GU) medicine and caring for gay men suspected that they were seeing patients with some features that suggested this new form of immune deficiency. From May 1983 or possibly a little earlier, Dr Anne Smith and I were meeting with Dr Sandy MacMillan, a GU medicine Consultant in the Royal Infirmary of Edinburgh and Mr. Derek Ogg of the Scottish Homosexual Rights Group to work out ways of communicating to gay men the message that they should refrain from donating blood. Dr MacMillan would have been restrained by clinical confidentiality from mentioning any specific cases, but I have a definite recollection that by that time he was aware that some of his male patients who were known to be gay were showing clinical features that suggested that they could be suffering from this new form of immune deficiency disorder.

The papers presented to the WHO conference in November 1983 provide a vivid contemporary picture at one moment of this evolution. The initial recognition that this emerging disease could be affecting patients with haemophilia, and so could be blood borne, had been based on detective work – investigation of the CDC's observation that the drug Pentamidine was being requested, for infection with Pneumocystis carinii in patients with hemophilia. Pneumocystis was not a recognised complication of haemophilia and was known to be a rare infection in the absence of severe.immune deficiency. Recognition of this pattern was only possible because of the system of central ordering and supply of this drug through the CDC.

Many of the early clinical features of AIDS (such as weight loss, fever and bowel disturbance) can be caused by many different conditions. For clinicians in Scotland where there were few cases, it would have been difficult to recognise that a patient who

was showing some of the features that had been described in a few reports from the USA was suffering from the "new" condition.

I learned at the WHO Geneva Conference in 1983 of the importance of creating an effective case definition when investigating the epidemiology of a clinical syndrome for which there is no specific and sensitive diagnostic test. At the end of 1983, Dr James Curran of the CDC was emphasising the importance of creating a narrow case definition that would ensure that all cases that fulfilled the definition could be confidently counted as having the new syndrome. This was summarised in the following passage from the final report of the November 1983 WHO AIDS meeting

> "There is no specific diagnostic test for AIDS. For surveillance purposes in 1981 the Centres for Disease Control adopted criteria for defining AIDS. These criteria contain reliably diagnosed marker conditions considered indicative of severe underlying deficiency with no identifiable cause. (Appendix 1) This definition has been useful for monitoring trends and detecting disease patterns, but it may underestimate the extent of the problem. Clinicians have recognised that a variety of chronic but non-specific symptoms and physical findings may also be related to the syndrome". (112) 10277.tif

4.1 Why was it necessary to buy commercial Factor VIII in early 1984?

I do not know if there is any single answer to this. Individual clinicians treating patients with haemophilia would have chosen the product to be used. One factor that could have lead to the use of a commercial product was a clinical decision that a particular product was necessary for an individual patient. It is for clinical haemophilia specialists to

comment on this.

A second factor that would have influenced the purchases of commercial products was the extent to which the supply of SNBTS factor VIII matched clinical demand at the time. I am entirely clear in my recollection that within the SNBTS a very high priority was being given to collecting and processing sufficient plasma from Scottish donors to meet an increasing demand for factor VIII concentrate with indigenous product. This was one of the main driving forces of the SNBTS at the time.

The quantities of factor VIII being used were increasing due to increased patient demand combined with clinical enthusiasm for more intensive treatment and there would also have been the influence of active marketing by the commercial suppliers of Factor VIII concentrate.

The definition of "demand" for a blood product such as factor VIII is a matter that is open to debate [11]10161.tif. This is discussed in a paper recently prepared for the WHO. The definition of demand has substantial implications for the view that is taken about the supply and prescriptions of factor VIII. The decision to administer larger or smaller amounts of factor VIII is in most cases not a life and death decision but a choice about levels of quality of life. The widespread belief at this time was that the risks of more intensive factor VIII therapy were far outweighed by the benefits; this was the basis of increasing demand.

In this situation the SNBTS could never have been confident that it could guarantee to meet a demand that was essentially open-ended and despite the concerns raised by Dr Boulton, I think it would not have been for the SNBTS as a supplier of product to propose the withdrawal of other suppliers' products when this may have lead to a shortage. I believe that it was accepted by the SNBTS and the SHHD (and considered as

matter of the professional independence of doctors) that those responsible for care of the haemophilia patients should decide on the relative risks and benefits of (a) continued use of commercial product versus (b) reducing the total amount of treatment available in the event that supplies of indigenous product were less than the demand.

4.2 When were clinicians able to begin using heat treated commercial concentrates?

Heat treated factor VIII concentrates were licensed by the UK Medicines Control Agency in February 1985. My understanding is that a heat treated concentrate (Hemofil T, Hyland) was available from June 1983 in the Netherlands and was later shown not to transmit HIV [12]10162.tif. I do not know to what extent this product was available in the UK. Another commercial dry heated factor VIII product (Armour) was also available, but was later withdrawn as it was found to be capable of transmitting HIV.

Appendix 1

Extract from the report of the Lindsay Tribunal, 2002, pages 155-156

Dr. Brian Colvin, Consultant Haematologist and Haemophilia Centre Director, gave evidence of the practice at the Royal London Hospital. In the early 1980s, in order to reduce the risk of hepatitis, children under the age of ten were, in general, not put on home treatment but were treated in hospital with cryoprecipitate. This general policy was subject to exceptions through clinical necessity. Children who required home treatment started receiving it between the ages of 10 and 15. NHS concentrates were used for home treatment and commercial concentrates were used for treatment in hospital where treatment with concentrate was necessary. The rationale for this policy was that it was thought preferable to try to provide for the reasonably predictable demand for home treatment from the relatively scarce NHS product and to have reserves of the more readily obtainable commercial product available to meet the much less predictable demand for special clinical use in hospital. These policies were apparently not changed in 1983.

The policy at Newcastle Haemophilia Treatment Centre was described by Dr. Peter Jones, Consultant Paediatrician, and Director of that centre during the relevant period. It seems in that centre from the mid-1970s children were treated in hospital with cryoprecipitate up to the age of six. Children who required home treatment were commenced on home treatment at approximately the age of six using concentrates. NHS concentrates were used where available for home treatment and where not available commercial concentrates. It would seem from Dr. Jones' evidence that in the great majority of cases patients of the centre would have received both NHS and commercial concentrates and that only in the case of a small number of patients was it possible to provide all their treatment from NHS concentrates. Again it seems the policy did not

change in 1983 and in particular children who had reached the age of six who required home treatment continued to commence treatment with concentrates after that date.

Professor Christine Lee, Haematologist, gave evidence of the policy of the Haemophilia Centre in the Royal Free Hospital, London. Cryoprecipitate was apparently used extensively in that centre until 1978 because the then Director was an enthusiast for cryoprecipitate. In 1978, under a new Director, concentrate began to replace cryoprecipitate. A mixture of NHS and commercial concentrate was used. Children were treated with NHS concentrate. By 1983 the use of cryoprecipitate at the centre had virtually ceased. The policy described by Professor Lee in 1983 involved use of DDAVP where possible for persons with mild haemophilia and otherwise treatment with concentrate either NHS or commercial. Professor Lee suggested that although the policy of using NHS product for children existed before 1983, it was not based on a view that NHS product was inherently better than commercial concentrate. After 1983 NHS product was regarded as safer and was used preferentially for children on that basis. Apart from this change of emphasis, it does not seem that the treatment regime changed significantly in 1983. Professor Lee described a period during 1984 when elective surgery would have been deferred

Appendix 2

The experience of the central figure in the recognition that AIDS was a blood borne disease. Dr Bruce Evatt was at the CDC in 1982

Text extracted from Evatt BL, J Thromb Haemost. (2006) 2295-301[1]. Note that in this extract, the references shown as *[12-13]* refer to the reference list of the published article.

… Consequently, plasma demand rose significantly, and the need for volume rather than quality drove the plasma industry. Plasma was often obtained from paid donors who had high risks of blood borne diseases (extremely poor, prisoners, alcoholics, etc). *[2]* As a result, clotting factor concentrates, derived from pools up to 20,000 donors with

inadequate donor screening and infective agent testing, almost uniformly infected patients with hepatitis. *[12-13]* Considering the enhanced quality of life and increased longevity, these high infectivity rates were deemed an acceptable risk by patients, physicians, industry and government--viral inactivation technology was not vigorously pursued.

The Epidemic Begins It was in this setting that a new blood borne disease, acquired immune deficiency syndrome (AIDS), was spawned in Africa and transmitted by social and sexual intercourse of populations at high risk for blood borne disease into the Caribbean, the United States (US) and other countries of the developed world.

First apparent in the homosexual population in the US in the last quarter of 1980, the disease possessed unusual properties that initially obscured it as a distinct infectious disease. Previously healthy victims had no specific symptoms but presented with either secondary infections or tumors associated with immune deficiency (i.e., *Pneumocystis carinii* pneumonia (PCP) or Kaposi's sarcoma). *[14,15]* A long incubation time made it difficult to identify' person-to-person spread. Laboratory methods needed to culture and identity of the etiologic agent were lacking. Leading scientists focused on non-infectious causes such as antibodies to sperm or reaction of the immune system to chemicals such as inhaled amyl nitrites that homosexuals used to maintain prolonged erections. *[16,17]*

On *July 2, 1982*, a request for pentamidine was received for a third hemophilia patient infected with PCP in Ohio. Investigation confirmed the presence of the immune disorder. We were now reasonably convinced that hemophilia patients were another risk group for AIDS. The author notified Dr. William Foege, Director of CDC, and drafted a letter for him to warn all the HTC directors. The Executive Director of the National Hemophilia Foundation (NHF) was notified of the implications and NHF's cooperation was enlisted

to provide support for further surveillance and investigations. The CDC published an MMWR article reporting the three patients and suggesting the probability of a blood borne infection as a cause of AIDS.[13] 10163.tif In July 1982, we reasoned that the time had come to shift US investigations towards a blood borne and sexually transmitted infection as a cause of AIDS. *[19]* The members of the blood banking and plasma industry, the affected patient groups, the hematology professional organizations, and government agencies needed to be briefed and an attempt made to reach a consensus position, and ideally, to concur on preventive action, such as blood donor deferral guidelines directed toward excluding high-risk groups from donating blood.

However, these actions could not be easily achieved. Although the implications of finding the syndrome in the four risk groups provided a strong suggestion of a possible blood borne disease, no direct proof existed that showed the syndrome was infectious or transmitted by blood. No agent had been found and no tests existed to screen potentially infected persons.

Confronting "Existing Wisdom" On **July 27, 1982**, CDC representatives met with a group of leaders from the blood industry, hemophilia groups, gay community organizations, and representatives from NIH and FDA, to present the evidence of a possible transmission by a blood borne agent. *[18]* If the attendees accepted this possibility, we reasoned that high-risk groups should be prohibited from donating blood until the issue could be clarified by future studies.

It was a long day. Detailed histories of the hemophilia cases were systematically presented, followed by data from the other risk groups and comparison of hypothetical risks posed by various etiologic theories to each risk groups (Table I). *[12,20]* Only the high risk for blood borne infections could explain a risk common to all four groups. But, rather than expressing alarm at a possible blood borne infection and suggesting ways to

reduce a blood borne risk, the audience expressed an almost universal reluctance to act.

The scientific community had yet to see "published evidence that the syndrome was indeed an infectious disease," let alone blood borne and sexually transmitted. Homosexuals were major blood donors in the large cities on the east and west coasts. It was thought that singling out homosexuals for exclusion would unnecessarily stigmatize them without evidence that they were indeed transmitting the disease. The blood industry, threatened by losing a large donor pool, strongly supported the position of the gay groups on this issue; "three hemophilia patients with the syndrome did not mean that they should spend millions of dollars" changing recruitment and screening practices. The hemophilia groups expressed concerns that the data of immune suppression in hemophilia patients could have reflected the effects of prolonged use of blood products and did not necessarily mean they had the new syndrome. They also feared a stigma of having a disease associated with homosexual patients and were concerned that reducing the use of clotting factor concentrates would bring back old issues of deformities and early death, the fate of hemophilia patients before concentrate treatment. The FDA, which had regulatory authority over the blood industry, had not yet accepted the collection of disorders related to immune deficiency as a single disease, and was also skeptical that hemophilia patients represented another risk group. Thus, no consensus was reached concerning blood donors.

Two important accomplishments occurred, however. **The official name of the disease, the Acquired Immune Deficiency Syndrome (AIDS), was established**. The new name facilitated an expansion of investigations beyond that of solely a homosexual problem. In addition, the CDC was encouraged to continue the studies of hemophilia patients. *[20]*

Finally, by **December, 1982, we identified an unequivocal transfusion** case, a 20 month old infant who developed AIDS following multiple transfusions, including a

transfusion of platelets derived from the blood of a male subsequently found to have AIDS. We were now convinced that in spite of the absence of an identified agent, the pattern of the epidemiologic evidence was sufficient to implicate a blood borne disease. *[21,22]* This evidence could no longer be ignored—in our opinion urgent changes in blood policy were needed to reduce the risk.

Many of us at CDC were dismayed by the outcome of the January 4th (1983) meeting. No recommendations would be forthcoming from the Assistant Secretary's Advisory Committee and actions of groups present at the meeting (with the exception of the NHF) suggested they would be happy if we were not involved in the blood transmission investigation. We decided, however, to raise the visibility of the theory of blood transmission by suggesting the US Public Health Service (PHS) issue a number of official AIDS-related recommendations on blood donations. We drafted a set of guidelines to be considered by the Assistant Secretary of Health and the other Public Health Service agencies, thereby bypassing FDA regulatory authority. This action was clearly a breach of protocol in that the responsibility for such guidelines lay with the FDA, but we reasoned it was worth the risk of severe criticism in order to move the issue from its dead end position. This draft included exclusion of high-risk donor groups and surrogate testing of screen donors. This draft was promptly rejected by the other agencies, but after appropriate amendments, the FDA, CDC and NIH agreed on a set of guidelines that was published by the PHS on March 4, 1983, although it was clearly short of what we, as individuals, at CDC wanted. By this time 12 patients with hemophilia and 6 possible transfusion cases had been identified. The publication of these guidelines marked the beginning of a slow change in public policy on transfusion associated AIDS.

[1] Evatt BL (2006) The tragic history of AIDS in the hemophilia population, 1982-1984. J Thromb Haemost. 2006 Nov; 4(11): pp.2295-301

[2] Barre-Sinoussi F,et al (1983) Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science. 1983 May; 220: pp.868-71.

[3] Popovic M, Sarngadharan MG, Read E, and Gallo RC (1984) Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. Science. 1984 May 4; 224 (4648): pp.497-500. (This is one of a series of papers published by this group on that date)

[4] Minute of Regional Transfusion Directors' Working Party on Transfusion Associated Hepatitis. 18 January 1983. Held at NWRHA HQ, Gateway House, Manchester.

[5] Ammann AJ et al (1983) Acquired Immunodeficiency in an Infant: Possible Transmission by Means of Blood Products. , 1983 Apr 30;1 (8331): pp. 956-8

[6] McClelland DBL (2010) Actions taken by SNBTS to protect patients from AIDS. September 10th 2010

[7] Willoughby MLN (1977) Chapter 18: Coagulation Disorders, in Paediatric Haematology. Churchill Livingstone. pp. 324 - 325

[8] Mason EC, Pepper DS, Griffin B (1981) Production of cryoprecipitate of intermediate purity in a closed system thaw-siphon process. Thrombos. Haemostas. 1981 Aug 28; 46(2): pp.543-6.

[9] Cash JD (2003) DDAVP and factor VIII: a tale from Edinburgh . J Thromb Haemost. 2003 April;1(4): pp.619-21

[10] Watt JG (1983) Acute Immunodeficiency Syndrome: Implications for Blood and Blood Products. Paper for WHO AIDS meeting, November 1983

[11] In a draft document that I recently co-authored for the World Health Organisation the following definitions of *use, demand* and *need* for whole blood or red cell units were proposed. Definitions along these lines could also be applied to factor VIII
Current use of blood: The number of whole blood or red cell units consumed by a defined number of facilities over a defined period of time (usually one year). Includes blood transfused for all clinical conditions and interventions as well as any blood that was fit for transfusion but was not transfused for any reason.
Current demand for blood: The current demand for blood is the number of whole blood units required to met all requests for blood transfusion for patients at a defined number of facilities over a defined period of time (usually one year) Current demand reflects disease

burden, health services offered (facility factors), access to health care, and prescribing practice, but is not directly affected by inadequate supply

***Population need for blood*:** The number of whole blood or red cell units that would be required to transfuse all individuals who require a transfusion, in a defined population during a defined period (usually one year) of time . This is a utopian view – assuming optimal access to optimal health care for all in the population

'Inappropriate' transfusion: Transfusion given to a patient in circumstances for which the benefit of that transfusion is not supported by evidence, clinical guidelines or expert consensus.

McClelland DBL (1983) Acquired Immune Deficiency Syndrome Emergencies. Report of a WHO Meeting, Geneva, 22 – 25 November 1983

[12] Van der Meer et al (1986) Absence of Seroconversion for HTLV-III in Haemophiliacs Intensively Treated with Heat Treated Factor VIII Concentrate. British Medical Journal, 292, 19 April 1986, p.1049

[13] Centers for Disease Control (1982) Epidemiologic notes and reports *Pneumocystis carinii* pneumonia among persons with hemophilia A. MMWR Morbidity and Mortality Weekly Report.1982; 31; pp.365-7.