



SCOTTISH EXECUTIVE

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Your ref:
Our ref: 2003/0022570OR

4 November 2003

Dear Mr

Thank you for your e-mail of 8 October to the Rt Hon Jim Wallace, Deputy First Minister, seeking support for a public inquiry into the infection of haemophiliacs with HIV and Hepatitis C through NHS treatment with blood and blood products in the 1970s and 1980s. I have been asked to reply.

You mention that Christine Grahame MSP, Convener of the Health and Community Care Committee, had called for a Public Inquiry. I have assumed you are referring to the discussion on Hepatitis C at the Committee meeting on 9 September which was attended by Malcolm Chisholm. (The full transcript of the meeting can be accessed on the Scottish Parliament website <http://www.scottish.parliament.uk/health/or/he03-0501.htm>.) During this session the Minister agreed to consider a paper which had been submitted to the 'Scotland on Sunday' and the 'Times', Scotland, in relation to the infection of haemophiliacs with Hepatitis C through treatment with blood products. He subsequently obtained a copy of the paper in question which was entitled "Haemophilia Directors' Hepatitis C Working Party Report for Year 1980-81". The paper appears to have been considered at a meeting of Haemophilia Directors in September 1982.

The point at issue was whether that document revealed new information about what those government officials knew, and whether in particular it confirms that they were aware from as early as 1974 that treatment with blood clotting factor concentrates carried a risk of infection with what we now know as Hepatitis C. The Minister has since responded to Christine Grahame MSP along the following lines.

The Minister acknowledged that there is no doubt that this document did confirm that Haemophilia Directors and the Department of Health and Social Security were aware of such a link, but is of the view that this does not constitute new evidence. The Minister is aware that there are numerous published articles in eminent medical journals, such as the Lancet, in the 1970s and 1980s that record information, interest and controversy on this issue and considers that it is important to consider the Haemophilia Directors' report in that context.

In particular, in the early 1970s Hepatitis C infection was widely regarded as benign, although there is no doubt there were some clinicians who strongly dissented from that view. As more information became available more clinicians began to voice concern – although not uncommonly the view was expressed that the benefits of the treatment outweighed the consequences of the resultant infection. Certainly up until 1985 at least there was no universal consensus that the Hepatitis C infection had serious consequences and many experts viewed it as a mild, non-progressive condition. This is recorded in the Scottish Executive's Report on Hepatitis C and Heat Treatment of Blood Products for Haemophiliacs in the Mid 1980s (October 2000) along with appropriate references.

NOT RELEVANT

From at least 1976, product information leaflets also contained statements that the risk of transmitting hepatitis could not be excluded. This information was directly available to all clinicians involved in the treatment of haemophiliacs with these products and also to the substantial proportion of patients who were practising home therapy (40% in 1978).

However, concern about the unknown long term outcomes from Hepatitis C infection was a driver for the initiative for UK self-sufficiency in blood products. The Scottish National Blood Transfusion Service was in the forefront of efforts to produce adequate supplies of non-commercial product.

We should be happy to provide you with copies of the Scottish Executive's Heat Treatment report together with the associated references (which include many contemporaneous articles in the medical press). We also have copies of other documents that show that the link between treatment with clotting factor concentrates and hepatitis infection was available to organisations representing patient interests.

You also mention HIV and I enclose for information the timeline, included with the Heat treatment report, which includes details on the discovery and isolation of HIV together with details of the availability of a HIV-safe SNBTS Factor VIII.

The Minister recognises that improved communication of risk between clinicians and patients is essential and efforts to achieve this form an important part of the Scottish Executive's strategy for NHSScotland. On the more general issue of the need for a public inquiry into events in the 1970s and 1980s, he remains to be convinced that this would serve any useful purpose. However he has stated that he is prepared to consider any new evidence which may emerge.

I hope this clarifies the position.

Yours sincerely

NOT RELEVANT

NOT RELEVANT

SANDRA FALCONER (MRS)



TIMELINE

When	Scotland	England	Scientific Literature
1975			Paper by Italian scientists describes “Asymptomatic liver disease in haemophiliacs”, asserts Factor VIII/IX possibly responsible because of large donor pools; also that available methods for universal donor screening unlikely to eliminate risk. (SNBTS ref. 11 ¹)
June 1978			US paper comments that liver abnormalities in haemophiliacs probably related to treatment with blood products and incidence of HBV. (ref. 13)
Sept 1978			<i>Lancet</i> paper identifies factor-concentrate replacement therapy as probably related to high incidence of chronic liver disease among haemophiliacs. (ref. 12)
1980			German scientists for Behringwerke

¹ Subsequent references in this section are all to papers included with the SNBTS submission



			publish report which suggests that pasteurising Factor VIII at 60°C for 10 hours frees it from hepatitis B risk – says further clinical proof needed for NANBH. (ref. 36)
September 1981	SNBTS begins its own research on pasteurisation.		
October 1981			Behringwerke get US patent for process to stabilise Factor VIII in pasteurisation (heat-treatment of liquid to 60° C). Although HBV was removed through this process, unclear at time whether this was because of purification or heat-treatment. Yields low – less than 25% of SNBTS's own production process of Factor VIII.
August 1982			US scientists at International Society of Haematology Congress report Factor VIII can be heated to 80° C but it was visibly less soluble than products in clinical use and it was unknown whether

NOT RELEVANT



			this heat treatment inactivated the relevant viruses. Chimpanzee studies were planned. (ref. 27)
September 1982			Italian scientists suggest non-A non-B chronic hepatitis is non-progressive. (ref. 14)
1982			Abstract in <i>Hepatology</i> suggests <u>insidious progression</u> of NANBH.
1982			US: 3 haemophiliacs develop new illness, which subsequently becomes known as AIDS.
1983		NOT RELEVANT	Further cases of this illness in recipients of Factor VIII.
1983			Manchester scientists suggest that liver biopsy on haemophiliacs not justified by incidence of liver damage (especially in the absence of proven therapy). Suggests liver disease in haemophiliacs an "overstated problem". (ref. 15)
1983	Scotland self-sufficient in SNBTS Factor VIII NY.		

NOT RELEVANT



Late 1983	SNBTS prepare batch of pasteurised Factor VIII for clinical evaluation.		HIV first isolated.	NOT RELEVANT
January 1984	First patient suffers adverse reaction, clinical study abandoned, and R&D programme revised.			NOT RELEVANT
March 1984			HIV first cultured for research.	
April 1984			Bayer (USA) publish patented method for pasteurisation of Factor VIII.	
June 1984	SNBTS collaborate with US's Alan Johnston on purification for pasteurisation process, in hope that it would improve pasteurisation and perhaps allow greater heat to be applied.			
October 1984	Samples from haemophiliacs at Edinburgh Centre tested using new HIV screening test. SNBTS informed that a number who had only ever received SNBTS products (i.e. none from abroad) are HIV+, indicating contamination of Scottish blood supply.			
November 1984			International Committee on Thrombosis	



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			and Hemostasis, concerned at the lack of a uniform approach in studies, draws up a protocol for evaluating the risk of hepatitis transmission by new products.
1984	SNBTS decide to keep trying to develop pasteurisation.	PFL Oxford manage to dry-heat a Factor VIII product ("8Y") to 80°C for 72 hours. Expected to provide greater protection against HIV. 10-times more purified than SNBTS NY product —believed by SNBTS to make the difference. No indication whether 80°C treatment would have an effect on hepatitis viruses. Production of 8Y undertaken with early model of freeze-drier, which was later recognised as crucial in the process. (ref para 7.14 of SNBTS submission)	Clinical studies suggest pasteurisation at 60°C for 10 hrs might be effective against hepatitis viruses (ref. 47).
August 1984 & July 1985			US scientists doing chimpanzee studies claim reduction of hepatitis infectivity

			following dry heat treatment to 60° C. (ref. 30,31)
Oct-Dec 1984	PFC production suspended during planned upgrade of facilities.		
November 1984	SNBTS scientists learn results of US work, that dry heat treatment at 68° C for one hour inactivates HIV. They already know that NY can withstand this level of heat for 2 hours. Decide to dry heat-treat existing stocks of NY.		
December 1984	All stocks of NY issued by PFC from now on – 12 months’ supply – have been dry heat-treated to 68° C for 2 hours – HIV-safe.		
January 1985	SNBTS put into production their developed process to dry-heat Factor VIII to 68° C for 24 hours.		
January 1985	SNBTS order specialised heat treatment oven to specification similar to that used by PFL.		
March 1985		All PFL (Oxford) Factor VIII Heat	



		treated – some at 80°C	
May 1985		All BPL (Elstree) Factor VIII heat treated – some at 80°C	
July 1985	SNBTS receive specialised oven (see above) and put to use.		<i>Lancet</i> article and letter suggests that clinical data from humans do not bear out the results of chimpanzee studies.
September 1985		All PFL/BPL Factor VIII (up to 40% of England and Wales requirement) heat treated at 80°C.	
1985			US paper suggests “no indication to alter current therapy patterns because of concern over plasma product-related liver disease”, but also points out that some studies suggest more insidious nature of disease than previously thought. (ref. 16)
1985			<i>Lancet</i> article by Sheffield scientists concludes chronic persistent hepatitis in haemophiliacs not as benign as hitherto supposed; an “understated problem”; suggests NANBH mainly responsible (ref. 17)

Autumn 1985	SNBTS develop highly-purified Factor VIII, but it does not stand up to dry heat at 80°C – NY samples included as control <i>do</i> withstand. They conclude that it is the process of freeze-drying which is important rather than purity, when it comes to tolerance of dry heat. Decide to concentrate on 80°C dry treatment of Factor VIII to increase safety margin for HIV (as this was the overriding concern at the time).		
October 1985	Clinical trial and introduction of Factor IX product DEFIX dry-heated to 80° C for 72 hours. (Safety studies had been needed prior to this due to risks of thrombosis).		
Feb 1986	SNBTS management endorse strategy concentrating on 80° C dry heat (see Autumn 1985).		
August 1986	SNBTS produce first full-scale production trial batches of Factor VIII		



	product Z8 (heated at 80°C for 72 hrs).		
September 1986		PFL/BPL report preliminary clinical data showing their 80° C dry-heat 8Y reduced risk of hepatitis transmission, and suggest fuller study be carried out. (ref. 53)	
December 1986	Z8 issued for clinical trials.		
April 1987	Z8 made available for routine clinical use.		
April 1987			Clinical studies redone to fit in with ICTH protocol suggest pasteurisation at 60°C for 10 hours effective. (ref. 48)
1988			French study of 60-68°C dry-heated products suggests heating at this level reduces NANBV contamination by 75%
1988	Look-back study shows that NY heat-treated in November 1984 and Jan/Feb 1985 had been prepared using HIV-infected donations, and that HIV virus had not been transmitted – thus demonstrating efficacy of the process as		

	far as HIV was concerned.		
May 1988			US patent granted to Alan Johnson for purification process
October 1988			Paper published in <i>Lancet</i> suggests 8Y (heated at 80°C for 72 hours) free from NANBH C risk (ref 60).
1989			Hepatitis C DNA code isolated (ref. 18)
1990			Letter published in <i>Lancet</i> suggests 8Y does not transmit hepatitis C risk (ref 61) and undertakes to continue to follow relevant patients.
1992			Paper by Finnish scientists reports that 68°C/72h dry-heated product had been in use in Finland 1985-1991, but the risk of contracting HCV with that product was now seen to be appreciable, before the advent of screening blood-donors for HCV.
November 1992			Report from UK scientists suggests that haemophiliacs exposed only to “super



			dry-heated concentrates" (for 72h at 80° C) presented no evidence of HCV infection. (ref. 63)
December 1992			Report on behalf of UK Haemophilia Centre directors confirms that 8Y treatment (dry heat at 80°C for 72 hours) seems to reduce risk of HCV transmission from 90% to 0-11%. (ref 62)
May 1993			Study by Haemophilia directors provides additional evidence that dry heat treatment for 72h at 80°C is effective in preventing HIV and HCV transmission (ref. 64)
January 1994			Paper by Italian scientists suggest heat-treated products (pasteurised or dry-heat treated at 68°C for 72h) effective in reducing risk of transmission of hepatitis C, and looks forward to even more effective virucidal treatment. (ref. 67)