SNBTS DOCUMENT REQUEST No:

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Penrose Inquiry: Response to a request from Mr Evans (18 May 2011) for background information and clarification on JDC's Witness Statement on Viral Inactivation (para 36.13 'We found ourselves alone, without active support from SHHD and MCA').

1.00 Background Notes

1.01 Further and related background notes have been lodged with the Inquiry team in a witness statement prepared in response to a letter from Douglas Tullis to Susan Murray dated 7 March 2011.

1.02 In the year that I was appointed SNBTS National Medical Director, there was published a historical review of the value, in the context of safety and efficacy, of state control of medicines(1). In 1984 an informative review of the workings of the Medicines Act in the United Kingdom was published(2).

1.03 In 1981 SNBTS Directors sought clarification on who had the legal duty of care with regard to the safety of PFC's products. They were advised that liability rested with the CSA's Management Committee, as it held the Manufacturing Licence. The only circumstance where the Director would be liable was 'if PFC staff took deliberate steps to contaminate a product'. This CLO opinion was described by the CSA official as 'preliminary and informal' and confirmation/further clarification was promised by CLO(3). To the best of my knowledge no CLO follow up ever materialised. It was a surprise to SNBTS Directors that no mention was made in this preliminary CLO advice of a responsibility of Ministers and their officials to product safety..

1.04 The absence of a CLO follow up led SNBTS Directors to pursue the matter further some months later, but this time included the legal position of all SNBTS Directors. On this occasion the issue was considered by the CSA's Management Committee (on which sat two senior SHHD officials). The Management Committee instructed its officials to advise the RTDs that 'the part played by the Regional Directors is that he /she has been designated in the Manufacturing Licence as the person, on behalf of the Management Committee, who is responsible for supervising the production operations and quality control'(4). It was still not clear to the Directors what the content of these instructions actually meant, but it seemed evident that a critical feature was the possession of Manufacturing Licences - a standard feature of the regulatory arrangements within the Medicines Act (1968).

1.05 Within months of this last communication the prospect of the CSA holding Manufacturing Licences was removed when SHHD announced that the CSA/SNBTS would now operate under Crown Immunity and thus outside the regulatory control of the Medicines Act (1968). It followed that the CSA/SNBTS

would not be permitted to seek the acquisition of these licences and the SNBTS would have to operate without the professional support/guidance of the Medicines Commission's Committee on Safety of Medicines and the MCA Inspectors during their mandatory inspections.

1.06 Repeated efforts (by myself) to obtain further clarification on how the CSA's legal duty of care would be discharged and the position of the SNBTS Directors, in the light of the introduction of Crown Immunity, failed, in the period up to December 1984, to generate responses from the CSA or SHHD.

2.0 Specific Responses

2.01 There is no doubt that in December 1984 there were significant doubts among some clinicians regarding the safety of heat treated Factor VIII products. As I recall the primary concern was the creation of neo-antigens, with the possibility of acute fatal allergic reactions and/or the development of Factor VIII inhibitors.

2.02 In the context of heat treated Factor VIII concentrates I was uncertain that we had the technology to detect denatured proteins/neo-antigens. I seem to recall, in discussions with Drs Pepper, Dawes and Foster this technical deficiency, was not unique to our laboratory.

2.03 There was no doubt that in December 1984, as an SNBTS management team came to consider the release of PFC's first heat treated Factor VIII product for clinical use, I was concerned at the magnitude of the responsibility we were taking. In the light of the events described above, I was aware that, because of the action taken by SHHD, 4 years had gone without a mandatory MCA inspection of PFC's good manufacturing practices. I did not believe that Crown Immunity brought us much comfort. We had consistently failed to get satisfactory answers to the questions: immunity from what and for whom? Moreover, it seemed possible that heat treatment might be considered to be an example of our deliberately contaminating a product. In short, making decisions which could immediately affect patients' lives, without the comfort/discipline of working within the regulatory scientific network of the Medicines Act (1968), which had been denied us by SHHD, was particularly stressful to me, and, I believe, some of my colleagues.

2.02 Despite a request for SHHD support (through Dr AE Bell (SHHD)), the responsibility to permit the release of the first PFC heat treated Factor VIII was not shared by SHHD or CSA officials, notably the Chief Pharmacist and/or the medical officer with responsibilities for regulatory matters. But it was shared by clinical colleagues and, through Dr Perry, informal support was obtained from a senior NIBSC staff member.

2.03 Events moved rapidly in the early months of 1985 and I believe several commercial companies were able to obtain rapid formal consent from the

Committee on Safety of Medicines to release heat treated factor VIII for clinical use on a named patient basis (i.e. without supporting clinical trial data) The imposition of Crown Immunity denied this option to the SNBTS and the legal position of those who took the responsibility to order the release of PFC's first heat treated Factor VIII, in the face of knowledge that HIV had gained access to the Scottish donor population, remains unknown. All the evidence pointed to the conclusion that Ministers and their officials at this time did not wish to engage in this (unique) batch release process event.

2.04 It is my best recollection that a key factor in the discussions which led us to the issue our first dry heated Factor VIII for clinical use was the information brought back from a conference in the Netherlands (Groningen) in the autumn of 1984. This information came from a US commercial company that had dry heat treated Factor VIII in a manner similar to our product and no adverse clinical reactions had occurred and the in vivo half life of the VIII appeared normal. I had been given advanced warning that this announcement would be made at this conference by a close friend who was the conference organiser (Dr Cess Smit-Sibinga) and we had agreed that it was imperative that Dr Peter Foster should attend the conference. In late 1984 my request for funding to enable Dr Foster to go to the conference had to be cleared by SHHD. It was refused. There followed several heated conversations and, I believe, through the good offices of Dr Bell (SHHD) this decision was reversed and Dr Foster went to Groningen.

2.05 I would suggest that the comment that was of interest to Mr Evans that 'we found ourselves alone and without active support of SHHD and MCA' could be viewed as a significant understatement.

References

1. Penn RG. The state control of medicine: the first 3000 years. Br.J.Clin.Pharmacol. (1979) **8**: 293-305.
2. Andrews PA et al. A regulatory view of the Medicines Act in the United Kingdom. J.Clin Pharmacol. (1984) **24**: 6-18
3. Communication on product liability from Mr Wooler (CSA) to Dr Cash (SNBTS) dated 18 December 1981 (C3-43)
4. Communication from Mr Wooler (CSA) to Dr Cash (SNBTS) dated 16 June 1982