Witness Name: Professor Edward Tuddenham
Statement No.: WITN3435001
Exhibits: WITN3435001/1, WITN3435001/2
Dated:

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT
OF PROFESSOR EDWARD TUDDENHAM

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 5 September 2019.

I, Professor Edward Tuddenham, of the Royal Free London NHS Foundation Trust, Pond Street, London, NW3 2QG, date of birth GRO-C 1944, will say as follows: -

Section 1: Introduction

1. I qualified with MBBS from Westminster Hospital Medical School in 1968. Following qualification I completed the usual course of pre-registration House Officer posts at Queen Mary's Hospital Roehampton in London and at the Royal Victoria Infirmary Bournemouth between November 1968 and December 1969.

2. Thereafter I completed a series of Senior House Officer and Registrar rotations at the United Liverpool Hospitals between October 1969 and December 1971.

3. I then began to specialise in haematology. I took up a Lectureship in Haematology at the Welsh National School of Medicine, University Hospitals of Wales between March 1972 and December 1975.

4. Thereafter I practised abroad as a Research Associate at the Department of Medicine Division of Haematology, University of Connecticut School of Medicine in the USA between January 1976 to December 1977.

5. I then returned to the UK to take up my first Consultant post, working as a Locum Consultant, and then appointed to Senor Lectureship at the Royal Free Hospital Haemophilia Centre, a post I held from January 1978 to July 1986.

6. At the same time, I was appointed Co-Director, with the late Dr Peter Kernoff, of the Katharine Dormandy Haemophilia Centre and Haemostasis Unit at the Royal Free Hospital School of Medicine, a post I held until October 1986. I also took up the post of Senior Lecturer at the Katharine Dormandy Haemophilia Centre and Haemostatis Unit in September 1978, also remaining in this post until October 1986.

7. My role as Senior Lecturer in haematology and Co-Director of the Katharine Dormandy Haemophilia Centre and Haemostasis Unit was to treat haemophiliac patient's being treated at the unit and also to conduct research. One of the major areas of my research concerned purification of factor VIII, which was a central problem in the treatment of haemophilia.

8. Between November 1986 to June 1987 I was Visiting Research Fellow at the Department of Molecular Biology, Genentech Inc. in San Francisco and also at the Laboratory of Molecular Embryology at the National Institute for Medical Research. My work as Visiting Research Fellow at the Department of Molecular Biology, Genentech Inc. was focused on identifying variations in the human factor VIII gene. The complete cDNA and genomic cloning of factor VIII led directly to production of synthetic factor VIII. It also led to discovery of common polymorphisms within the factor VIII gene that are useful for carrier detection and antenatal diagnosis. We were also able to localise some of the mutations causing haemophilia in individual patients.

9. In November 1986 I left the Royal Free Hospital to take up a position as Director, Haemostasis Research Group, at the Medical Research Centre, a position I held until June 1994. In July 1994 I became Director of the Haemostasis Research Group at the Medical Research Centre Clinical Sciences Centre, a position I have held from July 1994 to December 2005.

10. In April 1994 I became Professor of Haemostasis at Imperial College London, Faculty of Medicine, remaining in post until December 2005.

11. My work at the Medical Research Council focussed on factor VIII, tissue factor and factor VII, using methods of molecular biology and structural biochemistry to elucidate the molecular pathology of vascular disease, haemophilia and thrombosis.

12. During this period I was also Honorary Consultant Haematologist at Hammersmith Hospital between June 1990 and December 2005.

13. In January 2006, I returned to the Royal Free Hospital as Professor of Haemophilia at the Katharine Dormandy Haemophilia Centre and Haemostasis Unit, a position I held until August 2011. During this period I was also Professor of Haemophilia at University College Hospital Medical School.

14. At the same time as joining the Royal Free Hospital as Professor of Haemophilia, I also took up a position as a Consultant Haematologist at the Royal Free Hospital, a position I still hold. I retired from full time practice in 2011, but continue to work at the Royal Free Hospital two days a week.

15. From September 2011 to date I have been Emeritus Professor of Haemophilia at University College London.

16. In addition to positions detailed above I have held a number of consultancy posts in the past with companies involved with developing treatments for haemophiliacs. Between 1982 and 1986 I was a consultant for Speywood Laboratories, who were developing synthetic factor VIII to treat haemophilia in collaboration with Genetech Inc. I have also been a consultant with BioMarine, a US company involved in developing gene therapy for haemophiliacs using our patented technology. I have also been a consultant for Freeline Therapeutics, a biopharmaceutical company with focus on gene therapy for haemophilia and other genetic diseases.

17. In addition to my medical degree, I became a Member of the Royal College of Physicians (UK) in 1974 (MRCP). I became a Member of the Royal College of pathologist (UK) in 1975 (MRCPath).

18. I obtained an MD from the University of London in 1985. I became a Fellow of the Academy of Medical Sciences in 1998.

19. In the past I have been a member of the British Society for Haematology and the American Society of Haematology. In the 1980's I was also an advisor to the Haemophilia Society.

Section 2: Responses to criticism of W1000

20. At paragraph 28 of witness W1000's statement he claims that in a letter from myself to Witness W1000 dated 29 May 2008, I seem to deny responsibility for witness W1000 being given Factor VIII and it is suggested that I imply that I was not involved with his care.

21. With regard to whether I was involved with witness W1000 I wish to make it clear that I have been involved with his treatment during the periods I was working at the Royal Free Hospital. In that regard, I note from reviewing witness W1000 records, that he was a patient who was allocated to my colleague and Co-Director of the Katharine Dormandy Haemophilia Centre and Haemostasis Unit at the Royal Free Hospital School of Medicine, Dr Peter Kernoff. This can be seen by reviewing the clinical notes for witness W1000. Reference to the anonymised clinical notes for the period 25 September 1978 to 8 January 1987, (after which I left the Royal Free Hospital, not returning until January 2006, as described above), a copy of which I exhibit to this statement as WITN3435001/1, discloses that there are two consultation sheets dated 31 December 1979 and 1 December 1981 which clearly state that witness W1000 was under the care of Dr Kernoff.

22. The system in the Haemophilia Centre at the time was that patients would be seen by whichever clinician was seeing patients in the clinic that day, or who was on call that day. Both I and Dr Peter Kernoff were Co-Directors of the Katharine Dormandy Haemophilia Centre and Haemostasis Unit at the Royal Free Hospital School of Medicine. Therefore who patients were seen by was dependant on who was in the clinic seeing patients on that day. If Dr Kernoff was not available, I would see his patients and visa-versa. There were other clinicians working in the unit and they would also see patients at clinics.

23. Reference to the anonymised clinical notes at exhibit WITN3435001/1, discloses that I saw witness 1000 with a junior doctor on the 24 June 1981. Witness W1000 had suffered a traumatic injury to his left shoulder and I agreed that he should be

prescribed "BPL", (which stands for Blood Product Laboratory), a form of factor VIII prepared in the UK, on the 24 June 1981. I was also involved prescribing other blood products. For example I prescribed cryoprecipitate to witness W1000 on the 26 November 1980, when he had suffered repeated epistaxis, (a nosebleed), for 3 days.

24. As described above, whilst I was a Director of the unit, I was one of a number of clinicians involved in witness W1000's care. Reference to exhibit WITN3435001/1 discloses that he was also prescribed BPL by a colleague on the 12 May 1981 following an incident of spontaneous epistaxis which initially did not resolve with a prescription of concentrate. The notes also disclose that colleagues prescribed cryoprecipitate on at least 9 occasions between 25 September 1978 to 8 January 1987.

25. With regard to witness W1000's specific contention that in my letter of 29 May 2008 I seem *"to be denying any responsibility and implying that he was not involved in my care"*, my comment in my letter to witness W1000 is taken out of context. Reference to the relevant section of the letter discloses that I say as follows:

"In the two tests dated 1992 and 1994 the results read positive (by EIA) and Indeterminate (by RIBA) but there are no PCR or RNA results in the notes so who concluded that you were a natural clearer and why? ***Answer:*** *Again I can't find this recorded in the contemporary written notes (which entirely relate to individual bleeding episodes) or in the letters of the time. The responsible clinicians for your case were Dr Peter Kernoff (now deceased) and Dr Christine Lee (retired). If anything was said to you about it I assume it was by one of those two. Since treatment for hepatitis C had barely started then it may have been a moot point and no such conclusion was made at the time."*

26. It is clear from my response to witness W1000 in this letter that I am talking about a period of his care between 1992 and 1994 at which I was not working at the Royal Free Hospital. As stated above, I left the Royal Free in October 1986, and did not return to the Royal Free Hospital until January 2006, twelve years after the period of treatment to which this section of the letter to witness W1000 related. Therefore my comment in my letter of 29 May 2008 that I was not responsible for witness W1000 care during the period in question was entirely correct.

27. I note that at paragraph 35 of the statement of witness W1000 it is claimed that the comment in the letter dated 4 April 2013 from Stephen Evans, Head of Complaints and PALS at the Royal Free London NHS Foundation Trust dated 4 April 2013, that states that I was not aware that any of my colleagues were deliberately giving products they knew to be more dangerous than other products, contradicted what I said to the Hampstead and Highgate Express, which was published in their article dated 5 October 2016. Again, this has to be set in context.

28. The comments which I gave to the Hampstead and Highgate Express related to the treatment of haemophiliacs in the late 1970's and 1980's. It is important to note that until 1989 there was no assay which could be used to test blood products for the presence of Hepatitis C. Prior to 1989, haematologists were aware that patients were developing symptoms of hepatitis and this was called non A, non B Hepatitis.

29. With regard to HIV it was not until 1983/84 that scientists discovered the virus which causes AIDS. The first test which could identify HIV in blood was not available until 1984. During the late 1970's and early 1980's therefore the virus which causes AIDS had not been identified. It was not until 1984 that the first two cases (of what became known as HIV) being diagnosed in haemophiliacs was reported in the United States. At the time therefore, there was only a gradual awareness that there was a virus, subsequently identified as HIV, which could be disseminated through blood products.

30. Until 1985 there was no means to identify whether any particular blood product contained HIV and no way to identify whether a product contained Hepatitis C until 1989. To remove blood borne viruses, heat treated commercial FVIII was introduced for general use in the UK in December 1984, and heat treated BPL 8Y became available in July 1985.

31. Whilst it is correct to say that there were varying risk factors associated with receiving different types of blood products, it is necessary to be careful not to over-simplify the issues which faced the clinicians at the time. The main blood products which haemophiliacs received during that period comprised cryoprecipitate, BPL, (to which I refer above), and Factor VIII, which was received from the United States.

32. Cryoprecipitate is prepared from, and contains fibrinogen, von Willebrand factor, Factor VIII, Factor XIII and fibronectin. Cryoprecipitate is given in separate units, and each unit is obtained from a single donor.

33. BPL, and Factor VIII are products which are both obtained from large donor pools. Therefore, for example, for a single transfusion of Factor VIII, many thousands of patients may have contributed blood products, and the same is true for BPL. Because there are more donors involved in producing Factor VIII and BPL, there is a larger chance that these products can pass on Hepatitis C or other blood borne viruses, if one of the donors is infected.

34. However it is important to understand that the risk of giving cryoprecipitate is not negligible either. Whilst the risk of infection by a single unit of cryoprecipitate is much smaller than when receiving a transfusion of Factor VIII or BPL, haemophiliac patients over the course of their treatment, (and this includes witness W1000), received multiple units of cryoprecipitate. A patient who received multiple units of cryoprecipitate is also at risk of being infected with Hepatitis C, because of the number of individual patients who will have donated blood in order to supply the cryoprecipitate.

35. In addition, cryoprecipitate is not appropriate treatment for all patients with haemophilia or von Willebrand disease in all circumstances. If a patient with the above conditions has a serious bleed which is difficult to control, or a serious injury causing significant bleeding and it is necessary to achieve haemostasis, then it is more effective to treat with Factor VIII, or BPL which delivers a much more concentrated dose of Factor VIII, (which is an essential blood clotting protein). Delivering the required dose of Factor VIII through a transfusion of cryoprecipitate is more difficult and is sometimes completely impracticable. The reason for this is that cryoprecipitate, because it is supplied in single units from a single donor, contains a much smaller amount of Factor VIII. Therefore in order to deliver the same dosage of Factor VIII using cryoprecipitate would need a transfusion of multiple units of cryoprecipitate. This would take a long time to transfuse, which is problematic in an emergency situation. Secondly, there is a danger of volume overload which is potentially dangerous for the patient. In addition, with large volumes of cryoprecipitate the patient can receive a large dose of fibrinogen which itself can cause bleeding.

36. For that reason, there were many situations where it was necessary or more appropriate to treat a patient with BPL or Factor VIII compared to cryoprecipitate.

37. The other issue of relevance is that even if patients had wished to be treated with cryoprecipitate, because it was perceived the risk of being infected with blood borne

viruses was lower if they received this product, (which, for the reason indicated above, is not necessarily correct), there was simply not sufficient cryoprecipitate available from UK donors, for all patients to be treated with this product had they wished to be.

38. Set against that background, my response to the issue raised by Witness W1000 at paragraph 35 of his statement is as follows.

39. Whilst witness W1000 states that there is a contradiction between my comments to the Hampstead and Highgate Express in their article published on 5 October 2016 and the statement in the letter form Steven Evans to witness W1000 from the Royal Free London NHS Foundation Trust dated 4 April 2013, that is not the case. Reference to the letter of the 4 April 2013 discloses that it is said that:

"he also stated that he is not aware that any of his colleagues were deliberately giving products they knew to be more dangerous than other products"

40. I consider this statement to be correct. For the reasons explained above, in the period I worked at the Royal Free Hospital in the late 1970's to mid-1980's, it was not possible to identify using any assay whether a particular blood product given to a patient was infected with a blood borne virus.

41. Furthermore for the reasons stated above, in many cases, it was not appropriate or possible to treat a patient effectively using only cryoprecipitate, and there was not enough cryoprecipitate available to treat all patients had they wanted it.

42. For that reason, as far as I am aware, it was not the case that any clinician at the Royal Free Hospital deliberately gave a patient blood products which they knew to be more dangerous than other products. Whilst I can only comment from what I knew at the time, from my perspective, clinicians were aware that there was a small risk of passing on a blood borne virus with any of the blood products discussed above. In those circumstances it was necessary to balance the risks against the benefits of prescribing a particular blood product. Where the situation which presented was an immediate one connected with treating a patient who often urgently needed blood products, in some circumstances to stop a potentially fatal bleed, the issue was whether to treat the immediate problem associated with the bleeding that could be potentially fatal, balanced against the risk of transmitting a potential infection resulting in hepatitis.

43. In many situations, the decision to use BPL or Factor VIII over cryoprecipitate was based on the clinical circumstances and also the clinicians' knowledge that BPL or Factor VIII was a more effective product.

44. It is also worth noting that in the 1970's/1980's whilst the existence of the virus we identified as non A-non B Hepatitis was known of, at the time patients infected with this virus appeared to recover quickly from this infection. It only became known, much later, that the virus subsequently identified as Hepatitis C could have serious health consequences. My colleagues first published their observation that there was a high risk of non A non B hepatitis after infusion of both NHS and commercial concentrates in 1985 (Br J Haematol. 1985 Jul;60(3):469-79. High risk of non-A non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin; Kernoff PB, Lee CA, Karayiannis P, Thomas HC). As noted above, the episode of hepatitis after such infusions was apparently mild and transient.

45. With regard to the issue raised that it was not a "policy issue" to tell every Royal Free patient that switching to other treatments would reduce the dangers of contracting blood borne viruses, I have covered these issues above. I confirm that there was no policy not to tell patients of the risks as far as I am aware. However as I set out above, the circumstances in which a patient was given Factor VIII as compared to cryoprecipitate varied, depending on the clinical circumstances. Secondly, there was not enough product available to allow every patient to receive cryoprecipitate or BPL had they wanted it. The issue was not therefore one of policy, but a reflection of the circumstances which pertained at the time.

46. As indicated above I confirm that with the consent of witness W1000 I have accessed his medical records, as exhibited above, in connection with preparation of this statement.

Statement of Truth

I believe that the facts stated in this witness statement are true.

Signed GRO-C

Dated 7th October 2019

Table of exhibits:

Date	Notes/ Description	Exhibit number
25 September 1978 to 8 January 1987	Clinical notes (anonymised).	WITN3435001/1