Witness Name: Dr John Giddings
Statement No.: WITN4571001
Dated: 24 September 2020

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF DOCTOR JOHN CHARLES GIDDINGS

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 9 August 2020

I, Dr John Giddings, will say as follows: -

Section 1: Introduction

1. My name is Dr John Charles Giddings and my address is known to the Inquiry. My date of birth is GRO-C 942.

2. My professional qualifications are PhD, FRCPath., FIBMS and CSci. I am a retired Biomedical Scientist and Academic.

3. I was a Biomedical Scientist serving the Haematology Departments of Cardiff Royal Infirmary and University Hospital of Wales, Cardiff, between 1962 and 1981. I was then a Lecturer and Senior Lecturer at the University College of Medicine between 1981 and 2007. I retired in 2007.

4. I have been kindly assisted in drafting the below by the provision of various articles on request by the Library team at Cardiff – although they have informed me of strict copyright protocols and so I have not supplied the relevant articles with this statement.

5. I also undertook the following appointments during my career:

    a. Invited Fellowship, Alfred Hospital and Medical School, Melbourne, Australia, in 1984. I was also a Lecturer at Westmead Hospital, Sydney, Commonwealth Serum Laboratories, Melbourne, and the Royal Children's Hospital, Queen Victoria Medical Centre, Victoria, Australia in the same year.

    b. I was a Visiting Lecturer at the University of Pavia, Italy between 1980 and 1990.

    c. I was a Visiting Lecturer in Nara Medical College and Osaka Medical College, Japan, between 1991 and 2001. I still have a relationship with Nara and, from time to time, assist them with research projects.

    d. I lectured at the European School of Haematology in Paris in 1986 and 1992.

    e. I was a Visiting Professor in the University of Ulster, Northern Ireland, between 1998 and 2004.

    f. I was an Evaluation Expert, and Chair of the Specialist Haematology Committee, Belgian Office for Scientific, Technical and Cultural Affairs, 2001 to 2006.

    g. And a Consultant in Haematology, Clinical Studies, for Pfizer Ltd, UK, between 2003 and 2006 (as to which, see paragraph 70 below).

h. I have also been a Visiting Professor and Honorary Fellow at Kobegakuin University in Japan for nearly 30 years. I also still have that relationship now.

6. In terms of my links to other organisations during my career, I have performed the role of External Examiner (and Chief Examiner) for various degree courses at Monash University, Melbourne, Australia (1984), The Institute of Biomedical Sciences (1978-1992), the University of Portsmouth (1988-1992), Nottingham Trent University (1985-1995), Manchester Metropolitan University (1990-1995), Newcastle University of Northumbria (1995-1997), Sheffield Hallam University (1985-1989) the University of West of England (1985-1990).

7. I have previously been a member of: the British Society for Haemostasis and Thrombosis (Founding Member, 1979), the International Society on Thrombosis and Haemostasis (1971-2007), the Steering Committee of the UK National External Quality Assurance Scheme ('NEQAS', 1975-2000), the Editorial Board of the British Journal of Biomedical Sciences (1969-1985), European Thrombosis Research Organisation (1989-1997), Expert Panel of Research Referees, Medical Research Council (1990-2000), Panel of Assessors at Wellcome Trust (1994-1997) and Advisory Panel, International Society on Thrombosis and Haemostasis (2003).

8. In terms of my commercial activity, I was a co-inventor of a monoclonal antibody against human factor IX (in 1982). I have authored or co-authored more than 150 papers in peer-reviewed journals, 2 books on advanced topics in Haemostasis and Thrombosis, and 18 chapters in international textbooks on Haematology and Haemostasis. I can provide further information to the Inquiry on these publications if helpful.

9. I have not provided evidence to, or been involved in, any other Inquiries, investigations, criminal or civil litigation in relation to human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Creutzfeldt-Jakob disease ("vCJD") in blood and/or blood products.

Section 2: Decisions and actions of the Cardiff Haemophilia Centre and your decisions and actions

10. My Doctorate qualification is scientific (PhD), not medical. I was not involved in direct decisions about clinical management.

11. I was first appointed as a Medical Laboratory Technician in Pathology at The Cardiff Royal Infirmary ("CRI") in 1962. I was employed mainly in the Haematology Department, although during the first two years, I was seconded for teaching and training to different sections of Pathology, including the Blood Transfusion Laboratory, Biochemistry, Histopathology and Microbiology.

12. In 1965, I was transferred to work part-time in the new specialised laboratory directed by Dr Arthur Bloom (as he was then) - established to diagnose and investigate disorders of blood coagulation. At that time, this laboratory consisted of one small room with facilities for Dr Bloom, one senior technician and me. There were no facilities for patients. I started to work full-time with Dr Bloom in 1966.

13. I obtained the Professional Qualifications of The Institute of Biomedical Sciences in 1967 (Associateship) and in 1970 (Fellowship). I was promoted to Chief Biomedical Scientific Officer in 1968.

14. The Cardiff Haemophilia Treatment Unit was developed during this time, after an especially difficult episode of bleeding in orthopaedic surgery in a patient with mild haemophilia in 1966.

15. The role of the blood coagulation laboratory expanded considerably – demonstrated by my appointment and various other medical and scientific staff. My own clinical contact with patients was limited to liaising with medical and nursing staff on the hospital wards for the administration of therapy and the collection and analysis of blood samples before and after treatment.

16. I moved to the University Hospital of Wales ("UHW") in 1970 to assist with the commissioning of the Haematology Laboratories and Haemophilia Centre (the "Centre") at the new hospital. The new department opened in 1971. I continued as the Chief Scientific Officer in the Coagulation Laboratory leading a dedicated scientific team providing support for the diagnosis and treatment of blood clotting abnormalities.

17. During the 1960s and 1970s my role focussed on the laboratory investigation and analysis of blood coagulation in a range of patients with acquired and congenital disorders of haemostasis. The number of patients with haemophilia at the time was relatively small although, on occasions, they placed considerable demand on laboratory services. The development of laboratory techniques resulted in an increase in the diagnosis of different coagulation factor deficiencies. As far as I can remember, there were around one or two new families with haemophilia identified annually.

18. The clinical Haemophilia Centre at UHW was situated close to the laboratory, and expanded further, especially for the treatment of increasing number of patients that did not require hospital admission (i.e. out-patients and the provision of products for home therapy). My clinical interaction with patients was always limited (although I would speak to patients informally when they were at the Centre from time to time) – and consisted principally of collecting blood samples and analysis of response to treatment.

19. I obtained my PhD in 1975. I was appointed as Lecturer at the University of Wales College of Medicine and UHW in 1981, became a member of the Royal College of Pathologists in 1986 and a Fellow in 1996, and was registered as a Chartered Scientist in 2003. Most of my responsibilities after I became a Lecturer remained within the hospital laboratories and the Centre, but they centred around training and research in haemostasis and thrombosis. I had even less involvement with patients from 1981. As such, I am afraid that my ability to answer any questions regarding patients after this time is extremely limited. I retired as a Senior Lecturer in 2007.

20. With regard to "senior colleagues" involved in the care and treatment of patients during my time at CRI/ UHW/ the Centre (I am not quite sure how one defines the term), many staff from Haematology and other specialties in medicine were involved in the care and treatment of patients with bleeding disorders during the early years of my career and up to the time I became a Lecturer. In addition, several visitors from other parts of the UK and internationally came to Cardiff for different periods of time to develop their experience and further their qualifications – I understand a number of these are already listed in documents presented to the Inquiry.

21. I have listed below the medical and other colleagues that I can remember (note, I do not know the dates of their employment and so this list is not in chronological order but simply produced from memory – I have included later employment where I know of it, in parenthesis):

Medical Staff

Dr John Lilleyman (as he then was, now Professor, Sir) (Sheffield Children's Hospital)
Dr Chris Ludlam (Edinburgh)
Dr Stuart Mayne (Derby)
Dr Viv Mitchell (Leicester)
Dr Edward Tuddenham (London)
Dr M. Khurshid (Swansea)
Dr Elizabeth Moffatt (Newport)
Dr Keith Myers (Merthyr Tydfil)
Dr Ashley-Jones (Nottingham)
Dr Huw Parry (Bangor)
Dr Has Dasani
Dr Peter Cumber (Carmarthen)
Dr Saad al-Ismael (Swansea)
Dr Colin Hewlett
Dr Graham Standen (Bristol)
Dr Paul Bentley (Cardiff)

Dr David Hutton (Cardiff)
Dr Paul Trenchard (Cardiff, BTS)
Dr Tony Napier (Cardiff, BTS)
Dr Philip Cachia (Scotland)
Dr Simon Brown (London)
Dr Malcolm Liddell

Nursing Sisters

Ms Mildred Jones
Ms Jenny Jones

Research

Dr Ian Peake (Sheffield)

Social Worker

Ms Mary Dykes (Cardiff)

Other Departments in Cardiff Royal Infirmary and UHW

Dr Peter Beck (Department of Medicine)
Dr David Davies (Paediatrics)
Dr Peter Verow
Dr Roger Verrier-Jones (Paediatrics)

It is likely that this list is not complete, and I do not think I am qualified (or necessarily remember) all their roles and responsibilities at the time or as time progressed.

22. In the early years I was aware that Professor Bloom (as he became) used to contact several contemporaries experienced with treating haemophilia including Dr Rosemary Biggs (Oxford), Dr Katherine Dormandy (Royal Free

Hospital), Professor Roger Hardisty (Great Ormand Street Hospital), Professor Ilsley Ingram (St Thomas's Hospital) and Professor Blackburn (Sheffield). I can also remember wide-ranging discussions about treatment at Scientific meetings with International associates, including for example Professor Inga Marie Nilsson (Malmo), Professor Jan Sixma (Utrecht), Professor Pier Mannucci (Milan), Professor Oscar Ratnoff (Cleveland, Ohio) and Professor Harold Roberts (Chapel Hill, North Carolina).

23. International visitors that worked for extended periods of time during the late 1970s and early 1980s included Dr David Lillicrap (Ontario), Dr John Rowell (Brisbane), Dr Franco Piovella (Pavia) and Dr Akira Yoshioka (Nara). These individuals became recognised experts in the treatment of haemophilia and thrombosis. In addition, Dr Junichiro Yamamoto and Dr Yasuto Sasaki (Kobe) came to the Centre from the laboratory of Professor Utako Okamoto who was the leading world authority on the use of tranexamic acid as an anti-fibrinolytic agent and as a practicable haemostatic therapy.

24. As I mentioned above, I recall the number of patients under the care of the Centre increasing over the years I was there, but I cannot recall exact numbers and I am hesitant to estimate any figures. I was also not involved and cannot remember whether or when any formal policies or protocols for the management of patients with haemophilia were introduced.

25. I was not involved in the selection or purchase of blood products for use at the Centre. My recollection is that, during the 1960s and 1970s, decisions that were made by others were based on prevailing clinical circumstances, and the availability of national (UK) supplies.

26. I am afraid I also cannot comment on decisions regarding treatment of individual or categories of patients. Until the mid-1960s, the treatment of bleeding in patients with haemophilia relied mainly on Fresh Whole Blood or Fresh Frozen Plasma ("FFP"). I remember that some crude factor VIII-rich concentrates had been produced in the UK and other countries in Europe, but they were not widely available. The development of cryoprecipitate in 1964 was

a major advance, and this became the mainstay for haemophilia therapy. I recall on one occasion in around 1965 or 1966 where a freeze-dried Factor VIII concentrate was obtained from outside the UK for the treatment of a young man with mild haemophilia who had suffered a life-threatening injury to his thigh. Initial treatment with large volumes of cryoprecipitate had only limited success in controlling bleeding and had exhausted supplies. Higher concentrations of Factor VIII were considered essential for emergency surgical intervention.

27. I am not aware of:

    a. Any relationship between the Centre and pharmaceutical companies manufacturing or supplying blood products; or,

    b. Any external organisations with responsibility for the selection and purchase of blood products at the Centre.

28. With regard to alternative treatments to factor concentrates available for people with bleeding disorders in the 1970s and 1980s, I can recall epsilon-amino-carproic acid ("EACA") being used to cover dental procedures in the patient with mild haemophilia referred to directly above. And D-amino D-arginine vasopressin ("DDVAP", Desmopressin) was used in some patients with mild haemophilia or mild von Willebrand's disease.

29. In the early 1960s, EACA and tranexamic acid (Cyclokapron) were being introduced in different clinical specialities to stabilise haemostatic clots and reduce the severity of surgical and dental bleeding. These pharmacological agents appeared to limit the amount of factor VIII needed to cover dental extractions, but soon appeared to be of little other value in the treatment of haemophilia because they were only really effective in minor bleeds and some clinical trials at the time (e.g. Rizza, CR (1980) J. Clin. Path. 33 (Suppl) 14, 50-54) indicated that these products did not reduce the number or severity of bleeding episodes.

30. Studies in Italy in the late 1970s had shown that DDAVP could be effective for the treatment of minimal bleeding episodes or to cover minor surgery in mildly affected patients with Factor VIII deficiency. It was known not to be suitable for more serious injuries or major surgery, and it is not effective in severely deficient patients or in Factor IX deficiency.

31. Inter-departmental seminars covering many aspects of Clinical and Laboratory Haematology were held weekly at the time. I remember one occasion when the topic of DDAVP treatment was discussed. It was clear that the response to the product with regard to Factor VIII was unpredictable, at best modest, and sometimes negative. I recall that other studies showed that DDAVP promoted mechanisms related to the dissolution of blood clots (fibrinolysis) which it was considered could have been counterproductive. And there were concerns regarding potential side-effects, particularly relating to cardiovascular events and the possibility of intracranial bleeding. I have read much more recent studies which suggest that there might be certain patients who might benefit from treatment with DDAVP (e.g. Loomans et al: Haematologica 2018 Volume 103(3): 550-557, and the editorial by Mannucci in the same edition of this journal) but this is decades after the events relevant to the Inquiry.

32. I was not involved in any policy decisions regarding the use of cryoprecipitate, home treatment, prophylactic treatment, or factor concentrates for children.

33. One major instance I recall regarding the use of factor concentrates for people with mild or moderate bleeding disorders is referenced above. I also remember that some patients classified as 'moderate' based on their basal coagulation factor levels required almost as much treatment (including prophylaxis) as those classed as 'severe'. There were some individuals identified with a 'mild/ moderate' deficiency, and some female 'carriers' of the haemophilia gene, that required treatment for intermittent or traumatic bleeding episodes. In addition, I remember one particular patient with an additional rare genetic disorder that required special clinical management.

34. I am not aware of any viruses or infections other than HIV, HCH and HCB being transmitted to patients at the Centre.

Section 3: Knowledge of, and response to, risk

35. When I began my career, difficulties with blood-borne infections were well-recognised. The risks associated with 'needle-stick' injuries and open wounds, for example, were known, and were commonly emphasised in teaching procedures for taking blood samples and first aid care.

36. The "Australia Antigen" (known as the Hepatitis Associated Antigen in the early 1970s) had been described, and a number of laboratory tests had been developed for detecting the antigen and the antibody. These were well-documented in contemporary texts. More sensitive screening tests for the antigen (which was then shown to be a component of the hepatitis B virus) did not become available, however, until after the mid-1970s.

37. In the 1980s, a high incidence of what was then termed non A non B hepatitis ("NANBH") was demonstrated in haemophilia patients after a first exposure to Factor VIII concentrates. There were no reliable laboratory tests for NANBH at that time. It was not until around 1989 that the hepatitis C virus was fully characterised, and a reliable diagnostic laboratory test approved. The test did not become available worldwide until September 1991.

38. I am not qualified to comment on advisory/ decision-making structures in place at the time to consider and assess risks of infection associated with the use of blood and/or blood products. I would say though that I believe it was common practice at the Centre to balance the advantages and disadvantages of risks associated with treatment of individual patients.

39. In terms of my understanding of the relative risks of infection from the use of commercially supplied blood products and/or NHS blood products, I can only really comment on this in respect of my time in the Centre up to 1981.

40. It was appreciated that Factor VIII concentrates prepared from plasma collected from many donors was less safe than single donor cryoprecipitate. It was also evident, however, that patients with severe haemophilia would be exposed to multiple doses of cryoprecipitate. In the early 1970s, it was believed that products made from voluntarily donated blood may be less likely to transmit hepatitis than those prepared from the blood of paid donors. Nevertheless, I can recall reports indicating that even large-pool UK concentrates transmitted hepatitis. I recall that NANBH was characterised further in the mid- to late-1970s. The clinical impact of this appeared (at least initially) to be small. Surveys of haemophilia treatment during the 1970s showed no increase in the incidence of jaundice and very few deaths associated with liver disease.

41. I do not recall any specific occasions where I discussed with Professor Bloom the risk of infection associated with the use of blood and/or blood products.

Hepatitis

42. I have explained my initial and evolving knowledge of Hepatitis above. I am not qualified to explain, nor do I have specific knowledge as to what further enquiries and/or investigations were carried out at the Centre regarding the risks of transmission of hepatitis. Nor was I involved (nor know anything about) what actions the Centre took to reduce risks to patients in this regard.

43. As to liver function tests ("LFTs"), in the 1970s the range of LFTs expanded to include measurements of serum bilirubin, aspartate and alanine transferases, alkaline phosphatase, gamma glutamyl-transpeptidase and pseudocholinesterase. I cannot remember the timescale from when they were introduced. Also, I was not involved in decisions about the purposes of such testing in relation to individual patients.

HIV and AIDS

44. I first remember reading about HIV/AIDS in the general population of the USA in the mid to late 1970s. Originally termed Lymphadenopathy-Associated Virus

(or "LAV"), the virus was shown in the early 1980s to be the same as that termed human T-lymphotrophic virus, type 3 (HLTV-III) and later identified as the cause of AIDS. At that time, there was no consensus about the cause of AIDS, how it spread or the number of patients with haemophilia that could be infected. There were even alternative theories about the causes of the disease. In 1982, only two haemophiliacs who had developed AIDS were reported worldwide. Thereafter, the number of reported cases increased gradually and, by 1985, the infection was recognised as a serious complication in the treatment of these patients.

45. By this time, I was no longer directly involved with the Centre. As such, I am not in a position to comment on any HIV-related enquiries/ investigations/ actions/ treatments connected to or by the Centre over the relevant period.

Response to risk

46. I was not directly involved with the Centre after 1981. My recollection from the 1960s and 1970s is that Professor Bloom (and his colleagues) would discuss options for treatment and potential dangers of infections (particularly hepatitis B and other forms of hepatitis) from blood products with patients and their families. I did not generally observe these conversations, but I had a good rapport with a number of patients, and on occasion when they were at the Centre, they spoke to me about these sorts of matters.

47. In 1969, Professor Bloom was instrumental in the formation of the Cardiff Branch of the Haemophilia Society. I was pleased to assist with arrangements for events over several years where patients and families attended to discuss, albeit informally, their problems and hopes for the future. I recall that Professor Bloom was always very strict about patient confidentiality and insisted that any personal information about matters such as consequences of different treatment options were only communicated directly with the relevant patients and families in his clinic.

48. I later became friendly with the dedicated specialist Social Worker (Ms Mary Dykes) that had been appointed at the Centre around late 1986 to early 1987 to assist with HIV/AIDS. I recall her telling me that Professor Bloom encouraged her to support some young men that were keen to establish a link with similarly affected individuals and families. This group later became recognised (and respected) nationally as "the Birchgrove Group".

49. I remember that heat-treated products were introduced in the UK in the early 1980s. However, by this time, I was not directly involved with the Centre. As such, I do not have any further knowledge as to what happened there in terms of their use of the products in the 1980s and thereafter, or any decisions made in connection with the same.

50. I have been referred to minutes of a meeting of the UK Haemophilia Centre Directors on 17 October 1983 [PRSE0004440] where cryoprecipitate was discussed. I was not present at this meeting. I did not discuss treating patients with cryoprecipitate during this period, nor did Professor Bloom express any retrospective doubts about his apparent position on this matter in my presence. I was not directly involved with the Centre after 1981.

51. The minutes also include an explanation from a Dr Chisholm regarding availability of commercial concentrates v. cryoprecipitate ("unlimited supplies") in her region. My recollection is that there were certainly not unlimited supplies of cryoprecipitate in Cardiff. However, given the timeline (and my expertise), I am not in a position to say what decisions may have been taken in relation to its use at the time.

52. In terms of steps taken regarding risks of infection, and in retrospect, it was only in the mid-1970s that hepatitis was recognised as a frequent complication in patients with haemophilia, and it was only in the mid-1980s that progressive liver disorders were beginning to be reported.

53. The view at the time by the majority of those at the forefront of haemophilia treatment was that the problem of hepatitis was tolerable, especially because

the benefits of concentrates appeared (at that time) to outweigh the risks. Severe liver disease was not identified as a major cause of death in haemophilia. Intracranial haemorrhage and post-surgical or traumatic bleeding were the main fatal events. Patient information was important here.

Section 4: Treatment of patients

54. As explained above, my role at the Centre was principally concerned with the diagnosis of coagulation disorders, together with support services for assessing blood clotting responses to replacement coagulation factor therapy. These processes were necessary to inform patient discussions regarding treatment, but I did not have those discussions myself and was otherwise not involved in clinical management/ patient treatment at the Centre.

HIV

55. I cannot remember precise details, but I think that the first time I heard about patients at the Centre being infected with HIV was around late 1983 or 1984 (which was after I left the Centre). I recall Professor Bloom updating me about recent advances with tests for the diagnosis of AIDS, and telling me that he was concerned about some results in one of his patients that he had just seen in his out-patient clinic. He also said that he was preparing a report on this patient to the UK Committee on the Safety of Medicines. I am afraid I do not recall any more details.

Hepatitis, delays, etc

56. I have covered my thoughts on these matters and lack of patient interaction/ involvement in decision-making above.

Consent

57. Blood samples were commonly taken from patients to assess response to therapy, and and I was often reminded by Professor Bloom to ensure that

patients or parents were kept informed of the results. In the 1970s plasma samples from patients with severe haemophilia (0% factor VIII) were vital for accurate assays of clotting factor activity. Some adult patients in this category were regularly asked to provide blood for these purposes and were content to do so. I cannot remember any instance where the request was refused. There was always an excellent relationship between the patients and laboratory personnel.

58. I was not involved in any formal consent procedures. Professor Bloom and his colleagues would discuss options for treatment and the dangers of infections (particularly hepatitis B and other forms of hepatitis from blood products) with patients and their families.

59. I assisted with a study conducted in 1982/83 by Professor Bloom and Dr Elizabeth Moffatt, and it is clearly stated in that report that "Informed consent was obtained from all patients and normal volunteers".

PUPS

60. As mentioned above, my doctorate qualification is scientific (PhD) and not medical. I was not involved in direct decisions about clinical management.

Treatment of patients who had been infected with HIV and/or Hepatitis

61. See paragraph 60 above.

Recombinant

62. I am afraid I also cannot comment on this for the reasons mentioned above (i.e. not involved with products that were developed after the change of my employment).

Research

63. As I mentioned in paragraph 8 above, I have authored/ co-authored more than 150 papers in peer-reviewed journals. I am happy to provide a list of the same at the Inquiry's request. I also authored two books on advanced topics in Haemostasis and Thrombosis and 18 chapters in international textbooks of Haematology and Haemostasis.

64. As to publications which might be relevant to the Inquiry's Terms of Reference:

    a. Bloom, A.L., Giddings, J.C., Bevan, B., Letton, M and Drummond, R.J. (1969) *Comparison of quick and slow thaw methods of producing cryoprecipitate antihaemophilic factor from fresh and 24-hour old blood.* Journal of Clinical Pathology, 22, 447-452. This study was designed to investigate methods that could maximise the yield of Factor VIII activity in cryoprecipitate. No patients were involved.

    b. Beck, P. Giddings, J.C. and Bloom, A.L. (1969) *Inhibitor of factor VIII in mild haemophilia.* British Journal of Haematology, 17, 283-288 and Beck, P. Giddings, J.C. and Bloom, A.L. (1970) *Inhibitor of factor VIII in mild haemophilia*. British Journal of Haematology, 18, 107. These reports were related to an anonymised description of the laboratory diagnosis and treatment of two patients with mild factor VIII diagnosed with an inhibitor of FVIII. I was not involved in the consent procedures, but I do remember talking to one of the patients later, and he was especially pleased to know that the paper had been accepted for publication.

    c. Giddings, J.C., Bloom, A.L., Kelly, M.A. and Spratt, H.L. (1983*) Human factor IX inhibitors: immunochemical characteristics and treatment with activated concentrate.* Clinical and Laboratory Haematology. 5, 165-175. This publication describes the immunological characteristics of inhibitors in two anonymised patients (I believe one was from Cardiff) with factor IX deficiency. The results of treatment with activated factor IX

concentrate (FEIBA) are also illustrated. I am afraid I cannot recall how administrative matters regarding consent (to the extent is was required), etc, were arranged for this study.

d. Moffatt, E.H., Giddings, J.C. and Bloom, A.L. (1984) *The effect of desamino-D-argenine vasopressin (DDAVP) and naloxone infusions on factor VIII and possible endothelial cell (EC) related activities.* British Journal of Haematology, 57, 651-662. This investigation assessed the effect of *in vivo* and *in vitro* DDAVP on a range of possible endothelial cell markers in normal subjects and in anonymised patients with mild haemophilia and vWd. The publication clearly stated in that "Informed consent was obtained from all patients and normal volunteers".

65. I cannot remember details of the funding arrangements, but I cannot think of any necessity for contributions for these studies from outside the University.

66. I was not involved in any epidemiological studies.

Transfusion

67. I was trained in Blood Transfusion Science at Cardiff Royal Infirmary and The University Hospital of Wales. In the 1960s and early 1970s, I undertook 'out of hours' duties to cross-match and prepare blood for transfusion. My role at the time was solely to analyse blood samples prior to transfusion. This covered not only patients with hereditary bleeding disorders but also for other transfusions, e.g. to cover general surgical procedures or for use in Accident and Emergency cases.

Records

68. I was not involved in policy decisions at the Centre. I do not know what the policies were in relation to matters such as information on death certificates or retention policies.

69. I have no knowledge of the Centre maintaining "separate" files for some or all patients. I did not take any information about Centre patients outside of the hospital.

Section 5: Pharmaceutical companies/medical research/clinical trials

70. The only association with a pharmaceutical company I had during my career was in the form of a clinical trial for Pfizer in 2003 on The Effects of Pregabalin on Platelet Function in healthy individuals (this did not involve the Centre). The funding for this research was paid directly to the University of Wales College of Medicine. The only payment I received was a modest sum for my participation in one or two meetings with other scientists that were held as the study progressed and at conclusion of the trial.

Section 6: Other issues

71. There have been no complaints against me.

72. I have been referred to a "Haemophilia Litigation report" dated June 1990 [DHSC0001297]. I had no involvement in providing information or assistance for this report.

73. With regard to Professor Bloom's comments at around p. 27 of the report (i.e. in respect of commercially produced products, they were *"produced from pooled plasma and are presumed to have the same risks with regard to viruses as commercial factor IX concentrates (and presumably factor VIII concentrates). The latter observation is not certain because data are not available; most treated inhibitor parties also receive factor VIII"*): This is a complex topic that Professor Bloom highlighted in two respected publications in the late 1970s and 1980s (B.J. Haem (1978) 40, 21-27 and B.J. Haem. (1981) 49, 319-324). Specific protocols utilised in patients with clotting factor antibodies could depend on inhibitor concentration together with individual responses to different treatment products.

74. In this context, pages 27-30 in Professor Bloom's Litigation Report focuses specifically on patients with inhibitors (antibodies) against clotting factors, and the products that Professor Bloom refers to were produced mainly for the treatment of this relatively small number of individuals. The 'activated' factor IX concentrates were devised especially for this purpose. The rationale for this type of therapy is different from that in uncomplicated cases and is not easy to explain in lay terms. For example, it might seem very odd that factor IX-based concentrates were used to treat patients with factor VIII deficiency. Nevertheless, overall, I believe the above quote is correct. My interpretation of this is that the 'commercial factor IX concentrates etc' mentioned in this paragraph refers to the usual non-activated products used at that time to treat patients without inhibitors.

75. I was not involved with the use of activated concentrates (e.g. FEIBA) after 1990, but I think that it is particularly interesting that very recent clinical trials have emphasised that this type of treatment can be dangerously thrombogenic even in the context of the most advanced treatment regimens (see Shima, (2020) Int. J. Haemat. 111, 16-19).

76. In addition, I am aware that Immune Tolerance Induction ("ITI"), utilising repeated infusions of factor VIII or factor IX concentrates (thankfully now 'virus-free') has become the mainstay of treatment for patients with inhibitors Also, in more recent years non-factor therapy, for example, based on unique monoclonal antibodies manufactured in laboratories, has been shown to be effective in this very difficult-to-treat category of patients. (again, referenced in the publication by Professor Shima; 2020, above).

77. As to Professor Bloom's observations regarding porcine factor VIII in the report (at pp. 29-31), I have some recollections of porcine (and bovine) factor VIII being used in the 1960s or early 1970s. In one case, reported in the research studies mentioned above, porcine factor VIII was given to cover open reduction and internal fixation of a fractured femur. Resistance to this therapy occurred after nine days, however, and recurrent haematoma formation eventually necessitated amputation. Administration of bovine factor VIII before amputation

resulted in severe reaction with rigors, purpura, thrombocytopenia and increased bleeding.

78. I cannot remember the details of other specific circumstances involving porcine factor VIII, except for the disappointing and relatively rapid development of resistance detected by assays of factor VIII activity together with thrombocytopenia. I have no knowledge of these animal concentrates being used after this time.

79. I stated my opinion of Professor Bloom in a eulogy at the time of his death in 1992. My opinion, respectfully, based on my experiences of him at the time, has not altered based on what I have read in the media and elsewhere. My experience of him was that he was committed to his patients and his intentions were always directed at improving clinical care. He spent many hours working day and night close to the bedside of dangerously ill patients. In many cases the results were immediately lifesaving and he massively improved the quality of life of many patients. I do not accept what commentators say regarding his motives in using certain blood products for his patients. I consider the summary provided by Professor Mannucci in his paper, *AIDS, hepatitis and hemophilia in the 1980s: memoirs from an insider.* Journal of Thrombosis and Haemostasis, 2003, 1: 2065-2069 to be a fair and accurate representation of the position at the time. I truly believe Professor Bloom's intentions were honourable and selfless. I also believe no experts involved in the treatment of haemophilia in that era could have foreseen the tragedy that would affect so many lives some time later.

Statement of Truth

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

Signed GRO-C

Dated 24th September 2020