Witness Name: Mrs Linda A Frith
Statement No.: WITN6407001
Annex: WITN6407002 - WITN6407012
Dated: 16 November 2021

INFECTED BLOOD INQUIRY

WITNESS STATEMENT OF LINDA ANN FRITH

I Linda Ann Frith of an address known to the Inquiry will say AS FOLLOWS:

1. I provide this statement in response to a request dated 21 July 2021, from the Infected Blood Inquiry under Rule 9 of the Inquiry Rules 2006 ("the Rule 9 Request"), in my capacity as former Sales Development Manager at Cutter Laboratories ("Cutter UK"), a division of Miles Laboratories Limited, an affiliated company of Bayer plc ("Bayer").

2. I have carefully considered the Rule 9 Request and, in preparing this statement, I have sought to assist the Inquiry to the extent I am able to do so. However, the Rule 9 Request seeks information in a number of technical medical/scientific and regulatory areas that were outside my knowledge and experience in my role in sales and marketing of products in the UK. In particular, I am not able to provide information in response to Questions 26, 45, 52, 53, 54 and 58(e),(f) and (g) of the Rule 9 Request. Miles Laboratories Limited employed people with responsibility for these technical and regulatory matters, including senior staff with particular knowledge and expertise in these areas. However in view of the fact that between 30 and 40 years has elapsed since the events which are the subject of the Rule 9 Request took place, I have been advised by Bayer

that, to the best of their knowledge, such persons have left the company and are either deceased, infirm or cannot now be located.

3. I also wish to advise the Inquiry that I have health issues that impact my ability to provide reliable evidence in relation to the matters identified in the Rule 9 Request. In April 2005, I suffered a sub-arachnoid haemorrhage which has significantly affected my memory. After six to nine months of recovery, I returned to work but had to retire six months later as I found it difficult to absorb and comprehend information. I continue to suffer from memory difficulties, particularly in pressurised or stressful situations, when I can experience memory blanks. In addition, in 2017, I was diagnosed with breast cancer. I subsequently received treatment with chemotherapy on 19 occasions and continue to take anticancer drugs. I believe such treatment has also impacted my memory and ability to recall information quickly, particularly when under pressure. Information regarding my health issues and their implications in the context of the Rule 9 Request is provided in the medical report provided to the Inquiry on 2 November 2021.

Documents

4. The Rule 9 Request asks that I provide any documents that I hold which are relevant to the Inquiry's Terms of Reference. I confirm that I do not hold any such documents.

5. In preparing this statement, I have relied upon documents identified by the Inquiry and certain other material which has been shown to me by my solicitors, Arnold & Porter, and is either referenced using the Inquiry's numbering system or is attached in an annex to this statement. The annex comprises of:

   a. A Chronology and Timeline of Events, submitted by Bayer to the Archer Inquiry, provided at WITN6407002;

   b. A report prepared in 1994 by Dr Milton Mozen, Head of Research at Cutter Inc, for the purposes of a US Institute of Medicine report and

also submitted to the Krever Inquiry in Canada, provided at WITN6407003; and

c. Additional documents of relevance (WITN6407004 - WITN6407012) which I understand have been disclosed to the Inquiry previously but for which my solicitors have not been provided an Inquiry reference number.

Section 1 : Introduction

(1) Please set out your name, address, date of birth and professional qualifications.

6. My name is Linda Ann Frith and my address is known to the Inquiry. My date of birth is GRO-C 1950.

7. I attended Chelmer Valley High School in Bromfield, Essex between 1963 - 1968 and achieved O Levels in Art, General Biology, Geography, Mathematics and Physiology, Human Anatomy and Hygiene.

8. In 1971, I passed the Intermediate Examination of the Institute of Medical Technology and, in 1973, the Associate Examination of the Institute of Medical Technology, qualifying in Haematology and Blood Transfusion.

(2) Please set out your employment history, including the various roles and responsibilities that you have held throughout your career and the dates when you held them.

9. I left school at the age of 17 in 1968 and obtained a job with the Blood Transfusion Department, which was within the Department of Pathology based at the Chelmsford and Essex Hospital. I later worked for the Haematology Department within the Department of Pathology. After qualifying as an Associate of the Institute of Medical Laboratory Technology, I was given increased responsibilities including on-call during nights and at weekends. My role was predominantly related to haematology and blood transfusion cross-matching blood, and I dealt with emergency blood transfusions when on-call. I also gained some

knowledge of haemophilia and its treatment, as well as familiarity with Factor concentrates, which were sometimes stocked in the department.

10. In October 1977, I joined Wellcome Diagnostics as a Sales Representative for the South East of England. The products I dealt with in this role were immunologically based diagnostic tests for bacteriological typing and autoimmune disease. In 1981, I was given responsibility for the installation of radioimmunoassay machines in blood transfusion departments in Scotland. Then, in 1982, I transferred to the role of Product Manager for radioimmunoassay kits used by biochemistry departments in pathology laboratories.

11. In 1984, I responded to a newspaper advertisement for a job at Cutter UK, a division of Miles Laboratories Limited. I was interviewed by Mr Brian Dyos (Managing Director at Cutter UK) and Mr Jack Wood (Vice President of Cutter International) and recruited as a Sales Development Manager, tasked with establishing a small sales team at Cutter UK, based at Stoke Court, Stoke Poges, near Slough. In 1988, my roles was expanded to Sale and Marketing Manager.

12. I worked at Cutter UK until 1990, when I was advised that the company would be closing its operations in Stoke Poges and integrating its business into Bayer plc, in Newbury. I was given the option of either being made redundant or joining Bayer plc. I decided to join Bayer and was appointed Senior Product Manager in the marketing department. I had responsibility for the product Canesten, an antifungal preparation. In 1992 I was made South East Thames hospital manager for Bayer, with additional responsibility for training of sales representatives. This role involved overseeing the teaching hospitals in the South East of England as a representative of Bayer. I was responsible for various products including those related to high blood pressure.

13. In 2002, I obtained a job with Novartis Pharmaceuticals UK Ltd working for a short period as a Sales Representative with responsibility for their specialist oncology products. However later that year, I moved to Gilead

Sciences, as a Hospital Representative working with an antifungal product.

14. I retired from the pharmaceutical industry in 2005, as a result of the health issues described in paragraph 3 above. Since then, I have had a few part time jobs at The Chatham Dock Yard Trust and as an invigilator at a school in Brightlingsea. I have also worked at M&S at Christmas time.

(3) Please set out your membership, past or present, of any committees, associations, parties, societies, organisations or groups relevant to the Inquiry's Terms of Reference, including the dates of your membership and the nature of your involvement.

15. I am not, and have not previously been, a member of any committees, associations, parties, societies, organisations or groups relevant to the Inquiry's Terms of Reference.

(4) Please confirm whether you have provided evidence to, or have been involved in, any other inquiries, investigations, criminal or civil litigation in relation to the human immunodeficiency virus ("HIV") and/or hepatitis B virus ("HBV") and/or hepatitis C virus ("HCV") infections and/or variant Cretzfeldt-Jakob disease ("vCJD") in blood and/or blood products. Please provide details of your involvement and copies of any statements or reports that you provided.

16. I have not provided evidence to or been involved in any such inquiries, investigations, criminal or civil litigation.

(5) Please describe your roles, functions and responsibilities at Cutter Laboratories Limited, a/the division of Miles Laboratories Limited during the time that you worked there. If they changed over time please provide details.

17. When I joined Cutter UK in September 1984, Brian Dyos was the only other employee working exclusively for Cutter UK. He was responsible for the overall management of the UK business.

18. Initially, there was no designated sales function in the UK. There had previous been a sales representative, Barry Barber, who had been responsible for sales across the UK. He had left Cutter UK, to join Alpha Pharmaceuticals Ltd, before I arrived in 1984.

19. In my role as Sales Development Manager, I worked closely with and reported to Brian Dyos. I was responsible for communicating information regarding product developments, stock availability and prices to customers (principally Haemophilia Centre directors), producing sales reports and passing on details of any product quality issues reported to me by customers to both Brian Dyos and to Marie Tatt, Regulatory Affairs Manager, who was based at Bayer plc in Newbury. Marie Tatt dealt with the product licences for Cutter's products, testing of samples from individual batches of products by the National Institute for Biological Standards and Controls (NIBSC) and batch release and reporting of suspected adverse drug reactions to the regulatory authorities. Product orders were placed directly with Brian Dyos by customers.

20. Cutter UK's offices at Stoke Court were located in "the Miles Building" and I am aware that other employees of Miles Laboratories Limited also worked from there, including Brian Elliott, Medical Director and the Chairman and Managing Director, Dr Marcello Costi. However I had little contact with them or with divisions of Miles Laboratories Limited other than Cutter UK.

21. My responsibilities at Cutter UK included sales of the company's Factor VIII concentrate Koate and, following the grant of a product licence in February 1985, Koate HT. I am also aware that Cutter produced Factor IX concentrates although I do not believe these were ever licensed in the UK.

22. I received training from Brian Dyos in relation to Cutter's products and I also obtained information from Cutter in the US. I would additionally spend time in the library at Kings College Hospital (to which I had access), reading material relating to haemophilia treatments. Much of my

knowledge of Factor concentrates was, however, gained from the Haemophilia Centre directors. They were very well informed regarding the various products and the associated research and communicated developing knowledge and best practice between themselves, including at regular meetings. I would attend training at the various Haemophilia Centres and would meet with the Haemophilia Centre directors. The directors would often discuss published papers reporting the latest research and I, in turn, would pass such papers on to other Haemophilia Centre directors, even though it is likely that they would already have been aware through other channels.

23. In early 1985, I recruited a sales representative, Walid Marzouk and a second representative, Anne Walton, was recruited in April 1986. The two sales representatives took over the sales role in the North West and North East of England, respectively. I supervised the sales representatives and provided initial training on the products. They subsequently attended training organised at the Haemophilia Centres, where I introduced them to my contacts, the Haemophilia Centre directors and haemophilia nurses.

24. From August 1986, when Cutter's immunoglobulin product, Gamimune N was licensed, I also had sales and marketing responsibility for that product and this occupied a substantial part of my time until I joined Bayer plc in 1990. The launch of Gamimune N resulted in an increase in the sales team at Cutter UK; Walid Marzouk left and five other sales representatives were recruited.

(6) Please confirm whether you were employed by Cutter Laboratories Limited, a/the division of Miles Laboratories Limited (the UK based company) or by Cutter Laboratories Limited (the US company) or both or a different legal entity (and if the latter, please provide details).

25. I was employed by Cutter UK (a division of Miles Laboratories Limited) from 1984 until 1990, when I joined Bayer plc and ceased being involved in the sale and marketing of blood products (see paragraph 12).

(7) Please identify senior colleagues at Cutter (whether in the UK or in the US) who were involved in decision-making as regards the assessment of risks of infection, viral inactivation measures, the response to the risks of HIV/AIDS or any of the other matters set out below.

26. My role at Cutter was limited to sales and marketing in the UK. I do not therefore know which Cutter employees were involved in decision-making in relation to such issues. However my general impression was that such matters were taken seriously, considered diligently within the company and communicated to regulatory authorities. I set out below my recollection of the senior colleagues from the UK and US with whom I interacted.

27. As previously explained, my main contact and line manager in the UK was Brian Dyos, Managing Director at Cutter UK. While he was well informed on the scientific aspects of Cutter's products, his principal role was focused on sales and business development. Jack Wood, Vice President of Cutter Inc, visited the UK on a regular basis and would discuss the UK business with Brian Dyos. I was not present during those discussions.

28. I would contact Peter DeHart, Group Product Manager - Plasma Products, at Cutter US for information required in order to respond to specific questions from Haemophilia Centre directors in relation to Cutter products. I recall that he visited the UK on a number of occasions and met with Haemophilia Centre directors. I also had interactions with Gary Mull, Product Manager, Cutter US in relation to the supply of Koate-HT into the UK particularly if we were experiencing shortages and I needed to try and obtain additional stock.

29. Marie Tatt, Regulatory Affairs Manager was responsible for communications with the regulatory authorities, including in relation to reporting of adverse events. She liaised closely with senior colleagues at Cutter in the US, including Eli Greene, International Regulatory Affairs and Peter DeHart, regarding licensing of products and any safety concerns raised in relation to Cutter products. Eli Greene travelled to the UK several

times each year to meet with Marie Tatt and Brian Dyos and to visit various Haemophilia Centres. As far as I recall, I was not present during those meetings.

(8) Please describe your understanding of the relationship between Cutter Laboratories Limited, Division of Miles Laboratories Inc, and Cutter Laboratories Limited Company in the USA (please note that the companies are referred to below generally as "Cutter"). The enclosed letter of 21 February 1986, in which you seek advice from Cutter International, with employees of Cutter US cc'd in BAYP0000008_098 (tab 49) and enclosed fax from 8 October 1986 from Elias L Greene BAYP0000009_011 (tab 81), may assist you by way of reference.

30. As previously explained, Cutter UK was a division of Miles Laboratories Limited. There was however frequent contact between Cutter UK and Cutter Inc. in the US. As indicated above, Jack Wood, Vice President of Cutter Inc, travelled frequently to the UK and would agree business strategies for Cutter UK with Brian Dyos.

31. As confirmed by documents CGRA0000607 and CGRA0000584 provided to me by the Inquiry, representatives from Cutter Inc, including Jack Wood, Pete DeHart, Gary Mull and Eli Greene visited the UK regularly and met with clinicians in the UK to discuss products and to provide training to myself and other sales representatives.

32. I would contact colleagues at Cutter US in relation to queries regarding Cutter's products and also with respect to the arrangements for import of adequate supplies of Cutter products. While I was not responsible for Regulatory Affairs, I was aware that supplies of Cutter's products despatched to the UK had to be accompanied by certain documentation, consistent with applicable UK regulatory requirements. This is illustrated by document BAYP0000008_098 dated 21 February 1986, identified by the Inquiry, which involves a request from me to Gary Mull at Cutter Inc for samples and protocols for the lots of Koate HT that were to be shipped to the UK, so that these could undergo examination by NIBSC and be

approved in good time for supply to the UK market. I also reminded Gary Mull of the requirement at that time that batches of Factor concentrates supplied in the UK should be accompanied by a statement confirming that the plasma used to prepare the batch of product was non-reactive following testing for HTLVIII antibody.

33. Document BAYP0000009_011, identified by the Inquiry, is a fax from Eli Greene to Marie Tatt confirming that similar interactions occurred between regulatory functions in the UK and Cutter Inc in the US.

(9) To the best of your knowledge, please identify the various blood products which were supplied in the UK by Cutter in the 1980s and early 1990s.

34. When I joined Cutter in September 1984, the only licensed Factor concentrate supplied by the company in the UK was Koate. An application for a UK product licence had been submitted in relation to Koate HT and I believe that some Koate HT was supplied on a named patient basis (i.e. in response to unsolicited requests by haematologists to treat particular patients under their personal responsibility) prior to grant of the licence in February 1985. Non-heat treated Koate was no longer supplied in the UK after January 1985. I have been shown a letter from Cutter UK to the DHSS dated 26 September 1986 and the Abridged Product Licence Application for Koate-HS (WITN6407004 and BAYP0000014_022 respectively) indicating that, in September 1986, Cutter subsequently applied for a product licence for a further Factor VIII concentrate, Koate HS, which incorporated a viral inactivation method involving heating in solution. While I'm sure I was aware of Koate HS at the time, I have no recollection of this product now and understand it was never licensed in the UK.

35. Cutter's Factor IX concentrates, Konyne and Konyne HT, were not licensed in the UK. Non-heat treated Konyne was supplied to a limited extent on a named patient basis. From early 1985, a heat-treated Factor IX concentrate, Konyne HT, prepared by Cutter Inc was supplied in the UK

again to a limited extent on a named patient basis. This product was not, to the best of my knowledge, licensed in the UK.

36. In addition to Factor concentrates, Cutter's intravenous immunoglobulin product, Gamimune N was licensed in the UK in August 1986 and was supplied from around that time.

37. I do not recall anything about Plasbumin, although I have been shown a Key Indicator Report from December 1984, dated 30 January 1985 (BAYP0000024_047) which indicates that this was an albumin product. I cannot remember this product being sold in the UK and I do not know if it was licensed.

Section 2: Knowledge of, and response to risk

(10) When you were working at Cutter in the early 1980s, what did you know and understand about:

(a) the risks of infection associated with blood and/or blood products generally; and

38. As explained in my response to Question 2 above, when I joined Cutter in 1984, I had some familiarity with blood and blood products, including Factor concentrates, as a result of my previous role in the Department of Pathology at Chelmsford and Essex Hospital. From my work in Chelmsford, I was aware of the fact that blood and blood products could transmit hepatitis. By September 1984, AIDS had been widely reported in mainstream media and I was also aware that AIDS was thought to be transmitted through blood.

39. The risks of infection transmitted through blood and blood products were addressed by Cutter in the US through donor testing to try and exclude infected donations. However the sensitivity of tests for hepatitis B were limited and other viruses (i.e. so-called non-A non-B hepatitis ("NANB hepatitis") and the AIDS agent) had either not been identified or tests were not available. In addition to donor testing, during my time at Cutter, efforts

were made to use strategies, such as heat treatment, which aimed to inactivate viruses that were present in donated blood and plasma.

(b) the risks of transmission of hepatitis (including HBV and Non-A Non-B Hepatitis)? The enclosed document, a letter from 1986 to Dr Wensley (BAYP0000008_121 (tab 54) may assist by way of reference.

40. Please refer to my answer to (a). As explained above, the risk of transmission of hepatitis through blood and blood products was well known by the early 1980s.

41. I have reviewed document BAYP0000008_121, identified by the Inquiry, which is a letter I wrote to Dr Wensley on 18 March 1986. In the letter I referred to data presented by Dr Kernoff, from the Royal Free Hospital, comparing the rates of infection with NANB hepatitis following treatment with dry heat treated Factor concentrates supplied by different fractionators and enclosed an abstract, which had been submitted to the World Federation of Haemophilia (WFH) by Professor Allain, relating to rates of NANB hepatitis following treatment with Koate HT. Based on these data, I referred cautiously to the fact that the dry heat treatment method of viral inactivation used in Koate-HT seemed to reduce but not eradicate the risk of NANB hepatitis associated with use. The letter illustrates the point made in my answer to (a) above that, at that time, the hepatitis C virus, responsible for most cases of NANB hepatitis, had not been isolated and diagnosis of infection therefore relied upon non-specific tests of liver disorder, including raised levels of liver enzymes such as alanine aminotransferase ("ALT"). I do not recall writing this letter but I believe the purpose was to provide some information and scientific data to Dr Wensley which could be of use to him.

(c) How did your knowledge change and develop over time? What were the sources of your knowledge?

42. I refer to my answers to (a) and (b) above.

43. I recall that my knowledge of the risk of infection with the AIDS agent and hepatitis via blood and blood products developed principally through internal discussions with and training provided by Brian Dyos and others within Cutter, my own review of published papers and information, and published papers provided by the Haemophilia Centre directors during my regular meetings with them. The Haemophilia Centre directors were well informed and communicated information on treatments and products between themselves at national level and internationally. Many of them were actively involved in research (I can recall specifically: Professor Arthur Bloom in Cardiff; Professor Savidge at St Thomas' Hospital; Professor Kernoff at the Royal Free Hospital; and Dr Peter Jones in Newcastle) and would discuss the results of their studies with me. In addition, I attended larger meetings such as the WFH, which was held every four years and attended by haemophilia experts internationally. I recall, in particular, a meeting of the WFH which took place in Milan in June 1986.

(11) To the best of your knowledge, what was the state of knowledge within Cutter more generally in the 1980s about the risks of infection associated with blood and/or blood products?

44. I refer to my answers to Question 10 above. I am not aware of knowledge within Cutter, other than that which was passed on to me.

45. However, I have been shown the report of Dr Mozen (WITN6407003) and a Chronology and Timeline of Events (WITN6407002) which describes developing knowledge of the risk of infection associated with blood and blood products in the context of actions taken by Cutter. In view of my role in sales and marketing in the UK, I was not involved in the matters set out in Dr Mozen's report and do not have detailed knowledge of the matters set out in the Chronology and Timeline of Events at (WITN6407002). However, these documents are consistent with the knowledge and information available to me from my time at Cutter and respond to the Inquiry's question.

(12) What advisory or decision-making structures were in place at Cutter to assess the risks of infection associated with the use of blood and/or blood products?

46. The risks of infection associated with blood and blood products generally and Cutter products in particular, were assessed by Cutter Inc and information was provided to Cutter in the UK as described in my responses to Question 7 and Question 8 above. While I had no responsibility for decision-making on risks of infection and this was not within my knowledge or experience, I was aware that Cutter Inc was constantly reviewing its processes in order to develop products that were not only effective but also, to the extent possible, did not transmit infections.

47. Whenever I received information from Haemophilia Centres suggesting any concerns in relation to the safety of Cutter products (including possible transmission of infection), I would pass this on to Marie Tatt in Regulatory Affairs, who would, to the best of my knowledge, conduct further investigations, liaise with Cutter Inc and report to the UK regulatory authorities consistent with UK requirements.

To the best of your knowledge, on what sources did Cutter rely on for information about those risks?

48. I refer to my response to Question 10 above. I have no direct knowledge of the sources of information relied upon by Cutter, but believe that such sources probably included information from the published literature, meetings with experts and regulators and from its own research including that described by Dr Mozen in his report at WITN6407003.

(13) Insofar as you are able to do so, please provide a chronological account of the steps taken by Cutter during your employment to reduce the risk of people being infected with hepatitis (in particular Non-A Non-B Hepatitis) as a consequence of treatment with Cutter products.

49. As indicated above, I am not a scientist, my role at Cutter was in sales and marketing rather than in the scientific and technical parts of the business

and I did not have comprehensive knowledge of all the steps taken by Cutter to reduce the risk of hepatitis associated with the company's products.

50. However, while I was not involved in the preparation of Cutter's Factor concentrates, the efforts made by the company to eradicate viruses from its Factor concentrates are set out in the report of Dr Mozen (WITN6407003) at section 7.

51. Although I was not familiar with the matters described by Dr Mozen, I was generally aware of certain measures introduced by Cutter to reduce the risk of viral transmission through its blood products, such as those set out below:

    a. The datasheets for Cutter's Factor VIII and Factor IX concentrates included, at all material times, a warning to clinicians advising them that these products had been prepared from pooled plasma from many donations and that the transmission of hepatitis viruses should be assumed;

    b. Plasma donors were screened for infection and the details of such screening developed over time;

    c. Donations of plasma underwent testing for markers of infection, consistent with FDA requirements and again such testing changed over time;

    d. Virally inactivated products were developed, including:

        i. Koate HT (dry heat-treatment at 68°C for 72-77 hours);

        ii. Konyne HT (dry heat-treatment at 68°C for 72-77 hours); although a product licence application was submitted in the UK, I understand this was not ultimately granted by the UK licensing authority;

iii. Koate HS (heated in solution 60°C for 10 hours); again although a product licence application was submitted in the UK, I understand this was not ultimately granted by the UK licensing authority;

iv. Koate HP (solvent detergent method); similarly, while a product licence application was submitted in the UK, I understand this was not approved by the UK licensing authority.

e. When I first joined Cutter in 1984, I was informed that the company was seeking to develop concentrates containing recombinant coagulation Factors. This work continued and eventually resulted in Kogenate, a recombinant Factor VIII concentrate, licensed in the UK after I stopped working with blood products.

52. At this stage, some 30-40 years after the relevant events took place, I am not able to recall the dates of implementation of the measures described or details of the licensing of the blood products listed above. However, I refer to the Chronology and Timeline of Events, submitted by Bayer to the Archer Inquiry, provided at (WITN6407002).

(14) What if any steps were taken to ensure that:

(a) NHS bodies and/or clinicians purchasing and/or using Cutter products were made aware of the risks of hepatitis? The enclosed document, a letter from you to Dr Bevan in January 1986 noting the inactivation of HTLV-III in Koate HT (BAYP0000008_077) (tab 46) and a further letter from you to Dr Prentice, Dr Lee, Dr Smith and Gardiner from October 1986 (BAYP0000009_030) (tab 83) may assist you with answering this question; and

53. The principal way in which Cutter communicated information regarding its Factor concentrates to NHS bodies and clinicians was through the product information (datasheets and package inserts) which were approved by the regulatory authority as properly reflecting contemporaneous scientific and

medical information before they were put into circulation. NHS bodies and/or clinicians purchasing Cutter's Factor concentrates were made aware of the risk of hepatitis through prominent warnings on the packaging and in the datasheets, indicating that the products might transmit hepatitis. I have been shown some examples of these documents, including for the period before I joined Cutter UK; copies of which, together with the relevant warnings, are referenced below.

a. The package insert for Koate dated March 1981 (BAYP0000019_025) emphasised the risk of hepatitis associated with use and stated in bold capital letters:

   "**THIS PRODUCT IS PREPARED FROM HUMAN VENOUS PLASMA. EACH INDIVIDUAL UNIT OF PLASMA AND EACH LOT OF FINAL PRODUCT HAS BEEN FOUND NONREACTIVE FOR HEPATITIS B SURFACE ANTIGEN USING A LICENSED THIRD GENERATION ASSAY. HOWEVER, THIS TEST DOES NOT PRECLUDE THE PRESENCE OF HEPATITIS VIRUS. SEE WARNING.**"

   A warning also appeared in a prominent box as follows:

WARNING

Antihemophilic Factor (Human) Koate™ concentrate is a purified dried fraction of pooled plasma obtained from many paid donors. The presence of hepatitis viruses should be assumed and the hazard of administering Koate concentrate should be weighed against the medical consequence of withholding it, particularly in persons with few previous transfusions of blood and plasma products.

Kasper and Kipnis[4] have concluded that those who have had little exposure to blood products have a high risk of developing hepatitis after introduction of clotting Factor concentrates, such as this product. For those patients, especially those with mild haemophilia, they recommend single donor products. However, for patients with moderate or severe haemophilia who have received numerous infusions of blood and plasma products, they feel that the risk of hepatitis is small. They believe that the clotting Factor concentrates have so greatly improved the management of severe haemophilia that these products should not be denied to appropriate patients.

b. The package insert for Koate was amended in December 1981 (BAYP0000019_087) to update the warning in relation to the risk of hepatitis as follows (new wording is underlined):

"THIS PRODUCT HAS BEEN PREPARED FROM LARGE POOLS OF HUMAN VENOUS PLASMA COLLECTED FROM MANY PAID DONORS. EACH INDIVIDUAL UNIT OF PLASMA AND EACH LOT OF FINAL PRODUCT HAS BEEN FOUND NONREACTIVE FOR HEPATITIS B SURFACE ANTIGEN (HBsAG) USING A US FEDERALLY APPROVED TEST OF AT LEAST THIRD GENERATION SENSITIVITY. UNFORTUNATELY, THIS TEST DOES NOT PRECLUDE THE PRESENCE OF HEPATITIS VIRUS. SEE WARNING.

NO KNOWN LABORATORY TEST METHOD CAN OFFER ASSURANCE THAT PRODUCTS DERIVED FROM HUMAN BLOOD WILL NOT TRANSMIT HEPATITIS"

c. The Package leaflet for Koate, which was issued in March 1984 (WITN6407005), included a warning about AIDS, and read as follows:

WARNINGS

Koate™ concentrate is a purified dried fraction of pooled plasma obtained from many paid donors. Although each unit of plasma has been found nonreactive for hepatitis B surface antigen (HBsAG) using a U.S. Federally approved test with third-generation sensitivity, the presence of hepatitis viruses in such pools must be assumed.

Kasper and Kipnis[5] have concluded that those who have had little exposure to blood products have a higher risk of developing hepatitis after introduction of clotting factor concentrates. For such patients, especially those with mild haemophilia, they recommend single donor products. For patients with moderate or severe haemophilia who have received numerous infusions of blood or blood products, they feel that the risk of hepatitis is small. They believe that that clotting factor concentrates have so greatly improved the management of severe haemophilia that these products should not be denied to appropriate patients.

Isolated cases of Acquired Immune Deficiency Syndrome (AIDS) have been reported in haemophiliacs who have received blood and/or coagulation factor concentrates including Factor VIII concentrates. It is not known if the disease is due to a transmitted specific agent, secondary to multiple antigen exposures, or to some other mechanisms. The physician and patient should consider that Factor VIII concentrates may be associated with the transmission of AIDS and weigh the benefits of therapy accordingly.

d. The package insert for Koate HT dated May 1985 (WITN6407006) included the following boxed warning:

WARNINGS

Antihemophilic Factor (Human), heat-treated, Koate HT concentrate is a purified dried fraction taken from large pools of fresh human plasma obtained from many paid donors. Although each unit of plasma has been found non-reactive for hepatitis B surface antigen (HBsAg) by an FDA approved method, the presence of hepatitis viruses in such pools must be assumed.

Kasper and Kipnis[5] have concluded that those who have had little exposure to blood products have a higher risk of developing hepatitis after introduction of clotting factor concentrates. For such patients, especially those with mild hemophilia, they recommend single donor products. For patients with moderate or severe hemophilia who have received numerous infusions of blood and plasma products, they feel that the risk of hepatitis is small. They believe that the clotting factor concentrates have so greatly improved the management of severe hemophilia that these products should not be denied to appropriate patients.

Isolated cases of Acquired Immune Deficiency Syndrome (AIDS) have been reported in hemophilics who have received blood and/or coagulation factor concentrates including Factor VIII concentrates. It is not known if the disease is due to a transmitted specific agent, secondary to multiple antigenic exposures, or to some other mechanisms. The physician and patient should consider that Factor VIII concentrates may be associated with the transmission of AIDS and weigh the benefits of therapy accordingly.

e. The boxed warning in the Koate HT package insert was revised in July 1986 (WITN6407007) to read as follows:

WARNINGS

Antihemophilic Factor (Human), heat-treated, Koate HT is prepared from pooled units of plasma which have been individually tested and found nonreactive for hepatitis B surface antigen and antibody to human T-lymphotropic virus III (HTLV-III) by FDA approved tests. Other screening procedures are used to eliminate high risk plasma donors and the heat treatment step in the manufacturing process is designed to reduce the risk of transmitting viral infection. However, testing methods presently available are not sensitive enough to detect all units of potentially infectious plasma, and treatment methods have not been shown to be totally effective in eliminating viral infectivity from the product.

Individuals who have not received multiple infusions of blood and plasma products are very likely to develop signs and/or symptoms of some viral infections, especially non-A non-B hepatitis as shown in recent data. [reference]

Fletcher et al [reference] have concluded that those who have had [limited] exposure to blood products have a higher risk of developing hepatitis after introduction of clotting factor concentrates. For such patients, especially those with mild haemophilia, Kasper and Kipnis [reference] recommend single donor products. For patients with moderate or severe haemophilia who have received numerous infusions of blood and plasma products, they feel that the risk of hepatitis is small. They believe that the clotting factor concentrates have so greatly improved the management of severe haemophilia that these products should not be denied to appropriate patients. The physician and patient should consider that Factor VIII concentrates may be associated with the transmission of hepatitis and weigh the benefits of therapy accordingly.

54. Document BAYP0000008_077, identified by the Inquiry, is a letter dated 31 January 1986 from me to Dr Bevan at St George's Hospital, London. The letter described the viral inactivation process applied to Koate HT (68°C for 72 hours), stated that studies had shown that the HTLVIII virus and other viruses which were known to be difficult to eradicate were inactivated by the Cutter process and referred to the results of initial studies for NANB hepatitis conducted in chimpanzees, which had shown no evidence of infection in the animals tested. I do not remember this letter; however, I recall that I was careful to ensure that any information I provided to clinicians was based on published or other scientific data.

55. I have also reviewed document BAYP0000009_030, a letter dated 21 October 1986 sent by me to several clinicians, which was again identified

by the Inquiry. I do not recall this letter, however it seems to represent part of a pack of material relating to Cutter Factor concentrates and at least part of the contents would have been drafted by Cutter colleagues and given to me to send to clinicians who requested it. It is likely that the letter summarises information provided in the 'inactivation booklet' and the abstract of the paper by Professor Allain, presented at the International Congress of the WFH in Milan in June 1986, which are listed as attachments to the letter. The letter refers specifically to the data presented by Professor Allain which showed that the heat treatment process used in preparing Koate HT was "*effective in eliminating HTLVIII and also results in a significant reduction in the incidence of Non-A, Non-B hepatitis in haemophilic recipients*".

(b) patients treated with Cutter products were made aware of the risks of hepatitis?

56. Throughout the period while I worked for Cutter UK, there was no regulatory requirement for pharmaceutical companies to provide information directly to patients. As the Factor concentrates supplied by Cutter in the UK were available on prescription only, Cutter provided information to prescribers in relation to such products, including through the product information described at paragraph 53 above. The treating clinicians could then discuss the products and the associated risks tailored to the medical condition and circumstances of the individual patient. Cutter did not participate in those discussions and, while I saw patients very occasionally at meetings, I do not recall speaking to any of them.

Please describe, to the extent that you are able to, the information that was provided by Cutter to NHS bodies, clinicians and/or patients about the risks of hepatitis. The following documents may assist you in answering this question:

- ***A letter from you to Professor Bloom from March 1986 (See: BAYP0000008_109); (tab 52)***
- ***A Trip report by Gary Mull from June 1986 (See: CGRA0000584)(tab 68);***

- ***A letter to you from Jack Wood on 29/07/1986 regarding a meeting with Dr Peter Jones (See: CGRA0000607) (tab 75); and***
- ***Letters from 1986 to from A Walton of Cutter to various clinicians sharing a paper by J P Allain (See: BAYP0000008_155 (tab 58), BAYP0000008_250 (tab 69), and BAYP0000009_050 (tab 84)).***

57. My responses to Question 14 (a) and (b) above are repeated. Documents CGRA0000584 and CGRA0000607, identified by the Inquiry, are trip reports prepared by Gary Mull and Jack Wood of Cutter Inc following visits to the UK, which describe meetings with clinicians to discuss viral inactivation data and the safety profile of Factor concentrates.

58. In document CGRA0000607, Jack Wood described his meeting with Dr Peter Jones, Director of the Newcastle Haemophilia Centre. He stated:

> *"I reviewed with Dr. Jones once again the Cutter viral inactivation data and was pleased by his response that in all his discussions with United Kingdom haemophilia directors and those outside of this country there is a consensus that the Cutter data is the most reliable and if it was applied to HIV tested plasma should produce without question a HIV-safe product. He does feel that hepatitis-safety is not proven by Cutter on Koate-HT, but agrees the data does suggest it is as safe as the Alpha product he is currently using."*

59. In document CGRA0000584, Gary Mull refers to visits to the Oxford and Royal Free Hospital Haemophilia Centres. In 1986, Dr Kernoff, at the Royal Free Hospital, was co-ordinating studies on Alpha's wet heat treated Factor VIII concentrate, Profilate-HS and he expressed the view that this was the safest product for treating haemophilia available in the UK and safer, in terms of NANB hepatitis, than dry heat-treated concentrates such as Koate HT. Dr Kernoff was not willing to participate in any studies investigating other wet heat treated concentrates, such as Koate HS. Gary Mull also documented the interest of Dr Kernoff and other clinicians in the development of recombinant Factor VIII products.

60. Document BAYP0000008_109, identified by the Inquiry, is a letter dated 6 March 1986 from me to Professor Bloom at the University Hospital of Wales, in which I confirmed that all batches of Koate HT arriving in the UK would be prepared from material tested for HTLVIII and found to be non-reactive and attached a product profile sheet on Koate HT. I cannot now remember what information would have been included in the product profile sheet, although it seems likely that this would have reflected the datasheet, including the warnings regarding the risks of hepatitis.

61. Document BAYP0000008_155, identified by the Inquiry, is a letter dated 3 April 1986 from me to Professor Bloom, in which I referred to the abstract submitted to the WFH by Professor Allain where he described six patients treated with Koate HT who had not seroconverted to HTLVIII or developed raised ALT levels, which could suggest hepatitis. Since the date of Professor Allain's abstract, data relating to a further three patients demonstrating similar results had become available. In the letter, I said:

> *"I was anxious that you should be aware of this study as it shows that Koate HT has a process that is capable of reducing NANB infectivity as well as other claims which have been made by the manufacturers of the wet product."*

As previously mentioned, the hepatitis C virus had not at that time been isolated and there was no specific test for infection with the NANB agent. The results obtained by Professor Allain were, in those circumstances, encouraging although they did not indicate that NANB hepatitis was eradicated from Koate HT.

62. Document BAYP0000008_250, identified by the Inquiry, is a letter dated 2 July 1986 from Anne Walton, Senior Sales Representative to Dr Hows, at the Hammersmith Hospital, in which she referred to the study by Professor Allain described at paragraph 41 above and noted that *"Dr Allain concluded that the data suggest that Koate HT carries no risk of LAV/HTLVIII transmission and a low risk of transmitting non A non B hepatitis."* Document BAYP0000009_050, identified by the Inquiry, is a

letter from Anne Walton to Dr Adelman, Lincoln County Hospital, dated 3 November 1986, which contains substantially the same information.

63. In summary, therefore, the documents identified by the Inquiry provide examples of scientific data being provided to clinicians in relation to Cutter products, including evidence indicating that Koate HT was associated with a reduced risk of transmission of NANB hepatitis. We were however careful not to suggest that the heat treatment process used in Koate HT eradicated NANB hepatitis transmission.

HIV and AIDS

(15) What was your knowledge and understanding of HIV (previously known as HTLV-III) and AIDS and in particular the risks of transmission from blood products during your time working at Cutter? What were the sources of your knowledge, and did they change over time? How did your knowledge and understanding change over time?

64. My answer to Questions 2 and 10 are repeated. Before joining Cutter in September 1984, my knowledge of HTLVIII and AIDS had principally been obtained from reports in the mainstream media, as a result of which I believed that this was mainly a disease affecting gay men, although by the time I joined Cutter in late 1984 the possibility of transmission of AIDS through blood and blood products had been recognised. After joining Cutter, I learned more about the condition as described in my response to Question 10. Cutter had already developed Koate HT, incorporating a viral inactivation process that was subsequently confirmed to be effective against the AIDS agent. An application for a product licence for Koate HT was submitted to the Department of Health in November 1984 and approved by the Licensing Authority in February 1985. From January 1985 (BAYP0000024_091), Cutter supplied only heat-treated Koate for use in the UK.

(16) How and when did you first become aware that there might be an association between AIDS and the use of blood products? You may find the documents at BAYP0004203_002 (tab 1), BAYP0000024_233 (tab 39)

and BAYP0005737 (tab 35) of some assistance to you when considering this question. We note that BAYP0004203_002 predates your employment with Cutter.

65. As indicated in my responses to Questions 10 and 15 above, by the time I joined Cutter in September 1984, the possibility of transmission of the AIDS agent through blood and blood products had been recognised.

66. The first document identified by the Inquiry, BAYP0004203_002, is an internal memo from Merrill Boyce of Cutter Inc to Jack Wood dated 6 August 1982, which referred to a newsletter from the US National Hemophilia Foundation reporting three cases of AIDS in haemophilia patients and describing concerns that the agent might have been transmitted through blood products. The memo described the uncertainty surrounding the cause of AIDS at that time, together with suggestions that the condition might be due to chronic viral infection, potentially with hepatitis. Merrill Boyce stated that Cutter was actively involved in investigating the issue and would be co-operating closely with the US Bureau of Biologics and the Center for Disease Control. As the Inquiry notes, this document pre-dates my employment at Cutter UK by over two years.

67. Document BAYP0005737, identified by the Inquiry, is a copy of an article published in the journal, Clinica on 12 April 1985, which refers to a recent letter from Dr Peter Jones, Director of the Newcastle Haemophilia Centre, to the British Medical Journal. In that letter, Dr Jones had suggested that AIDS was transmitted to the US via plasma collected in Africa in the 1970s. At the end of the article, Dr Elliott of Cutter was reported to have described Dr Jones's assertions as "inconceivable". The origin of AIDS is a matter outside my knowledge and expertise.

68. Document BAYP0000024_233, identified by the Inquiry, is a memo dated 20 May 1985 from Walid Marzouk, Sales Representative for the North West of England, to me regarding information provided to him by Dr Jones in relation to the AIDS situation in the US. The memo states that "*HTLVIII*

antibodies have now been found in volunteer donors who have previously been referred to as a low risk group" and that this, plus the fact that "*HTLVIII antibodies are now found in female prostitutes and there is enough evidence to suggest that this is being transmitted to normal heterosexual males*", "*suggest that HTLVIII is more contagious than originally thought*". This information indicated that AIDS was more widespread in the US population than had previously been believed and was not limited to so-called high risk groups.

(17) To your knowledge, what enquiries and/or investigations did Cutter carry out in respect of the risks of transmission of HTLV-III, HIV and/or AIDS, prior to 1985? What was your involvement in such enquiries and investigations? You may find the document at BAYP0000025_038 (tab 17) and ARCH0002291_004 (tab 3) of some assistance when considering this question.

69. As indicated above, I am not a scientist and, in view of my role in sales and marketing, I was not involved in investigating the risks of transmission of HTLVIII, HIV or AIDS prior to 1985 or at any other time. Furthermore, I joined Cutter UK in September 1984 and therefore had little opportunity to make enquiries prior to 1985.

70. Document ARCH0002291_004, identified by the Inquiry, is a Cutter Statement of Policy, entitled "Acquired Immune Deficiency Syndrome", dated 28 January 1983, some 18 months before I joined Cutter UK. The Statement of Policy indicated that very little was known about the cause of AIDS, but that US Government health authorities had identified three population groups as appearing to be more at risk: gay men; intravenous drug users; and, recent visitors or inhabitants of Haiti. In addition, a further small group was emerging as having a risk of contracting AIDS, persons receiving blood or blood products. In these circumstances, the Statement of Policy stated:

"Cutter is initiating a program for the selection of plasma donors in order to reduce the possibility of AIDS being transmitted through blood-derived products.

This program requires potential plasma donors to read a statement concerning the serious nature of AIDS. A donor who acknowledges being a male homosexual, a user of intravenous drugs or a recent resident or visitor to Haiti will not be accepted as a plasma donor.

This donor acceptance policy will be enlarged appropriately as further information about the disease becomes available. Cutter has intensively involved its people and resources to contribute to a resolution of this segment of the AIDS problem".

71. The Inquiry has also identified document BAYP0000025_038, a letter dated 10 October 1984 from Dr J.N Ashworth, Vice President, Scientific Affairs, Cutter Inc to Marie Tatt in response to certain queries regarding sites of plasmapheresis raised in Ireland. I was not copied into this correspondence. The letter stated that Cutter did not use plasma collected at centres situated in the so-called high risk areas, but pointed out that there was no way to control movement of donors. Dr Ashworth also referred to a recent recall of American Red Cross Factor VIII, prepared from plasma from unpaid volunteer donors, after one such donor had been found to have AIDS. He said that, despite the absence of any test for AIDS, Cutter was doing everything possible at that time to eliminate potential AIDS donors from the donor pool and that Cutter planned to screen donors for HTLVIII as soon as a test became commercially available. This letter reflects my general impression that Cutter took the possibility of transmission of AIDS through its Factor concentrates very seriously and took what steps were possible to try to reduce this risk.

72. The Chronology and Timeline of Events submitted to the Archer Inquiry by Bayer and provided at WITN6407002 also includes information regarding actions taken by Cutter to reduce the risk of transmission of the AIDS agent prior to 1985, in the context of relevant regulatory statements and requirements.

(18) When did you become aware of the risk of HIV and AIDS in Cutter products specifically? The enclosed document, a memo from Eli Greene in 1984 (BAYP0005496) (tab 20) may assist by way of reference. Were you made aware of this memorandum, or would you have expected to be made aware of this memorandum? If so and if not, what are your views on the substance of the memorandum?

73. My responses to Questions 10 and 15 above are repeated. While I was not responsible for investigating reports of possible viral transmission, I do not now remember any case where Cutter's Factor concentrates were confirmed to be the cause of AIDS. I do however remember that we received reports of hepatitis and I am aware that it was challenging to investigate the cause of viral infections in any individual case because, in general, patients received multiple treatments from many different sources.

74. Document BAYP0005496, identified by the Inquiry, is an internal memo dated 29 November 1984, from Eli Greene at Cutter Inc to various senior colleagues at Cutter Inc and Brian Dyos at Cutter UK. The memo states that a patient in Ireland who had been using Koate had been diagnosed as having Pneumocystis Carinii infection with a presumptive diagnosis of AIDS. The patient had been using Koate since 31 January 1984 but before that "*had a mixture of everything*". Professor Temperley of the Haemophilia Centre in Dublin had recalled all Koate from patients with supplies for home treatment. While the memo expressed the view that Koate was probably not the cause of AIDS in the Irish patient in view of the relatively short time he had been using the product and the typically long incubation period of AIDS, it recognised the difficulty proving this. The memo also pointed out that the lot of product used by the affected patient GRO-A had been used in Ireland for some time and asked where else the same lot had been supplied.

75. The memo dated 29 November 1984 was not copied to me and I do not recall seeing it, although it is quite possible that Brian Dyos showed it to me. I would have expected to have been alerted to the issue, particularly

if the same lot of Koate had been supplied in the UK, so that I would be prepared if I received questions from Haemophilia Centre directors or other healthcare professionals.

76. I have been shown further documents which relate to the case of AIDS in Ireland; these are referenced below.

    a. A letter dated 6 December 1984, sent by Cutter Inc to Professor Temperley in relation to the case (BAYP0000025_102) which stated:

        "Since AIDS runs a general incubation period of 14 months to two years, and the CDC considers 5 years the maximum, it is entirely possible that the products your patient received prior to 31 January, 1984, could have transmitted the AIDS virus.

        […]

        To date, we know of no case of AIDS which has been specifically traced to use of Koate or Konyne Factor IX Complex Human, nor have we been notified of such by the CDC or FDA, and no specific Lot, including NC 8502A has been suspected."

    b. An internal memo from Eli Greene dated 12 December 1984 (BAYP0000025_106), which confirmed that Mike O'Donnell, Cutter's distributor in Ireland, had called to confirm that Professor Temperley had asked to speak with him urgently and that "*Koate has been completely exonerated from blame in the AIDS case*".

(19) Insofar as you are able to do so, please provide a chronological account of the steps taken by Cutter during your employment to reduce the risk of infection with HTLV-III, HIV and/or AIDS as a consequence of treatment with Cutter products. (See the enclosed document from 1986: BAYP0000008_116) (tab 53)

77. I refer to my response to Question 13 above. I believe that the measures taken to reduce the risk of infection with the AIDS agent would have been similar to those taken to reduce the risk of hepatitis, particularly prior to the identification of HTLVIII in 1984.

78. As previously explained, my role at Cutter was in sales and marketing rather than in the scientific and technical parts of the business and I would not have had comprehensive knowledge of all the steps taken by the company to reduce the risk of infection with HTLVIII, HIV and/or AIDS associated with Cutter's products. However, the main steps taken by Cutter specifically to reduce the risk of infection with HTLV-III, HIV and/or AIDS, of which I am aware, were:

    a. Enhanced screening of plasma donors and donations as described at paragraph 51 above;

    b. The development of the heat treatment process used for Koate HT and associated products; a product licence application for Koate HT was submitted in the UK in November 1984, shortly after I joined Cutter (see BAYP0000003_268, a letter from Miles to DHSS dated 13 November 1984);

    c. After the identification of HTLVIII, the introduction of screening of plasma donations for antibodies to HTLVIII in May 1985.

    Further details of the measures taken by Cutter are set out in the report of Dr Milt Mozen at WITN6407003 and the Chronology and Timeline at WITN6407002.

79. Document BAYP0000008_116, identified by the Inquiry, is a letter dated 14 March 1986 from me to Dr McVerry at St James University Hospital in Leeds, enclosing a copy of a booklet entitled "Inactivation of AIDS-associated viruses in antihemophilic factor products: the effectiveness of heat treatment". The letter stated that "*the heat treatment process used by Cutter on Koate HT, 68°C for 72 hours, is the most vigorous heat treatment of all commercial companies*" and proceeded to inform Dr McVerry that all batches of material received in the UK would be taken from 100% HTLVIII antibody tested donors.

80. I also refer to document BAYP0000009_030 identified by the Inquiry in relation to Question 14 and addressed at paragraph 55 above, which describes actions taken by Cutter.

81. In addition, the Timeline of Events at WITN6407002 and the report of Dr Mozen, at WITN6407003 reference the initiatives carried out by Cutter Inc to reduce the risk of transmission of infections, including viral inactivation processes applied to its blood products.

(20) To the best of your knowledge, what if any steps were taken to ensure that:

a. NHS bodies and/or clinicians purchasing and/or using Cutter products were made aware of the risks of HTLV-III, HIV and/or AIDS? You may find the enclosed letters to clinicians from 1983 (BAYP0000028_025 (tab 6) and BAYP0000028_076) (tab 8)) and a contract specification from 1985 (BAYP0000007_129) (tab 43)) of some assistance to you when considering this question.

b. patients treated with Cutter products were made aware of the risks of HTLV-III, HIV and/or AIDS?

Please describe, to the extent that you are able to, the information that was provided by Cutter to NHS bodies, clinicians and/or patients about the risks of HTLV-III, HIV and/or AIDS.

82. I refer to the response to Question 14 above.

83. The principal way in which Cutter communicated information regarding its Factor concentrates to NHS bodies and clinicians was through the product information (datasheets and package inserts) which were approved by the regulatory authority as properly reflecting contemporaneous scientific and medical information before they were put into circulation. I describe examples of product information, including the information that was provided in relation to the possibility of transmission of hepatitis and AIDS at paragraph 53 above. In summary, warnings regarding the possibility of transmission of infections through use of blood products were at all times

provided with all Cutter Factor concentrates supplied in the UK. A specific warning relating to the possibility of transmission of the AIDS agent was included in product information for Koate from March 1984, before the agent had been isolated (WITN6407005):

> *"Isolated cases of Acquired Immune Deficiency Syndrome (AIDS) have been reported in haemophiliacs who received blood and/or coagulation Factor concentrates, including Factor VIII concentrate. It is not known if the disease is due to a transmitted specific agent, secondary to multiple antigenic exposures or to some other mechanisms. The physician and patient should consider that Factor VIII concentrates may be associated with the transmission of AIDS and weigh the benefits of therapy accordingly".*

84. The Haemophilia Centre directors were in any event very well informed of the risks associated with use of relevant blood products as a result of effective communication between clinicians at both national level (through the Haemophilia Centre Directors Organisation) and internationally.

85. With respect to patients, my response to Question 14(b) at paragraph 56 above is repeated.

86. The two letters identified by the Inquiry in relation to this question, (BAYP0000028_025 and BAYP0000028_076) are dated 1983 which was before I joined Cutter UK and I therefore can add little to their content.

    a. Document BAYP0000028_025 is a letter from Brian Dyos to Dr Kernoff, Royal Free Haemophilia Centre, dated 8 February 1983. The letter indicates that Dr Kernoff had inquired regarding Cutter's selection procedures for plasma donors and was advised that, at that time, Cutter was instituting a programme of enhanced donor screening aimed to exclude donors from groups thought to be at high risk of AIDS and that there were no Cutter-owned or contracted plasma donation centres in the Cities of New York, Los Angeles or San Francisco (which were thought to be the high risk areas). Brian Dyos informed Dr

Kernoff that Cutter was closely following all AIDS developments and was in constant communication with responsible health authorities.

b. Document BAYP0000028_076 is a letter from Barry Barber, Sales Manager at Cutter UK, to Professor Bloom at the University Hospital of Wales, dated 5 April 1983. This letter also referred to the measures described in the previous letter to Dr Kernoff and additionally stated that the medical examination performed on all donors had been expanded to include questions specifically related to symptoms associated with AIDS, such as night sweats, drastic unexplained weight loss and recurrent fever. The physical examination included a check for enlarged lymph glands and a full body examination for suspicious lesions.

87. The Inquiry has also referred me to a contract specification dated 25 October 1985 (document BAYP0000007_129). I have no recollection of this specification and the NHS body with whom the contract was made is unclear. The specification confirms that plasma donors were screened according to FDA requirements (so far as I am aware this was always the case) and that, from March 1985, all donations had been tested for HTLVIII antibodies.

Section 3: Blood supply, donor pools and screening

(21) To the best of your knowledge, where and from whom did Cutter obtain source plasma? Please provide details. You may wish to consider BAYP0000002_169 [Tab 5] and BAYP0000003_225 [Tab 13] when answering this question.

88. I had no involvement in the arrangements for obtaining source plasma whilst working at Cutter UK and, although I may have been aware of some of this information at the relevant time, I cannot now remember it. I therefore cannot comment on document BAYP0000002_169 (a Cutter Laboratories Quality Assurance document dated 8 February 1983, which lists source plasma centres). I have reviewed document BAYP0000003_225, identified by the Inquiry, which is a letter dated 9 May

1984 from Professor Temperley in Ireland to Dr McCarthy at the National Drugs Advisory Board. Professor Temperley stated in the letter that he "*would be most unhappy about using FVIII concentrates whose original plasma was collected in New York, Miami and San Francisco*" which, Professor Temperley indicated in his letter, were associated with AIDS at that time. He referred to Cutter, amongst other companies, having given verbal guarantees that plasma used in their Factor concentrates was not collected from these areas, and stated that written guarantees would been helpful. The documents identified by the Inquiry in relation to Question 20 are also relevant to this Question 21 and I refer to my responses at paragraphs 82-87 above.

89. I have also been shown document BAYP0000009_030, identified by the Inquiry in relation to Question 14, which is a letter sent by me to several clinicians on 21 October 1986. The first section of this letter, in particular, sets out information relating to sourcing of plasma, as follows:

> *"Koate HT is prepared from pooled human plasma from at least 1000 healthy donors. All donors are required to read and sign a confidentiality questionnaire which states that they are not members of any of the high risk groups for AIDS. In addition, a medical examination is routinely given to all donors to ensure good general health; this includes questions specifically related to AIDS-like symptoms.*
>
> *No plasma is collected from the metropolitan areas of New York, San Francisco, Los Angeles or Miami where the majority of AIDS cases to date have been reported."*

(22) Please set out your understanding and evaluation of Cutter's risk reduction practices. When answering this question you may wish to consider BAYP0000012_074 [tab 103], BAYP0000032_006 [tab 102] and BAYP0000002_183 [tab 9].

90. I refer to my response to Question 19 above.

91. In view of my responsibilities in sales and marketing, I was not involved in developing Cutter's risk reduction practices. However, it was my understanding that Cutter took the possibility of viral transmission through its blood products very seriously and aimed to be at the forefront of efforts to reduce such risks.

92. The Inquiry has suggested that, in responding to this question, I should consider document BAYP0000032_006, which is a joint statement directed towards blood banks on AIDS related to transfusion. I understand that this statement, dated 13 January 1983, was prepared by the American Association of Blood Banks, the American Red Cross, and the Council of Community Blood Centers, with assistance from the American Blood Commission, National Gay Task Force, the National Hemophilia Foundation, and representatives from the American Blood Resources Association, the Centers for Disease Control, and the Food and Drug Administration (published Transfusion March-April 1983; 23(2): 87-88). The joint statement therefore predated my arrival at Cutter UK by some 18 months. However the joint statement advised:

> *"Given the possibility that AIDS may be spread by transfusion, we are obliged to respond with measures that seem reasonable at present. The lack of a specific test means that our major effort must revolve around two areas: (1) reduction in the use of blood and blood products and (2) reasonable attempts to limit blood donation from individuals or groups that may have an unacceptably high risk of AIDS…"*

The joint statement concluded:

> "*These recommendations are made with full realisation that the cause of AIDS is unknown and that evidence for its transmission is inconclusive. We believe however, that we must respond to the possibility that a new and infectious illness has surfaced. Until more information is available, we believe that the measures outlined above are prudent and appropriate".*

93. Document BAYP0000002_183, identified by the Inquiry, is a letter from Dr Ashworth, at that time Division Vice President, Scientific Affairs, Cutter Inc to Dr Fowler at the DHSS, dated 3 June 1983 which also predated my arrival at Cutter UK. In the letter, Dr Ashworth described the lack of knowledge concerning AIDS and the efforts made to exclude plasma donations by high risk groups.

94. Document BAYP0000012_074, also identified by the Inquiry in the context of this Question, is a contract with West Midlands Regional Health Authority for supply of Koate HT. The date of the contract is unclear, however the contract refers to testing of individual donations of plasma for raised ALT levels, a process introduced in 1986 (see responses to Questions 36 and 37 below), therefore the contract must be dated in or after 1986. The contract indicates that, at that time, Cutter's system of plasmapheresis was compliant with FDA requirements and included obtaining medical history and physical examination of donors, testing of each unit of donor plasma for antibodies to HTLVIII, radioimmunoassay of each unit for hepatitis B surface antigen, testing for raised ALT levels (potential evidence of deranged liver function) and heat treatment of concentrate at 68°C for 72-77 hours.

95. As previously indicated, I have been informed that the research efforts in relation to seeking to eliminate hepatitis and HTLVIII viruses from Cutter's Factor concentrates were led by the Head of Research at Cutter Inc, Dr Milton Mozen. I did not have any interaction with Dr Mozen during my time at Cutter; however, as stated above, I attach a copy of a report he prepared at WITN6407003.

(23) Please set out your understanding of Cutter's use of pooled plasma in its factor concentrate products. The enclosed Koate HT Notice under the Exemption from Licenses from 1984 (BAYP0000003_247) (tab 15) may assist by way of reference.

96. I have no detailed knowledge of Cutter's use of pooled plasma beyond that set out in the product information for Cutter's Factor concentrates at

paragraphs 53 and 89 above. This issue is however addressed by Dr Mozen in his report at WITN6407003.

97. I have reviewed document BAYP0000003_247, referred to by the Inquiry for the purposes of this Question, which is an application for a clinical trial exemption certificate in respect of Koate HT, dated August 1984. Part II, Section 3 of this document refers to the 'active constituents' of Koate HT and states:

> *"[…]*
>
> *The source material is pooled plasma obtained from at least 1000 healthy donors. It is collected by plasmapheresis at centres in the U.S.A licensed by the FDA and inspected by both the FDA and Cutter Laboratories to ensure compliance with the Code of Federal Regulations*
>
> *[…]".*

(24) Please set out your understanding of Cutter's assessment of the link between the number of donors and the level of risk of transmission. You may wish to consider the following documents, a memo from 1986 by Marie Tatt (BAYP0000008_263 - tab 71) and this Miles Laboratories statement from 1987, (BAYP0000010_096 - tab 89).

a. Please also set out your understanding of the infection risk a single donation, when pooled, could pose to an eventual recipient.

98. I am not a scientist and, if I was aware of any link between the number of donors and the risk of transmission of infections while I was working at Cutter UK, I can no longer recall this information. My responsibilities at the company were limited to sales and marketing and did not include such matters which fall outside my knowledge and experience. The documents identified by the Inquiry do not further assist me to answer this Question.

99. However, the report of Dr Milton Mozen (WITN6407003) considers the issue of pool size and may assist the Inquiry.

(25) Please set out your understanding of Cutter's donor testing and screening policies from the years 1984 to 1990, having regard to reducing the risk of transmission of HBV, HCV and HIV.

100. I was not involved in the testing and screening of donors while working for Cutter UK and therefore my response to this Question is based on documents identified by the Inquiry or otherwise shown to me.

101. My responses to Questions 13, 17, 21 and 22 above and the documents identified by the Inquiry for the purposes of those Questions, set out my understanding of Cutter's donor testing and screening policies during the period 1984 to 1990. In addition, I refer to the report of Dr Mozen at WITN6407003.

102. I understand that specific testing for Hepatitis C antibodies was introduced in 1990, following the identification of the causative virus and the availability of the first available antibody test. However, I believe this occurred after I ceased being involved in sales and marketing of blood products.

103. While I have no knowledge of the development of Cutter's donor testing and screening policies save as set out in paragraph 51 above, these matters are summarised in the Chronology and Timeline of Events at WITN6407002.

(26) Please outline your understanding of Cutter's use of Prison Plasma. You may wish to consider the following documents; Minutes of Biological Coordinating Committee meetings from November 1983 and 1985 (See: BAYP0004952 - tab 12, and BAYP0005729 - tab 33), and a note from the fractionators meeting in 1985, (CGRA0000545 - tab 36).

104. I have no knowledge of Cutter's use of prison plasma and cannot comment on the documents identified by the Inquiry.

Section 4: Communication and notification of risk

HIV

(27) Please describe your understanding and evaluation of Cutter's notification policies, including its response to discovering that a donor had tested positive to HIV. You may wish to consider the following documents regarding voluntary recall of material due to a plasma donation by an individual who was subsequently diagnosed with AIDS in late 1983, BAYP0004889_001 (tab 10), BAYP0004916 (tab 11) and BAYP0000009_007 (tab 80).

105. I am not a scientist and, in view of my role in sales and marketing, I had no involvement in decision-making in relation to notification policies and recalls. However during the period of time I was with Cutter UK we did institute recalls of products on several occasions, where particular batches were associated with hepatitis B infection. I do not remember any recalls of product associated with AIDS transmission while I was working at Cutter UK. The arrangements for recall are described in my responses to Question 30 and Question 32 below.

106. Documents BAYP0004889_001 and BAYP0004916, identified by the Inquiry, are internal memos of Cutter Inc dated 1983, approximately a year before I joined Cutter UK. I have no contemporaneous knowledge of the events referred to in these memos. However, the two documents indicate that, having been notified that a donor of plasma had subsequently been diagnosed with AIDS after his last donation, Cutter Inc voluntarily recalled one lot of Konyne and 15 lots of Koate, which contained plasma donated by the particular donor between November 1982 and September 1983, from 304 consignees in the US and 14 international consignees. None of these lots had been shipped to the UK and no product was therefore recalled from the UK. The lots were recalled as a precautionary measure as there was no evidence that the products were infected with the AIDS agent or transmitted the disease. At the time of the recall, no adverse reactions involving the relevant lots had been reported.

107. Document BAYP0000009_007 is a scientific paper comparing recipients of eight lots of Factor concentrates voluntarily withdrawn because one donor was known to have subsequently developed AIDS with a non-exposed cohort (Jason J et al. Effects of Exposure to Factor Concentrates Containing Donations from Identified AIDS Patients, A Matched Cohort Study. JAMA 3 October 1986). While the paper does not make this clear, the withdrawn lots appear to have been non-heat treated Factor concentrates. The study found that individuals exposed to the withdrawn lots of Factor concentrate showed no clinically important immunological or HIV serologic differences from the comparison group. The authors concluded that market withdrawals were an insufficient means of limiting the spread of AIDS in the haemophiliac population and that, since either wet or dry heat treatment appeared to be effective in inactivating HIV and related viruses, only viral-inactivated Factor products should be used in therapy for haemophiliacs. At the time of publication of this paper, all Factor concentrates supplied by Cutter UK were heat-treated.

(28) Please describe your understanding and evaluation of Cutter's response to the seroconversion of a patient treated with either:

Koate (See: BAYP0005496 - tab 20); and

Koate HT (You may wish to consider the following documents: BAYP0000010_087 (tab 91), BAYP0005985 (tab 93) and BAYP0000010_067 (tab 88) (regarding seroconversions in Italy)).

108. As previously explained, in view of my role in sales and marketing, I was not involved in Cutter's assessment of adverse events or the company's response to these. It is however my understanding that any report of seroconversion following use of Cutter's Factor concentrates would be carefully investigated, including in the context of any other reports associated with the same lot(s) of product.

109. Document BAYP0005496 identified by the Inquiry, is an internal memo dated 29 November 1984 from Eli Greene, Cutter Inc, to various senior colleagues at Cutter Inc and Brian Dyos at Cutter UK. This document was

also identified by the Inquiry in relation to Question 18 above and I repeat the response I provided, in particular at paragraphs 73 -75.

110. Documents BAYP0000010_067 and BAYP0005985, identified by the Inquiry, refer to reports of HTLVIII seroconversion in Italy in patients treated with Koate HT.

a. Document BAYP0000010_067 is a UK key indicator report, dated 24 March 1987, which included the statement "*Currently rumours are circulating about the late seroconversions in Italy, we are waiting for the US marketing statement before expressing any views to our users on the subject*".

b. Document BAYP0005985 is a report of the International Congress on Thrombosis and Haemostasis, held in Brussels in July 1987, which referred to the cases of HIV seroconversion in the three Italian patients treated with heat treated concentrates, mentioned in (a) above. The report indicated that each of these three patients had received treatment with products manufactured by two of three fractionators (one of which was Cutter).

111. I do not now recall these cases of seroconversions in Italy and was not involved in any investigation of the reports. However I have been shown the following additional documents in relation to this matter:

a. A report by Professor Mariani et al, on the '*HIV seroconversion in three hemophiliacs after heated clotting factor*' (BAYP0000010_060), which gave details of the patients' conditions and the heat-treated products they received. The report referred to different Factor concentrates by reference to the heat treatment process used, rather than by name and suggested that a relatively low temperature for a short time period (60°C for 30 hours) might be insufficient to inactivate HIV. This reference did not refer to Cutter's heat-treated Factor VIII concentrate which was, as previously indicated, heated at 68°C for 72 hours. The report concluded:

"[…]

These cases show that seroconversion developed after heated concentrates other than that associated with the two previously reported seroconversions. We could not ascertain which concentrate was involved in seroconversions, because each patient was treated with more than one concentrate heated with more than one method. Even though the latency period between exposure to HIV and seroconversion is not well established in hemophiliacs, one study suggests that such period might be of 6-7 months or less. Since seroconversions were detected 13 to 31 months after the last dose of unheated concentrate, inadequate heat inactivation of HIV is the most likely explanation for them. We cannot exclude though that they might be due to the HIV contained in unheated concentrates given prior to exclusive usage of heated concentrates.

[…]".

b. An internal Miles memo dated 6 February 1987, from M.M Sternberg to Dr Risse (BAYP0005899_001) which indicated that Jack Wood, Dr Rousell and Dr Mozen visited Italy for a thorough review of the reported cases. Dr Levy, a leading researcher provided advice to the company and "*categorically stated that the process developed at Cutter has been shown beyond doubt to inactivate HIV with large margin of over kill*". The results of the investigation in Italy were:

> *"Two of the cases were hemophilia B individuals who received small amounts of Konyne HT interspersed with large doses of Bebulin from Immuno. In both cases there is no way Konyne could be unequivocally implicated, although there seems no doubt that seroconversion to HIV did occur, in spite of the patients receiving heat treated preparations.*

The third patient suffers from hemophilia A and had received only heat treated products since January 1984, namely Behring HS product in 1984 and Koate HT since. He tested positive by ELISA and was confirmed by Western Blot".

c. A Miles interoffice communication dated 8 May 1987, from C. Moore to various Miles personnel in the US (BAYP0000010_111). The content related to a call with Dr Dale Lawrence from the US Centers for Disease Control, in which he mentions the possible seroconversion associated with Miles' products in Italy. C. Moore reported:

"I discussed the Italian situation as we know it and stressed that there was nothing concrete linking our product to the seroconversion. After discussing the cases with him, (he was already aware of most of the details) he agreed that seroconversions would not be linked to our product and was of no concern for the CDC.

[…]"

d. An internal memo dated 31 July 1987, from Dr Rousell to Eli Greene relating to 'UK-DHSS Enquiry about Professor Mariani's patients' (WITN6407008). This confirmed that it had not been possible for the clinicians or the affected patients to supply information about which lots of Factor concentrates the patients had received, but noted that the patients had previously received non-heat treated products and that "*To date seroconversion has never occurred in any patient who has received only heat treated concentrates.*"

112. While therefore, I had no involvement in the investigation of the reports from Italy, it is clear from the documents that Cutter Inc took these cases very seriously and did what they could to investigate these matters.

113. Document BAYP0000010_087, identified by the Inquiry, is an internal Cutter memo dated 22 April 1987 from me to Marie Tatt, notifying her of a report received from Dr Mitchell, Leicester Haemophilia Centre relating to

a case of hepatitis B seroconversion in a haemophilia patient treated with Koate HT as well as other blood products. This notification to regulatory affairs reflected Cutter procedure for handling such reports as described in the response to Question 34 below. I was not involved in the subsequent investigation of the report from Leicester, although a hand written note on the memo indicates that there was a delay in progressing it as a result of staff absence and the Easter holiday.

(29) Please describe your understanding and evaluation of Cutter's use of existing inventory whilst a new heat treatment method was formulated. (See: BAYP0000024_114 (tab 31), CGRA0000581 (tab 37) and BAYP0000008_330 (tab 76) which relate to correspondence regarding the conversion to heat treated product in the UK and supply of non-heat treated material in 1985 and 1986.)

114. Prior to grant of a product licence for Koate HT in February 1985, only non-heat treated Koate could be actively marketed in the UK. However, from the end of November 1984, Koate HT was supplied to some centres on a named patient basis in response to unsolicited requests from clinicians.

115. Document BAYP0000024_114, identified by the Inquiry, is a report of a trip by Jack Wood to the UK, dated 13 March 1985. The report confirmed that Koate HT had been "approved for sale" in the UK (which I understand to refer to the grant of a product licence), with the result that the product no longer needed to be distributed on a named patient basis. I refer to my response to Question 46 below which sets out further details about the approval of Koate HT in the UK: see paragraphs 187-189. The report indicated that, due to the limited availability of Koate HT and high demand in the UK, Cutter decided, in the short term, to offer stock proactively only to those customers who were already using Koate HT (presumably on a named-patient basis) but not to seek to expand its customer base. The approach suggested in the report is consistent with my recollection which is that Cutter was concerned to manage its stock situation and to assist clinicians to maintain continuity in the use of the same products for the

treatment of individual patients. The report also referred to reallocation of non-heat treated product to markets outside the UK which were not, at that time, fully converted to heat treated products. I had no involvement in those decisions.

116. Document CGRA0000581, identified by the Inquiry, is an internal Cutter Inc memo dated 15 April 1985 from Jack Wood to Gary Mull regarding 'Koate Returns from United Kingdom'. The memo confirmed that, in early 1985, non-heated treated Koate previously shipped to the UK was returned to the company. I was not involved in the arrangements for return of UK stock and have no knowledge of the matters discussed in the memo.

117. Document BAYP0000007_026, identified by the Inquiry, is an internal memo dated 12 June 1985 from Walid Marzouk to me, which indicated that the difficulties with supply of Koate HT during early 1985 improved towards the middle of the year:

> *"During May, Koate HT supplies from the US have improved. It is expected that improvements in supplies will continue until we are able to fully supply our clients. However, we will still be unable to reserve batches and obtain new business."*

118. Document BAYP0000008_330, identified by the Inquiry, is a letter dated 1 August 1986 from me to Dr Rizza at the Oxford Haemophilia Centre, regarding the products used in Oxford since the introduction of Koate HT. The letter confirmed that only heat treated product had been supplied since December 1984 (prior to February 1985 this had been supplied on a named patient basis). From May 1985, the lots of Koate HT supplied to Oxford had been partially screened for HTLV III antibodies and from March 1986, the Oxford Haemophilia Centre had been supplied with 100% HTLV III donor screened Koate HT.

Batch 50P069

(30) Please consider the following documents:

a. ***On 11 June 1986, Marie Tatt wrote to K Fernandez (Cutter USA) setting out information about three haemophiliacs who had developed hepatitis B who had all been using Koate HT (See: BAYP0000008_219 and BAYP0000008_207). Earlier, Professor Temperley advised Cutter on 6 June 1986 that he "thought it was likely that the batch of Koate HT was contaminated with hepatitis B virus and issued instructions for removal from circulation." The Cutter agent confirmed that remaining vials were recalled and quarantined. "This batch was distributed to a number of centres in the UK." (See: BAYP0000004_374 and BAYP0000008_234).***
b. ***On 16 July 1986, Marie Tatt wrote to the National Drugs Advisory Board ("NDAB"), Dublin about reports of hepatitis B in patients who had received Koate HT, batch 50P069.***
c. ***In the second half of 1986, Brian Dyos wrote to Willi Ewald outlining the actions taken in the UK in relation to Lot 50P069, (See: BAYP0000009_090)***
d. ***On 8 January 1987, Marie Tatt advised the DHSS that following the possible infection in Eire and further investigation Cutter USA decided to initiate a recall in December 1986, (See: BAYP0000004_406)***

Considering the six documents referenced above, and any other documents or information available to you, please set out the steps taken by Cutter in the UK, if any, to reduce the risk batch 50P069 posed, prior to the notification of possible transmission in the Republic of Ireland before the reports were received from Professor Temperley in June 1986.

119. My response to Question 13 at paragraphs 50-52 refers to Cutter's efforts to reduce the risk of transmission of hepatitis and is therefore repeated. Throughout the period I worked at Cutter UK, the product information for the company's Factor concentrates indicated that each lot had been tested and found non-reactive for Hepatitis B Surface Antigen (HBsAg) (see paragraph 53 above). However I understand that, due to limitations in the tests available, these results did not wholly exclude the possibility that Hepatitis B was present and did not test for NANB hepatitis. The product

information for Cutter's Factor concentrates therefore warned healthcare professionals that the presence of hepatitis viruses should be assumed.

120. Specifically in relation to Koate HT lot 50P069, I have been shown an NIBSC batch release certificate dated 2 October 1985, (WITN6407009) and have considered this together with document BAYP0000004_374, identified by the Inquiry, which is a letter from Miles to the Irish National Drugs Advisory Board dated 16 July 1986. These documents indicate that lot 50P069 underwent examination by NIBSC and was approved for sale or supply, after which it was distributed to a number of Haemophilia Centres in the UK and Ireland between October 1985 and March 1986. This lot was not sold in any other country.

121. I have also been shown a letter from Miles to DHSS dated 23 December 1986, following an investigation by Cutter Inc into the cases reported in Ireland (BAYP000004_401). The letter confirms that all UK Centres which had been supplied with lot 50P069 had been informed of the reports; however, in all instances the product had already been used for patient treatment, with no adverse effect. Cutter Inc's investigation showed that:

> *"1. The routine release test for Hepatitis B Surface Antigen (Radioimmunoassay) was repeated on retained samples of batch 50P069 and all results were negative. The tests were carried out in Cutter's QA laboratories in both Berkeley and Clayton.*
>
> *2. In compliance with regulations, all units of plasma used in production of Koate HT are routinely tested for Hepatitis B Surface Antigen and any unit found to be positive is destroyed.*
>
> *In order to further assure that none of Cutter's plasma-derived products are contaminated with HBsAg, the company has now initiated testing of plasma pools.*
>
> *During the validation of this procedure, retained samples from 90 pools were tested for HBsAg and one was found to be positive.*
>
> *The positive pool was used in the production of Koate HT batch 50P069."*

122. Document BAYP0000009_090, identified by the Inquiry, is a memo dated 15 December 1986 from Brian Dyos to Willi Ewald, which confirms the action taken by Cutter UK following receipt of the reports from Ireland. This memo indicates that all Centres in the UK which had received lot 50P069 had been identified and that I had notified all of them of the Irish cases, but that in all instances, the product had already been used with no adverse incident.

123. Document BAYP0000004_406, identified by the Inquiry, is a letter from Marie Tatt to Mr J Ayling at the DHSS, referring to the cases in Ireland reported by Dr Temperley and indicating that, after further investigation (which seemingly included testing of samples from the plasma pool used to prepare lot 50P069), Cutter Inc had decided to initiate a recall. Marie Tatt advised DHSS that no additional lots of product of any type, prepared from the pool which tested positive, had been shipped to the UK.

(31) Please consider the following documents:

(a) Correspondence and internal Cutter memoranda concerning the HBV infection of a child who used the Konyne product in 1986:

- ***i. Letter from G.M. Akin (Director of Medical Services at Cutter to Dr Mitchell, 28 February 1986 (See: BAYP0000008_102 [tab 51]);***
- ***ii. Internal Cutter memorandum, 15 April 1986 (See: CGRA0000602) [tab 59];***
- ***iii. Internal Cutter memorandum, 23 April 1986 (See: BAYP0000008_165 [tab 60]);***
- ***iv. Internal Cutter memorandum, 2 May 1986 (See: BAYP0000008_179 [tab 61]);***
- ***v. Internal Cutter memorandum, 16 May 1986 (See: BAYP0000008_189 [tab 64]);***
- ***vi. Internal Cutter memorandum, 4 July 1986 (See: BAYP0000008_259[tab 70);***

vii. Internal Cutter memorandum, 10 July 1986 (See: BAYP0000008_284[tab 72]);

viii. Letter from Marie Tatt, Regulatory Affairs Manager at Cutter to Dr Mitchell, 11 July 1986 (See: BAYP00000008_288[tab 73]) and

ix. Internal Cutter memorandum, 12 August 1986 (See: BAYP0000008_338[tab 77]).

(b) Correspondence and internal Cutter memoranda concerning the HBV infection of an adult patient who received multiple infusions of Koate HT during surgery:

i. Medical Incident Report (See: BAYP0000010_028 [tab 105], pp. 23)

ii. Letter, Dr Mitchell to you, 3 April 1987 (See: BAYP0000010_071 [tab 90]); and

iii. Letter, G M Akin (Associate Director, Miles Pharmaceuticals) to Dr Mitchell, 14 May 1987 (See: BAYP0000010_105 [tab 92].

iv. A letter co-authored by Dr Mitchell on these cases in the British Journal of Haematology (BJH), 1988, 69, 421-428 at 421 (See: IPSN0000156_089 [tab 94]).

Dr Mitchell gave the following evidence to the Inquiry in 2020; "I concluded that from this evidence (documents produced in Rule 9 to Dr Mitchell) that Hep B had been transmitted by these heat treated concentrates. Although Cutter did not accept this, they did not challenge our letter to the BJH." (See: WITN3174003 (tab 101))

Considering the documents and evidence listed above, what was your understanding of the difference of opinion that Cutter had with Dr. Mitchell as to the source of the HBV infection? Drawing on your personal knowledge and experience, in your view, why did Cutter not accept Dr. Mitchell's conclusion as to the source of HBV infection and challenge the letter to the BJH ? What, if any, mechanisms were there for resolving such disputes?

(a) HBV infection of a child who used the Konyne product in 1986

124. All adverse incidents were taken very seriously by Cutter, which were investigated by the regulatory team in the UK and considered with relevant personnel in the US. In my role in sales and marketing, I did not have direct responsibility for investigating adverse incidents. However, I was careful to report all suspected adverse incidents received from customers and to forward all such reports received from customers or from any other source to the regulatory team to be properly evaluated and reported.

125. Document BAYP0000008_102, identified by the Inquiry, is a letter dated 28 February 1986 from Dr Akin, Director of Medical Services at Cutter Inc, to Dr Mitchell, at the Royal Infirmary in Leicester and referring to a report of hepatitis in a patient who had received treatment with Konyne HT. Dr Akin requested information regarding the blood and plasma products received by this particular patient during the previous six months and details of the laboratory tests which had been performed.

126. Document CGRA0000602, identified by the Inquiry, is a report of a trip by Dr Roussell of Cutter Inc to Europe in March 1986, copied to a number of other Cutter personnel, which referred to possible transmission of Hepatitis B in a patient of Dr Mitchell's:

> *"Cutter UK also reported on the possible transmission of hepatitis B in patients receiving Konyne lot 20N028.*
> *Apparently six hemophilia B patients were treated by Dr. Mitchell at the Leicester Royal Infirmary. Three of these patients were immune to hepatitis B, as evidenced by having HBsAG levels prior to the Konyne-HT therapy. The other three were in fact negative. Of the negative patients, one child has now developed clinical hepatitis B.*
> *This child had been tested in June and August, 1985, and was HBsAG negative.*
> *Tested again in February, 1986, this child was confirmed to be HBsAG positive. Of the other two children, one has been transferred to Sheffield. This case will be followed up. The test results for*

hepatitis B surface antigen were not yet available in the third case. We will be informed of their follow up.

[…]"

127. Document BAYP0000008_165, identified by the Inquiry, is an internal memo from me to Marie Tatt dated 23 April 1986 in relation to the case reported by Dr Mitchell. I do not recall writing this memo, which indicates that the patient switched from NHS Factor IX to Konyne HT on 28 March 1985, HBsAg tests were negative up to October 1985, but were positive when tested in February 1986. The memo also notes that seven boys had been treated with the particular lot of Konyne HT in Leicester; of these three had previously been found to have antibodies to Hepatitis B and four had been negative. Of the four boys who had previously not had antibodies to Hepatitis B, the reported case was the only one to have seroconverted and test results were awaited in relation to a second, although the boy seemingly showed no signs of illness.

128. Document BAYP0000008_179, identified by the Inquiry, is an internal memo from Marie Tatt to Karen Fernandez of Cutter Inc dated 2 May 1986 which attached completed medical incident forms for the case reported by Dr Mitchell.

129. Document BAYP0000008_189, identified by the Inquiry, is an internal memo from me to Brian Dyos dated 16 May 1986 providing a 'situation report' on Koate-HT. I regularly reported to Brian Dyos on inventory and this letter sets out information about purchases of Koate HT by various Haemophilia Centres. I also reported on my visits to Haemophilia Centres and, under the heading 'Leicester' on the second page, I indicated:

"[…]

The follow-up on the Konyne HT reported to have transmitted hepatitis B was made. Only one boy out of seven was implicated. Three of the boys already had antibodies to hepatitis B surface antigen. Of the four, three were known not to have seroconverted and the fourth did not yet have the test results available, although he

was clinically well. All necessary forms had been completed and passed to Marie Tatt".

These figures, which suggest no seroconversions, seem inconsistent with those in the document I have referred to at paragraph 127 above.

130. Document BAYP0000008_259, identified by the Inquiry, is an internal memo from Anne Walton to me dated 4 July 1986. It confirms, amongst other matters, that Dr Mitchell had *"requested information on the follow up carried out on the batch of Konyne-HT which was reported to have caused HBsAG positivity in one of his patients".* I have been shown a further letter which was then sent from Marie Tatt to Dr Mitchell on 11 July 1986 (BAYP00000008_288) which apologised for the delay in responding to his request for information in relation to the lot of Konyne HT which was reported to have been associated with hepatitis in one of his patients.

131. Document BAYP0000008_284, identified by the Inquiry, is an internal Cutter memo from Karen Fernandez in the US to Marie Tatt dated 10 July 1986. This referred to Dr Akin's previous request to Dr Mitchell for information about the incident and the fact that Dr Akin had seemingly not received a response. The memo also described Cutter's investigation of the report by Dr Mitchell, noted that there had been no other reports of hepatitis related to this lot of Konyne HT and that the lot had passed all tests for HBsAg prior to supply. Furthermore, the memo stated: "*It is to be noted that the patient also received national product prior to, and around the same time, of administration of Konyne-HT*", indicating Dr Akin's view that the patient could have contracted hepatitis through NHS Factor IX.

132. Document BAYP0000008_338, identified by the Inquiry, is an internal memo dated 12 August 1986 from Marie Tatt, which provided the following observations in relation to the incident:

"2. Konyne HT: Leicester Incident

Apparently Dr. Mitchell was satisfied with the information provided as he has not raised the subject again. I will let you know if there are

any further developments but we are not actively following up this case at the moment."

(b) HBV infection of an adult patient who received multiple infusions of Koate HT during surgery

133. Document BAYP0000010_28, identified by the Inquiry, is a medical incident report relating to a report from Dr Mitchell regarding a patient with mild haemophilia who had become HBsAg positive following multiple infusions of Koate HT lot 50R004 pre and post coronary artery bypass graft surgery. The patient had also received two units of whole blood and 6 units of platelets during surgery . The patient had been vaccinated on 14 August and 19 September 1986, prior to surgery on 8 October. He was HBsAg negative on 25 September and 7 October 1986, but HBsAg positive on 19 February 1987.

134. Document BAYP0000010_071, identified by the Inquiry, is a letter from Dr Mitchell to me dated 3 April 1987, in relation to the incident described at paragraph 132 above.

135. Document BAYP0000010_105, identified by the Inquiry, is a letter from Dr Akin to Dr Mitchell dated 14 May 1987, summarising the investigation of the report relating to the man who had received multiple infusions of Koate HT in the context of cardiac surgery, confirming that Miles had not received any other reports of hepatitis in relation to lot 50R004 and that a review of all manufacturing records and quality assurance evaluations for the lot had been normal. The letter stated that each unit of plasma which had gone into the relevant production batch had been HBsAg negative, and radio immuno assay (RIA) testing of the lot itself had also been HBsAg negative. In view of the laboratory studies, together with the lack of other hepatitis reports relating to this lot, Dr Akin stated that Miles did not believe that Koate HT was the probable source of the hepatitis B infection reported by Dr Mitchell.

British Journal of Haematology report

136. Document IPSN0000156_089, identified by the Inquiry, is a report in the British Journal of Haematology, in which Dr Mitchell disagreed with the analysis undertaken by Cutter on the probable source of the hepatitis B in both the patients described above. Dr Mitchell's evidence to the Inquiry refers to this report, and to the fact that Cutter had not challenged this. As previously indicated, while I was aware of the reports by Dr Mitchell, I was not involved in the investigation of these cases. I do not know why Cutter did not respond to this article. However, it may have been the case that Cutter did not consider this an appropriate forum in which to discuss such matters.

137. I do not know whether any specific procedures were in place to resolve differences in opinions between Cutter and clinicians regarding the cause of suspected adverse drug reactions. This would not have fallen within my area of responsibility, however I would have expected that, if Dr Mitchell had not been satisfied by the response from Cutter, he would have notified Cutter accordingly.

Lot 50S021

32. Please consider the following documents:

a. ***On 13 February 1988, you wrote to Marie Tatt enclosing a Medical Incident Report relating to the possible transmission of hepatitis B from Lot 50S021 at Derriford Hospital, Plymouth. (See:BAYP0000011_020 [tab 95]).***
b. ***On 12 April 1988, you wrote to Marie Tatt advising of further reports from Liverpool Royal Infirmary and Bradford Royal Infirmary of possible hepatitis B infections "possibly due to this lot of Koate HT."; (See: BAYP0000011_056[tab 96]).***
c. ***On 13 April 1988, you wrote to Marie Tatt confirming "every customer who used Lot 50S021 was contacted and told of the possible Hepatitis B transmission and asked to return any***

product that had not been used." (See: BAYP0000011_058[tab 97])

Considering the three documents referenced above, and any other documents or information available to you, please set out the steps taken by Cutter in the UK, if any, to reduce the risk this Lot posed, prior to the notification of possible transmission at Derriford Hospital in February 1988

138. In my role in sales and marketing at Cutter UK, I did not have direct responsibility for risk reduction strategies or procedures. However, when I did receive notice of an adverse incident or received such a report from a customer, I would ensure this was forwarded to the regulatory team at Cutter UK, who were responsible for investigation and reporting of suspected adverse drug reactions. I was often in contact with customers about products due to the nature of my role, and assisted the regulatory team in terms of contact with Haemophilia Centres. In relation to steps taken by Cutter prior to the notification from Derriford Hospital, my response to Question 30 is repeated, particularly paragraph 119 above.

139. Document BAYP0000011_020, identified by the Inquiry, is an internal memo from me to Marie Tatt dated 18 February 1988, relating to an incident concerning the possible transmission of Hepatitis B to patients in Plymouth who had been treated with Koate HT, lot 50S021.

140. Document BAYP0000011_056, identified by the Inquiry, is a further internal memo from me to Marie Tatt dated 12 April 1988, referring to further incidents of possible transmission of Hepatitis B in Liverpool and Bradford associated with the same lot of Koate HT.

141. Document BAYP0000011_058, identified by the Inquiry, is a third internal memo from me to Marie Tatt, dated 13 April 1988. This memo indicated that "*every customer who used lot 50S021 was contacted and told of the possible hepatitis B transmission and asked to return any product that had not been used*". The various hospitals had been notified on 21 March 1988 and returned product from lot 50S021 had been replaced with Koate HT from a different lot. I believe that this document demonstrates that, in

instances where Cutter concluded, following investigation, that a particular lot of Koate HT was likely to have transmitted hepatitis B, the company acted appropriately to recall the affected lot.

142. I have been shown correspondence dated 24 May 1988 between Bayer and DHSS and NIBSC (BAYP0000005_056), confirming that the incidents of Hepatitis B described above, had been reported to the Committee on Safety of Medicines (CSM) in accordance with the yellow card system and that both DHSS and NIBSC had been notified of the recall.

143. While I was clearly aware of the reports concerning lot 50S021 at the time and was involved in the notification of hospitals who had received that lot, at this stage, some 30 years later, I have no recollection of the incident.

(33) To the best of your knowledge, please set out your understanding of Cutter's actions to reduce the risk of HBV during the period of 1986 to 1988, being the period Cutter was notified of contamination of Batch 50P069 and Lot 50S02.

144. As previously explained, my role at Cutter UK was in sales and marketing and I did not have responsibility for risk reduction strategies or procedures. However my responses to Questions 13, 22, 25, 31 and 32 above are relevant to this Question 33 and are repeated.

145. The documents confirm that the affected lots were recalled (see paragraphs 123 and 141 above).

146. Document BAY0000004_406, identified by the Inquiry in relation to Question 30, is a letter dated 8 January 1987 from Marie Tatt to DHSS relating to lot 50P069 and indicating that Cutter Inc quality assurance had confirmed that no additional batches of product, of any type, prepared from the pool of plasma which tested positive had been shipped to the UK.

147. I have been shown a letter from Ms Tatt to the DHSS dated 23 December 1986 (BAYP0000004_401), relating to the recall of lot 50P069. Ms Tatt confirms, in relation to testing, that:

"In compliance with regulations, all units of plasma used in production of Koate HT are routinely tested for Hepatitis B Surface Antigen and any unit found to be positive is destroyed.

In order to further assure that none of Cutter's plasma-derived products are contaminated with HBsAg, the company has now initiated testing of plasma pools."

Adverse Reaction Reports

(34) Please set out your understanding of Cutter's policies regarding adverse reaction reports that were filed in relation to Cutter's products in the 1980's. You may wish to consider the following documents when addressing this question: BAYP0000007_053 (tab 40), BAYP0000007_082 ((tab 41), and BAYP0000010_015 (tab 87).

148. As previously explained, my role at Cutter UK was in sales and marketing and I was not involved in reporting suspected adverse reaction reports to the regulatory authorities; paragraphs 124 and 138 above are repeated.

149. If I was notified by a clinician or by a Cutter UK sales representative of any adverse incident associated with a Cutter products, I would request further details and clarification of the reaction if necessary, as demonstrated by document BAYP0000010_015, identified by the Inquiry, which is a letter from Dr Macheta of the Manchester Children's Hospital to me providing further information in relation to two haemophilia patients found to be positive for HBsAG. I would pass all the information I received on to the regulatory team, who were responsible for investigating the report, including communicating with the relevant US personnel at Cutter Inc in relation to the incident and reporting to the regulatory authorities, as necessary.

150. Document BAYP0000007_053, identified by the Inquiry, is an internal memo dated 22 July 1985 from Walid Marzouk, a sales representative who reported to me, providing details of a suspected adverse reaction

associated with Koate HT lot 50P025 to Dr Elliott. Document BAYP0000007_082, identified by the Inquiry, is a key indicator report from Brian Dyos and myself dated 21 August 1985 which refers to the reports concerning lot 50P025 and describes the investigation by Dr Elliott and the advice he had provided. The document refers to *"routine reporting procedures"* which, in this instance, had been handled by Dr Elliott. This particular incident does not appear to have been related to infection but a "*possible PKA and/or glycine problem*".

151. In addition, document BAYP0000010_087, identified by the Inquiry in relation to Question 28, provides an example of my role in passing reports of suspected adverse drug reactions to regulatory affairs (Marie Tatt) and advising "*The Customer Services report will be completed as soon as possible and the additional information you require to complete the medical incident report*". See paragraph 113 above. I recall that the procedure for handling reports of suspected adverse drug reactions involved the completion of a Customer Services Report (CSR), which would be used by regulatory affairs to complete a medical incident form. I have been shown an example of a CSR and the corresponding Medical Incident Form from April 1987 (BAYP0000010_097 and BAYP0000010_099). The Customer Service "Desk" Procedure (BAYP0004912_005) confirmed that the CSR Form should be completed by Sales and forwarded to the Customer Service Department (CSD). The procedure is described as follows:

"

1. *If a serious report alleging human reaction, mislabeling, or microbial contamination, the following groups are immediately notified by phone: QA, Technology, Marketing, plant of manufacture, and Director of Medical Services and/or Director of Clinical Operations for human reactions. (NOTE: Sales has been specifically instructed to phone in any serious reports as soon as they become aware of them.)*

2. *Report is logged and entered into customer and product code reference files.*
3. *Copies of CSR sent to QA, Technology, Marketing, plant of manufacture, Regulatory Affairs, and medical representative (human reactions only.)*
4. *If requested by Sales, a standard letter acknowledging receipt of the CSR is sent to the customer."*

152. In relation to samples, the document confirmed that, if none were available from the customer, then the CSD would *"attempt to purchase product from Cutter inventory from the same lot(s) as the complaint material*".

153. Furthermore, the document set out that:

> *"If requested by Sales, the Customer Service Department drafts a final response letter based upon the specific CSR investigation and the previous complaint history of the product, component, and/or lot. (Exception: all patient reactions handled by the medical investigator.)"*

154. I have also been shown a letter from Marie Tatt to Mike O'Donnell at Accu-Science dated 8 July 1986 (BAYP0000008_265). Marie Tatt stated:

> *"The Medical Incident Report form is for Cutter's internal use. It is company procedure that I complete this form and send it to Cutter Regulatory Affairs in the U.S.A. whenever any problem with a product is reported by a customer in the U.K. or Ireland.*
> *The form is designed to enable Cutter to monitor for problem trends and investigate any product complaints as required by U.S. law. This should not be sent to any regulatory authority…"*

Product Labelling

(35) Please set out your understanding of Cutter's policies in relation to product labelling, specifically the addition, removal and/ or amendment of warning statements throughout the 1980's. You may wish to consider the

following internal memorandums from 1985 and 1986 when considering this question: BAYP0000007_126, (tab 42) BAYP0003604 (tab 48) and BAYP0000015_060. (tab 78)

155. My response to Question 14 above is repeated. Product labelling, including the inclusion of warning statements, was dealt with by regulatory affairs in Cutter and was not a matter within my responsibility. It is clear from the following documents that Cutter Inc was substantially involved in the contents of the labels used for UK products. If Marie Tatt in the UK wished to make any amendments to the labels forwarded by Cutter Inc, these changes would be discussed with colleagues in the US. These arrangements are evidenced by the following documents, identified by the Inquiry:

156. Document BAYP0000015_060 is a memo dated 15 September 1986, from Marie Tatt to Eli Greene at Cutter Inc, asking: "*Could the "WARNINGS" statement be amended for the UK? We would like to delete the reference to the Fletcher paper and potential transmission of Non-A, Non-B hepatitis*".

157. Document BAYP0003604 is an internal memo dated 20 February 1986, in which I asked Marie Tatt if certain changes could be made to the draft label for Gamimune-N for the UK. It is apparent that the draft label was that used for the US market, and I asked, among other things, whether it would be possible for statements not relevant to the UK market, such as "*Caution: US federal law prohibits…*" to be removed from the label.

158. Document BAYP0000007_126 is a telex dated 23 October 1985 from me to Gary Mull stating that Cutter UK would like the statement on HTLVIII Anti-body testing of plasma to appear on all future product imported into the UK. I ask "*would stickers be available for existing stock which has been tested*?".

Section 5: Cutter's efforts to reduce the risk of infected blood products

Alanine Aminotransferase Testing ("'ALT Testing")

(36) Please set out your understanding of Cutter's policies regarding ALT testing as a measure to reduce the risk of HCV. You may wish to consider the following letter from 1986 when addressing this question: BAYP0000008_077 [tab 46].

159. Cutter's polices regarding ALT testing would principally have been a matter for the scientific and medical teams and regulatory affairs at Cutter. I may have had some knowledge of such matters at the relevant time, but I cannot now remember these matters.

160. Document BAYP0000009_030, identified by the Inquiry in relation to Questions 14 and 21, is a letter I sent to Dr Prentice and other clinicians relating to Koate HT, dated 21 October 1986. This letter set out the following information in relation to ALT testing:

> *"Cutter Laboratories is also screening individual donors for alanine transaminase (ALT) levels. Any donation with ALT levels greater than twice the normal level is not used for production of Koate HT. By the end of this year, all batches of Koate HT will have been prepared from plasma screened for ALT levels in addition to HTLVIII antibodies and hepatitis B surface antigen…"*..

161. I have been shown an application dated 10 August 1987 (WITN6407010) to vary the product licence for Koate-HT to revise the wording of the package insert in relation to source plasma:

> *"Source plasma is collected according to the Cutter System of Plasmapheresis which incorporates all the FDA requirements for Source Plasma including testing of samples from all donors for antibodies to ~~HTLVIII~~ HIV.*
>
> *In addition Cutter test each donation for ALT levels. Only units found to have an ALT level less than twice the upper limit of normal for the test are used in the manufacture of Koate HT."* (revisions underlined)

162. I have also been shown the approval document (WITN6407011) which indicates that the variation was not approved by DHSS until eighteen months later on 27 February 1989.

163. Document BAYP0000008_077, identified by the Inquiry in relation to this Question, is a letter from me to Dr Bevan at St George's Hospital, dated 31 January 1986. However it does not refer to ALT testing.

(37) In a telex transmission from Karen Fernandez to Marie Tatt dated 29 September 1986 (See: BAYP0000008_373 - tab 79), it is noted that in "August of this year (1986) marked the date for 100% ALT screen incoming plasma from Cutter owned and contracted centers. However, because of existing inventories of non-screened plasma there will be a phase in period." A subsequent document records that ALT screened Koate HT will not be received until December 1986 (See: BAYP0000009_023 - tab 82). Please set out your understanding of why ALT screened Koate HT was not received in the UK earlier and whether this was communicated to clinicians/haemophilia centre directors.

164. I do not, at this stage, recall any discussions relating to this issue.

165. Document BAYP0000008_373, identified by the Inquiry, is a telex dated 29 September 1986 from Karen Fernandez to Marie Tatt, which includes the excerpt mentioned above. As with any manufacturing process it took a little time to produce a sufficient quantity of ALT screened Koate HT after such screening was introduced to meet global demand. The telex dated 29 September 1986 also included the following section:

> *"The next lot of Koate HT for the UK will be available late November - early December. According to Gary* [Mull]*, this lot will mark the beginning of a continuous supply of 100% ALT screened Koate HT for the UK".*

The telex additionally states "*This early availability of screened product is possible only due to segregation of the plasma and hand selection of the units going into the plasma pool*". I am not sure what this is referring to,

although it suggests that Cutter sought to supply concentrates prepared from ALT screened plasma as soon as this was possible.

166. Document BAYP0000009_023, identified by the Inquiry, is a telex from Gary Mull to me dated 15 October 1986 regarding supply of Koate HT to the UK. He stated that a lot of product at 250IU, which had been ALT-tested, would be available for shipping after sampling and also referred to two lots of product at 270 IU and 1000 IU, prepared from non-ALT-tested plasma, which would be available shortly. He asked whether the non-ALT tested lots should be sent to the UK and confirmed that product at 1000 IU, which had been ALT tested, would not be available until December. I have no recollection of my response to this telex, however as mentioned above it seems that after the switch to ALT tested plasma, there was a delay before sufficient stock was available.

167. I have no recollection of these events or what information regarding the transition to ALT-tested plasma was provided to UK Haemophilia Centre directors. However it seems likely that whether a product was prepared from ALT tested plasma would have been made known to Haemophilia Centre directors prior to supply. As indicated at paragraph 162 above, the product information for Koate HT was not revised to refer to ALT screening until February 1989.

Heat Treatment

Dry heat treatment vs Wet heat treatment

(38) On 17 January 1985, Marie Tatt wrote to E. L Greene confirming the product license for Koate HT would be issued "on receipt of written confirmation from us that we will include a statement in the data sheet that the product is heated at 68 degrees c for 72 hours and this is done to reduce the risk of infectivity. No need to mention that dry heat is used." (See: BAYP0000024_034) Please set out your understanding and evaluation of Cutter's decision to pursue a dry heating method of Koate.

168. While I was working at Cutter UK I was aware of the differences between the various methods of viral inactivation. However I was not employed in a scientific or regulatory capacity, have no expertise in such matters and, in view of the time that has elapsed, I can no longer remember the issues involved. The principal Cutter expert on matters of viral inactivation was Dr Milton Mozen and I refer to his report at WITN6407003.

(39) On 19 March 1985, Dr. Kernoff wrote to you confirming that the Royal Free Hospital would not be purchasing any Cutter Factor VIII for 1986/1985. (See: RFLT0000015). What steps, if any, did Cutter take in response to Dr. Kernoff's assessment?

169. Document RFLT0000015, identified by the Inquiry, is a letter from Dr Kernoff to me dated 19 March 1985, in which he stated that the Royal Free Haemophilia Centre had decided not to purchase Cutter product for the following year, as a result of his view that dry heat treated concentrates were more likely to transmit NANB hepatitis than wet heat treated products. I understood that he had conducted research for Alpha in relation to their wet heat treated product, including acting as principal investigator co-ordinating multi-centre studies on their behalf. His decision not to purchase Cutter products was based on his findings in the context of that research as well as other research in "virgin" patients, even though such studies had not included Cutter concentrates.

170. I have been shown my response to Dr Kernoff dated 22 March 1985 (WITN6407012). In this letter I express my disappointment but acknowledge the reasoning behind Dr Kernoff's decision to use wet heat treated products. I go on to state that:

> *"It has been well noted that certain dry heat treated products have transmitted Non A Non B hepatitis but I would like to re-emphasise that all manufacturers' dry heat treatment processes are very, very different. Cutter's process for Koate HT is unique. Trials are being conducted in Japan and by Professor Minucci in Italy. When the results are available I will certainly let you know the outcome."*

171. I do not know, at this stage, whether I wrote to Dr Kernoff again regarding this issue.

Retrovirus inactivation in Koate

(40) In late 1983 or early 1984, Dr Jay Levy, Associate Professor of Medicine at the University of California, San Francisco in collaboration with researchers at Cutter carried out a study to determine whether a retrovirus (mouse xenotropic Type C retrovirus) could survive the conditions used for preparing Koate. This retrovirus resembled that which was associated with the AIDS virus (LAV). It was determined that when subjected to Cutter's heating process of 68 degrees c for 72 hours, no retrovirus was detected. (See: BAUM0000003_001 Please set out your understanding of this study, and Cutter's response.

172. The Levy study was conducted before I joined Cutter and I would not have been aware of its implications at the time or the company's immediate response to its results. I do not now remember reading this study.

173. Document BAUM0000003_001, identified by the Inquiry, is a memo from Dr Milt Mozen to Jan Peterson dated 17 May 1984 describing studies conducted by Dr Levy at the University of California, San Francisco in collaboration with Cutter. The researchers found that fractionation of human plasma spiked with the model retrovirus had little effect in reducing activity of the retrovirus, whereas when Cutter's dry heat treatment process (68°C for 72 hours) was applied to the spiked plasma, no retrovirus was detected. The memo indicates that Dr Mozen concluded that the results of these laboratory studies were very significant. Dr Mozen's report at WITN6407003 describes Cutter's interpretation of and response to the study. The results of the study were released to the media.

174. In May 1984, when the above memo was written by Dr Mozen, Koate HT had already been licensed and was available on the market in the United States. Dr Levy's study would have been reassuring in that context.

However Koate HT was not licensed in the UK until February 1985 and, until a product licence was granted, I would have been very careful about making any statements in relation to Koate HT (including in relation to the implications of the Levy study) in view of the general prohibition on promotion of unlicensed medicinal products.

McDougal Study

(41) In late 1984, Cutter carried out an experiment with Dr Steve McDougal of the Center for Disease Control ("CDC") in Atlanta, Georgia. The results showed that LAV in Koate can be inactivated to a significant extent by the Koate HT manufacturing process. (See: CGRA0000447 [tab 18]). What if any impact did these results have on Cutter's decisions and actions?

175. As previously explained, I am not a scientist and my role at Cutter UK was in the sales and marketing department. I do not recall the study by Dr McDougall and would not have been in a position to know how the results of his study or the other data referenced in the document identified by the Inquiry affected Cutter's decisions and actions.

176. However, I have reviewed document CGRA0000447, identified by the Inquiry, which is a letter dated 26 October 1984 from Jack Ryan, President of Cutter Biological Inc, addressed to "Dear Hemophilia Treater". The letter describes recent research conducted by Cutter with Dr McDougall and with Dr Levy.

- The study conducted with Dr McDougall investigated the effect of the heat treatment process used for Koate HT on antihaemofilic Factor (AHF) spiked with lymphadenopathy associated virus (LAV), which had been described by Dr Montagnier and linked with AIDS. The study showed that, after heating at 68°C for 72 hours, an assay for LAV showed less than 10^2 particles, the lower limit of detection of the assay.

- The study conducted with Dr Levy investigated the effect of the Koate HT heat treatment process on Koate spiked with a virus he had isolated from AIDS patients, known as AIDS-related virus (ARV). The heat

treated Koate was then cultured in peripheral mononuclear cells and activity of reverse transcriptase (an enzyme involved in virus replication) was assessed. Preliminary results suggested that ARV was inactivated by the heat treatment process.

177. The letter to "Dear Hemophilia Treater" concluded "*Based on our belief that Koate-HT provides a true advancement in Factor VIII concentrate manufacture, Cutter is immediately converting manufacture of all Koate to Koate-HT.*"

(42) The document referred to in the above question shows a covering letter; "Dear Hemophilia Treater," could you please set out your understanding, if any, of the distribution of this information particularly in relation to the distribution to, if any, UK haemophilia centres.

178. I do not remember seeing a copy of the letter addressed to "Dear Hemophilia Treater" at the time it was written and I do not believe it was sent to UK haematologists; the terminology ("Hemophilia Treater") and spelling is American and this type of communication to UK haematologists would have been sent by the UK business (Brian Dyos, Marie Tatt or me) rather than by Cutter Inc. However it is possible that a copy of this letter was provided to Cutter UK for information purposes. It is in any event unlikely that a version of this letter or the information in it would have been sent to UK haematologists in October 1984. Koate HT was not licensed in the UK until February 1985 and the provision of information relating to the viral inactivation process applied to Cutter's heat treated product before that date (not limited to the published papers themselves) would have been viewed as contrary to the ABPI Code.

Cutter's discussion of viral inactivation studies

(43) On 19 February 1985, you wrote to Mr Farron of the Department of Pathology, Bristol Royal Infirmary. (See BAYP0000024_081). Please set out your understanding of Cutter's viral inactivation studies and the demand for

these studies from clinicians and government licensing bodies during your employment with Cutter.

179. I do not remember writing the letter dated 19 February 1985 to Mr Farron at the Bristol Royal Infirmary, however it is unlikely that I would have supplied the information referred to in that letter unless it had been requested. It is therefore probable that Mr Farron had asked me to send information on Cutter's viral inactivation processes when I met with him in Bristol. We did not often receive such requests from clinicians or hospitals, principally because the Haemophilia Centre directors were already very well informed as a result of effective communication within clinical networks both nationally and internationally.

180. Any requests from government licensing bodies for details of Cutter's viral inactivation studies would have been directed to Marie Tatt, who had responsibility for regulatory affairs. I have no knowledge of such matters, although I would have expected that copies of significant studies involving Cutter's products licensed in the UK would have been sent to the Department of Health.

181. For completeness, the attachments to the letter of 19 February 1985 (including the "Viral Inactivation Studies" Booklet) are no longer available and the letter provides only a brief summary, although I believe that the reference to "Hutchinson strain of non A non B hepatitis" was to studies conducted in chimpanzees. In general, if I had been given a summary of Cutter studies to pass on to clinicians, I would have been aware of the content, but, as a non-scientist, I would not have analysed this material critically.

182. As indicated above, Dr Mozen led Cutter's viral inactivation efforts. I refer to his report at WITN6407003 and to my responses to Questions 19, 22 and 40 above.

Price Increase due to Screening Requirements

(44) In March and April of 1986, you advised haematology departments and health authorities that the price per unit of Koate HT was increasing to incorporate the cost of HTLV-III antibody testing. (See: BAYP0000008_130 and BAYP0000008_153). Please set out the decision-making process which led to this price increase to customers.

183. I had no involvement in decisions on the price of Cutter medicinal products in the UK. Prices were set by Brian Dyos and Jack Wood and I simply notified customers of the price increase.

184. However, while I did not instigate any changes in price and was not involved in the associated discussions, I am not surprised that the increase in manufacturing costs associated with the introduction of enhanced screening of plasma donations resulted in an increase in the price of finished Factor concentrates.

Section 6: Withdrawal of Koate (switch to Koate HT)

(45) In late 1984, Koate HT entered the UK market following the market demand for heat treated Factor VIII. Please set out the events which led to Koate HT "being forced on to the market". (See: BAYP0000024_047)

185. I refer to my responses to Questions 29 above and 46 below in relation to this Question 45.

186. Document BAYP0000024_047, identified by the Inquiry, is a Cutter UK - Key Indicator Report for December 1984 written by Brian Dyos and me. I do not now remember why the sentence "*Koate HT was forced onto the UK market place by the market's demand for heat treated Factor VIII Concentrate*" was used in the report. However, this may have been intended to reflect the fact that Koate HT was not licensed at that time and was therefore only supplied in response to specific requests from individual clinicians ("named patient" supply) rather than being offered proactively by Cutter.

(46) In September 1984, Cutter received approval from DHSS for a clinical trial of Koate HT. The product licence for Koate HT, 0055/0107 was granted

on 18 February 1985. Please explain the supply of Koate HT in the UK between September 1984 and February 1985 (See: BAYP0000025_019 [tab 16], BAYP0000003_309 [tab 25])

187. Prior to the grant of a product licence for Koate HT in February 1985, all supply in the UK would have been in the context of clinical trials or as "named patient" supply. Document BAYP0000025_019 identified by the Inquiry, is a telex from Marie Tatt to P Bedogni dated 3 September 1984, indicating that the DHSS had granted a clinical trial exemption certificate permitting a clinical trial of Koate HT. Document BAYP0000003_309 is the product licence for Koate HT granted on 18 February 1985.

188. I have been shown a Cutter UK; Year End Review and Reports dated January 1985 (CGRA0000554 at page 8) which shows that, whilst Miles had anticipated that Koate HT would be launched into the UK market during the second quarter of 1985, it made what was described as a "hasty" appearance on a named-patient basis at the end of November 1984. This escalation in timelines is probably explained by the following passage from an internal Miles report dated 30 November 1984 (BAYP0000025_087 at pages 3-4) which I have been shown:

> *"AIDS has finally come to the United Kingdom with a force that has caused a virtual panic in the Department of Health. For one year this department has blocked every application for registration of its heat-treated factor VIII products and now in the space of one week they are in a panic responding to the newspaper demand for action concerning the AIDS risk to hemophiliacs [...] following these headlines the Department of Health has advised Cutter that every action will be taken to grant us registration by early December [...]The Hemophilia Treatment Centres are now also responding to the newspaper stimulus and requesting heat-treated Koate on a named patient basis. Cutter UK had in inventory 1000 vials of 500 IU Koate HT which has now been allocated and requests for other sizes have been received from the treatment centres."*

189. I have also been shown a Cutter/Miles internal memo dated 13 March 1985 (BAYP0000024_114 at page 1) which shows that, by February 1985, the UK market had been converted to heat-treated product and therefore no further non-heat-treated Koate was sold. The supply of Koate-HT is confirmed in a letter from Cutter to Dr Savidge at St Thomas' Hospital dated 13 March 1985 (BAYP0000024_113) which I have also been shown in which Cutter refused to sell Koate to the UK market, stating:

> *"...dramatic changes have taken place in the United Kingdom regarding heat-treated factor VIII products. Therefore, we at Cutter feel it is prudent to no longer effect sales of non-heat-treated product for use in the United Kingdom".*

(47) Please set out the process for the return of Koate regular material as referred to in these documents (BAYP0000024_090 (tab 29) and BAYP0000024_002) (tab 21)

190. My response to Question 29 (paragraphs 115-116) is repeated.

191. I was not directly involved in the arrangements for return of non-heat treated concentrates, which were organised by regulatory affairs. However it is my understanding that, after introduction of heat treated concentrates, Cutter UK accepted return of non-heat treated stock crediting the price in full. This view is supported by document BAYP0000024, identified by the Inquiry, which is a Cutter UK - Key Indicator Report for January 1985, confirming return of non-heat treated Koate amounting to 633460 IU and £50,618. Additionally, document BAYP0000024_002, identified by the Inquiry, is a list of product lots shipped to the UK in 1985, which showed credit invoices issued for return of non-heat treated Koate.

(48) On 15 May 1985, you wrote to Dr Tuddenham of the Royal Free Hospital offering supply of non-heated Koate at a reduced price. (See: CGRA0000561)

Could you please set out:

a. ***Why non heated Koate was being offered to Royal Free Hospital;***
b. ***Who authorised the supply of non heated Koate; and***
c. ***Whether non heated Koate was supplied to any other UK hospital or health authority after January 1985?***

192. I have no recollection of document CGRA0000561, identified by the Inquiry, which is a letter dated 15 May 1985 from me to Dr (now Professor) Tuddenham. However, I have been shown an extract from the evidence of Professor Tuddenham, when he gave evidence to the Inquiry on 22 October 2020, which seems to be relevant to this Question. Professor Tuddenham was asked by Counsel to the Inquiry about a letter dated March 1985 in which he had requested supplies of non-heat treated Koate for a hospital in Karachi, Pakistan. The transcript of the hearing on 22 October 2020 states:

> 12 Q And then, if we go to CGRA0000560, please, Henry.
> 13 I just wanted to ask if you're able to assist with
> 14 what this letter was concerned with. This is
> 15 a letter, March 1985, addressed to you. Not entirely
> 16 sure -- so, yes, it's in relation to Koate, and you're
> 17 being offered unheated Koate to cover the requirements
> 18 of the Fatimid Foundation. Is this anything to do
> 19 with treatment at the Royal Free or is this to do with
> 20 something else entirely?
>
> 21 A. It's not to do with treatment at the Royal Free. It's
> 22 to do with treatment at a Haemophilia Centre in
> 23 Karachi.

193. I understand that the Inquiry has declined to provide a copy of document CGRA0000560, shown to Professor Tuddenham and I do not otherwise have access to it. However I believe that the letter dated 15 May 1985 in which I stated that Brian Dyos had asked me to contact Professor Tuddenham regarding some non-heat treated Koate in Cutter's inventory with an expiry date of 13 July 1985, is likely to relate to this same request by Professor Tuddenham for supplies of product for use in Karachi.

194. I therefore believe that Question 48 is based on a misunderstanding by the Inquiry and my letter of 15 May 1985 was not an offer of non-heat

treated Koate to the Royal Free Hospital. As far as I am aware, non-heat treated Koate was not offered or supplied to the Royal Free Hospital or any other UK hospital or health authority after January 1985.

(49) On 25 February 1986, you were copied into a file note from Peter DeHart reporting on Dr Peter Jones (Newcastle Haemophilia Centre) speaking at an AIDS conference and where it was said that heat-treated Factor VIII did not completely inactivate the HTLV-III virus AIDS. He reported four (or five) instances of seroconversion following use of heat-treated concentrates (according to Cutter). (See: CGRA0000585) What actions, if any, did Cutter take in relation to these statements by Dr Jones?

195. Document CGRA0000585, identified by the Inquiry, is a file note prepared by Peter DeHart after attending an AIDS conference organised by Dr Jones in Newcastle in February 1986. While the file note was copied to me I do not remember receiving it. However, it is clear that the statement by Dr Jones was viewed as controversial. The file note indicates that Dr Jones referred to reports by two clinicians in the US and the Netherlands, describing seroconversion in patients who had received only heat treated concentrates for a year. Two other clinicians challenged Dr Jones' inference that seroconversion after one year of treatment with heat treated products implicated the heat treatment processes and suggested that the affected individuals had probably been infected prior to the introduction of heat treated product. Furthermore, Dr Jones did not identify the heat treated products which had been administered to the patients he described or provide any other details regarding their treatment and seroconversion. The file note indicates that Cutter intended to contact the US and Netherlands haematologists identified by Dr Jones for further information. I am not aware of the outcome of those discussions.

Section 7: Licensing

(50) On what basis were products allocated by Cutter to Haemophilia Centres on a 'named patient' basis? (See: BAYP0000024_085 [tab 27] BAYP0000024_250, [tab 30] BAYP0000016_073 [tab 100] and

BAYP0000005_091 (Ireland)) [tab 98] Please outline your understanding of the processes in place at Cutter when products were supplied on a named patient basis.

196. I was not responsible for deciding whether a product could be provided on a 'named patient' basis. I would forward any unsolicited requests for unlicensed products received by me from any Haemophilia Centre to Marie Tatt in regulatory affairs. Cutter would seek to fulfil all requests for named patient supply if clinicians requested such treatment, however the company did not offer such supply proactively. I refer to my response to Question 46, in which I explain the named patient supply of Koate HT from November 1984 up to the grant of a product licence in February 1985.

197. Document BAYP0000024_085 identified by the Inquiry, is a letter dated 25 February 1985 from me to Dr Prowse of Edinburgh and South East Scotland Blood Transfusion Service, providing information in relation to Konyne HT and a copy of the "Viral Inactivation Studies" booklet. I do not remember this letter. However I did not carry out sales and marketing activities in Scotland and it is therefore likely that the information provided in this letter was specifically requested by Dr Prowse. I do not believe I would have sent such information to Dr Prowse if he had not previously asked for it.

198. Document BAYP0000024_250 identified by the Inquiry, is a memo from Eli Greene at Cutter Inc to Steve Ojala in US regulatory affairs, reporting on a trip to the UK. The file note was copied to three people from Cutter UK, although not to me. In relation to named patient supply, the file note refers to heat treated Factor IX concentrate and states "*UK marketing is interested in a licence even though it is being sold on named patient basis*". This meant that, at that time, Cutter UK was supplying unlicensed Konyne HT for the treatment of specific patients in response to unsolicited requests from clinicians. I assume that Cutter UK wished to obtain a product licence for Konyne HT in order to promote the product.

199. Document BAYP0000016_073 identified by the Inquiry, is a letter from me to Mike O'Donnell of Accu-Science (Cutter's distributor in Ireland) dated 10 April 1990, relating to his request for Koate HS, but seeking to ensure that he did not receive more stock than he was likely to need. I do not remember writing this letter.

200. Document BAYP0000005_091 identified by the Inquiry, is a memo dated 2 September 1988 from Joyce Boult in regulatory affairs to Dr Marley which refers to an "*attached […] list of the named patients who have been approved by Dr. Scott of the NDAB for supply of Konyne HT via Dr. Temperley*". This list reflects the fact that products could only be supplied on a named patient basis if, amongst other requirements, the patient had been specifically named by their treating doctor.

(51) Konyne and Konyne HT were not licensed in the UK. Please outline your understanding as to why Konyne or Konyne HT were not licensed in the UK despite being supplied on a named patient basis. (See: BAYP0000008_071 [tab 104], BAYP0000035_017 [tab 99] BAYP0000024_250 [tab 30] and BAYP0000003_315) [tab 28]

201. I was not involved in the licensing of Cutter's Factor IX concentrates and have limited knowledge of the company's strategy in this respect. However, national requirements for Factor IX concentrate were, I understand, substantially less than those for Factor VIII concentrate and I believe that the Blood Products Laboratory was able to satisfy much of the demand.

202. I have reviewed document BAYP0000008_071 identified by the Inquiry, which is an undated document providing submissions by Cutter to the CSM in support of its application for a product licence for Konyne HT. This states that an application for a UK product licence for Konyne was initially made by Cutter in 1982 but was subsequently withdrawn because the application was not in the format required under DHSS guidelines. The application in respect of Konyne HT was seemingly unsuccessful because the CSM required additional clinical data confirming that the viral

inactivation processes applied to the product were effective in preventing transmission of viruses. This was inevitably a difficult issue because it required administration of product to patients who had not previously been treated with Factor concentrates. I had no involvement in preparing the submissions to the CSM for Konyne HT.

203. Document BAYP0000008_071 identified by the Inquiry, is a letter dated 23 February 1990 from Craig Simpson, Senior Registration Officer at Bayer UK to a colleague at Cutter Biological in the US, providing a report on the licence status of products supplied in the UK. The status report indicates that an application for a product licence for Konyne-HT had been submitted to the Licensing Authority in May 1985, but was ultimately abandoned.

(52) Could you please set out your understanding of the connection, if any, between licensing products in the UK and the supply of products in the Republic of Ireland? (See: BAYP0000003_262 and BAYP0000008_188).

204. All medicinal products supplied in the UK and Republic of Ireland required separate licences granted by the relevant Licensing Authority. Marie Tatt was responsible for communications with the authorities in both countries on behalf of Cutter. I have no knowledge of the connection between licensing products in the UK and Republic of Ireland.

205. Cutter had no affiliate in the Republic of Ireland and its business was handled through a distributor, Accu-Science. My responsibilities in sales and marketing were limited to England and Wales although I did have some contact with Accu-Science on an ad hoc basis (see, for example, response to Question 50) and, I believe, with Professor Temperley.

Section 8: Interactions with the DHSS, Haemophilia Centres, UKHCDO and the Haemophilia Society

(53) Please describe, in broad terms, your knowledge of Cutter's relationship with the Department of Health and Social Security ("DHSS") during the

period in which you were employed by Cutter and how, if at all, it changed over time.

206. My role at Cutter UK was in sales and marketing and other departments within the company dealt with regulatory aspects, including contact with the DHSS. I therefore have no knowledge of Cutter's relationship with the DHSS.

(54) Please set out your recollection of any specific interactions or meetings with the DHSS in which you were involved during the 1980s (and in particular any interactions or meetings in which issues relating to the safety of blood products generally or Cutter products in particular or licensing processes or risks relating to hepatitis or HIV were considered).

207. My response to Question 53 is repeated. I do not believe I was present at any meetings with DHSS or had any interactions with DHSS during the 1980s or at any other time.

(55) Please describe, in broad terms, your knowledge of Cutter's relationship with the Haemophilia Society in the UK during the period in which you were employed by Cutter and how, if at all, it changed over time. Please explain your role in that relationship. (See: HCDO0000279_009)

208. Patients with haemophilia, their carers and treating healthcare professionals were closely connected. I regarded getting to know the Haemophilia Society as one of my responsibilities, so that I could learn more about the issues that were important to affected patients and to the clinicians treating them, including effective treatment delivery and side-effects. I therefore attended Haemophilia Society meetings where this was permitted, although I was not asked to speak and there was no discussion of Cutter products. Sometimes the Haemophilia Society would request donations for activities involving its members; these were generally modest. In addition, Cutter UK did provide financial support to the Haemophilia Society, so that representatives could attend some of the larger haemophilia meetings, such as the WFH meeting which occurred

every four years (see response to Question 56 below). I do not remember any changes in the relationship during the time I was working at Cutter.

209. Document HCDO0000279_009, identified by the Inquiry, has not been disclosed by the Inquiry and is not otherwise available to me.

(56) Describe your understanding of Cutter's sales and marketing policies or strategies with regard to the Haemophilia Society in the UK during the 1980's, specifically:

a. Arrangements;

b. Financial Incentives; and

c. Non-financial incentives.

The following correspondence to David Watters in 1985 may be of assistance when considering this question, BAYP0006231, BAYP0006240 and BAYP0006241.

210. My response to Question 55 above is repeated. Cutter did not sell its products to the Haemophilia Society. Contact with the Society assisted Cutter to understand more about haemophilia and the issues faced by haemophilia patients. There was no direct financial benefit to Cutter resulting from its contacts with the Haemophilia Society although a greater knowledge of haemophilia allowed us to understand the benefits of treatment. Cutter UK therefore provided small donations to the Haemophilia Society as a goodwill gesture and expected no particular benefit in return.

211. Document BAYP0006231 identified by the Inquiry, is a letter from me to David Watters, Co-ordinator of the Haemophilia Society, dated 15 January 1985, in which I enclosed a cheque for £1000 for the purposes of the Society's Annual Residential Seminar. This was the first Haemophilia Society meeting I attended.

212. Document BAYP0006240 identified by the Inquiry, is another letter from me to David Watters, Co-ordinator of the Haemophilia Society, dated 15

May 1986 enclosing a cheque for £200 as sponsorship for a Haemophilia Society representative to attend the WFH congress in Milan.

213. Document BAYP0006241 identified by the Inquiry, is a further letter from me to David Watters, Co-ordinator of the Haemophilia Society, this time dated 18 December 1985 enclosing a cheque for £1,200 for the purposes of the Society's 1986 Residential Seminar.

(57) In early 1985, you attended a Haemophilia Society weekend in Bournemouth.

Please set out:

a. What occurred during this Haemophilia Society weekend;

b. Who else attended this weekend; and

c. Was it common practice for a Pharmaceutical company sales representative to attend these weekends (See: BAYP0006233).

214. I have limited recollection of the Haemophilia Society Annual Seminar in early 1985 and believe I was only present for part of the weekend.

a. During the weekend, the boys who attended participated in various activities and I think there were some presentations although I cannot now remember the content. There was no discussion regarding Factor concentrates and I did not discuss products with any attendees.

b. As far as I remember the seminar was attended by boys with haemophilia and their families, quite a few haemophilia nurses and some representatives from the Society. I do not remember any doctors being present. I did not speak to the patients who attended and, although I would have spoken to the nurses who attended, this would have been about general matters rather than Cutter products.

c. I attended most of the annual Haemophilia Society seminars while I was at Cutter. I do not know whether this was common practice and

I do not remember whether representatives of other pharmaceutical companies were present.

(58) Please:

a. Drawing on your own knowledge and experience, please outline the nature of your relationships with haemophilia clinicians and centres. The enclosed letter to Dr Kernoff from April 1985 may assist you in answering this question (BAYP0000024_172).

215. I would generally meet with Haemophilia Centre directors by appointment once every 3 months. The meetings took place at times convenient to the directors concerned, often between clinics, and would involve a discussion for about 20 minutes. I would ask them about their research and recent experiences in managing patients, including any problems that had emerged. The discussions involved little in the way of traditional "selling" as the directors were well informed and very knowledgeable about scientific developments, although, if I had become aware of a scientific paper of interest, I might provide copies to the directors. Sometimes we would discuss the price charged for Factor concentrates, although Brian Dyos was principally responsible for discussions with individual Haemophilia Centres on pricing matters.

216. In addition to these discussions, as previously described, Cutter would sponsor educational meetings organised by Haemophilia Centre directors for the Centre's staff. Furthermore, I would organise education for Cutter sales representatives as an introduction to haemophilia by Haemophilia Centre staff.

217. Document BAYP0000024_172 identified by the Inquiry, is a letter from me to Dr Kernoff dated 11 April 1985 in which I refer to returned Koate-HT, and then invite Dr Kernoff to visit Cutter in San Francisco at the time of a meeting in San Diego. This would have been the WFH meeting, which would probably have been attended by all Haemophilia Centre directors. I confirmed specifically that Professor Bloom and Dr Wensley would also be attending. I believe that those particular Haemophilia Centre directors

were invited to Cutter due to their interest in science and research. The WFH meeting would have given them an opportunity to speak with other scientists about developments in haemophilia treatments and to see Cutter's US facilities.

b. What was your understanding of Cutter's sales and marketing policies or strategies with regard to haemophilia centres and haemophilia centre directors in the UK during the 1980s, in relation to:

- ***i. Arrangements;***
- ***ii. Financial incentives; and***
- ***iii. Non-financial incentives (See: BAYP0000008_059).***

218. I am not aware that Cutter had any formal sales and marketing policies with regard to Haemophilia Centres and Haemophilia Centre directors.

219. The arrangements for interactions with Haemophilia Centres are described in my response to part (a) of this Question (see paragraphs 215 and 216 above).

220. Occasionally Cutter UK might provide small donations to assist in the activities of individual Haemophilia Centres or provide support, usually by a department fund, to allow a Haemophilia Centre director or one of their clinical colleagues, to attend a conference abroad.

221. Price was a key factor in Cutter's marketing strategy. However price was relevant only if a product was effective and acceptably safe. For this reason, we would seek to differentiate Cutter's products from those supplied by competitors by reference to the available scientific data on safety and efficacy.

222. Document BAYP0000008_059 identified by the Inquiry, is an internal memo from me to Jack Wood dated 16 January 1986. The memo refers to the decision by the Newcastle Haemophilia Centre to use only concentrates supplied by Alpha, in view of Dr Kernoff's data from the Royal Free Hospital which suggested that the Alpha concentrates had some advantages in eradicating NANB hepatitis. The memo confirmed the

relevance of clinical data, rather than simply price, to support choice of Factor concentrates.

c. Identify any particular haemophilia centre directors in the UK with whom Cutter had a close relationship in the 1980s (See: BAYP0000008_085, BAYP0000008_109 and BAYP0000008_155).

223. Cutter had closer relationships with the larger Haemophilia Centres because they were generally the most receptive to meeting with us.

224. The three documents identified by the Inquiry are letters between me and Professor Bloom of the Cardiff Haemophilia Centre. I do not believe Cutter had a closer relationship with Professor Bloom than it did with other Haemophilia Centre directors or that Cutter had a closer relationship with him than other companies. The fact that Professor Bloom did not consistently purchase Cutter products is shown by the memo referenced in my response to part (b) above. He was heavily involved in research and so was very knowledgeable about Factor concentrates.

d. Identify any haemophilia centre directors in the UK:

- ***i. from whom Cutter sought advice; or***
- ***ii. who provided consultancy services to Cutter;***
- ***iii. or who undertook research for or with Cutter during the 1980s and provide details. This letter from 1984 [BAYP0000025_091] may assist when considering this question.***

225. I do not know whether my colleagues at Cutter ever requested advice from Haemophilia Centre directors, and I do not recall advice ever being sought from them on a formal basis. I discussed scientific papers with Haemophilia Centre directors when I visited them, and asked them questions to enhance my understanding about haemophilia treatment generally, developments in research and papers that had been published.

226. While I would have regular discussions with Haemophilia Centre directors as described in my response to Question 57 above, I am not aware that

any directors provided formal consultancy services to Cutter UK save possibly in the research context.

227. However, I do not recall any Haemophilia Centre directors working for or with Cutter on research. Document BAYP0000025_091, identified by the Inquiry, is a letter from Walid Marzouk to Dr Mitchell, dated 2 December 1984. This confirms that Cutter would be willing to supply heat treated material free of charge for one patient for the purposes of a study. Walid Marzouk also enclosed an approved study protocol. While these documents suggest that Cutter was prepared to support research initiated by Dr Mitchell, they do not indicate that Dr Mitchell was conducting a study for or with Cutter.

e. What remuneration was provided by Cutter to haemophilia clinicians in return for the performance advisory and/or consultancy roles? Please provide details.

228. I have no knowledge of any remuneration provided by Cutter UK to any Haemophilia Centre directors or other haemophilia clinicians in the UK. So far as I am aware, there was never any expectation that the Haemophilia Centre directors would undertake any services for Cutter.

f. What regulations or requirements or guidelines were in place at the time concerning declaratory procedures for clinicians' involvement with a pharmaceutical company?

229. I am not aware what rules may have been in place during the period I was at Cutter UK in relation to declaratory procedures for clinicians, however I believe this is likely to have been a matter determined by their employers.

g. Describe, in broad terms, Cutter's relationship with the UK Haemophilia Centre Directors Organisation ("UKHCDO") and set out your recollection of any specific interactions or meetings with UKHCDO in which you were involved during the 1980s.

230. I do not recall any involvement with the UKHCDO.

(59) Please explain, in as much detail as you are able to, any other matters that you believe may be of relevance to the Infected Blood Inquiry, having regard to its Terms of Reference and to the current List of Issues.

231. I am aware of no additional matters.

Statement of Truth

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

Signed GRO-C

Dated 16th November 2021