Witness Name: Peter Coombes
Statement No.: WITN6409001
Exhibits: SHPL0000067_009
Dated: 15 March 2022

INFECTED BLOOD INQUIRY

WRITTEN STATEMENT OF PETER COOMBES

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 9 August 2021.

I, Peter Coombes, will say as follows: -

I. Preliminary observations

i. Before answering the questions raised with me by the Inquiry I think it would be helpful to make some preliminary comments that I think are relevant to my written answers. I retired from Immuno Limited in 1997. After that time I did some occasional consultancy work but I had ceased to work in the pharmaceutical industry by 2003. The questions raised by the Inquiry require me to try to recall detailed events, often involving complex medical and scientific matters, from between 30 and 50 years ago. I have tried my best but have found this very difficult. In respect of a number of the questions I either have no recollection or my recollection, while being best I can give, may not be correct as I may have forgotten or confused matters as a result of the passage of time.

ii. The Inquiry's questions refer to IMMUNO AG and Immuno Limited as though they were the same company but the UK company had a different role from the Austrian based business. The Immuno company in the UK, where I was employed, was a distribution company. It was responsible for the sale and distribution of products and acted as a point of liaison for IMMUNO AG with UK regulators; Immuno Limited did not develop or make the products. Unfortunately a number of questions ask for information that, because of my role and the work undertaken by Immuno Limited my employer, I do not have the knowledge to answer.

iii. I have been asked to consider 61 questions, many with sub questions, and to consider more than 90 documents. I have read the documents provided to me by the Inquiry and considered the questions diligently over many days and have done my best to answer them. Where questions seem to me to be unclear I have tried to identify what I think is the point being raised and answered on that basis.

iv. For ease of reference, the questions raised in the Rule 9 Request are included below in **bold** and *italics* before my responses.

Section 1: Introduction

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

1.1 My full name is Peter John Coombes. I was born on GRO-C 1947. I live in the south of England and my address is known to the Inquiry.

1.2 I have a Bachelor's Degree in Pharmacy and a Diploma in Pharmaceutical Chemistry.

2. ***Please set out your employment history including the various roles and responsibilities that you have held throughout your career, as well as the dates, insofar as relevant to the Inquiry's Terms of Reference. In particular, please set out the timeline of your work with Serological Products Ltd., Immuno Ltd. and Baxter Healthcare Ltd, including:***

(a) ***The positions that you held within these companies; and***

(b) ***The responsibilities that each of those positions entailed.***

2.1 The dates I set out for various roles I have held are approximate and given to the best of my memory.

2.2 Between 1968 and 1973, I worked as a retail pharmacist for both Boots and another pharmacy chain in Yorkshire called Selles.

2.3 Between 1973 and 1976, I worked as a medical representative in Yorkshire for a company called Serological Products Ltd, which I believe changed its name to Immuno Limited in 1976. As a medical representative I visited hospitals in Yorkshire and across the north east, east Midlands and south Scotland. I think at the time the company had a contract with the Department of Health, held jointly with another company, which I recall was initially to supply approximately a million units of Factor VIII per year. I was providing information to doctors about the company's products.

2.4 From 1976 until 1997 I worked in Immuno Limited's Head Office, in Sevenoaks.

2.5 Between 1976 and 1979 I was a Sales Executive, where my role was to set up a sales department and train and supervise field staff in the UK and Ireland.

2.6 Between 1979 and 1982 I was a Marketing Manager, with responsibility for sales, budgeting, training of staff, hospital and regional contracts.

2.7 Between 1982 and 1984 I was the Marketing Director with responsibility for reporting sales at board level to Immuno Limited. As Marketing Director I was also responsible for developing new business, for example trying to arrange UK distribution agreements with other pharmaceutical or diagnostic companies.

2.8 Between 1984 and 1997 I was the Managing Director and reported to the Chairman and board on all UK operational matters. This included

supervision of warehousing and distribution in relation to our Wholesale Dealer's Licence. From 1980 I was also the EC registered 'Qualified Person' and had responsibility for product batch testing. My other responsibilities included Adverse Reaction Reporting and Medicines Inspectorate site visits.

2.9 Following the takeover of the Immuno group by Baxter in 1996-97, I supervised the transfer of the Immuno Limited business to Baxter. This was completed in November 1997 and though I was offered a role at Baxter I opted for voluntary redundancy.

2.10 From 1997 to 2003 I was a self-employed consultant working in various areas of the pharmaceutical industry unrelated to blood products and I also worked on a project undertaking market research for the French blood transfusion service.

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.***

3.1 During my career I was a member of various organisations which may be relevant to the Inquiry's Terms of Reference. I cannot recall the dates of my memberships but they included being a member of: the Royal Pharmaceutical Society, the Royal Society of Medicine, the UK Haemophilia Society, the World Haemophilia Society, the British Society of Blood Transmission and the British Society of Haematology, the Association of the British Pharmaceutical Industry (ABPI), and at one point I was the ABPI representative on the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Diagnostic Committee .

4. ***In so far as you are able to, please describe your understanding of the corporate and functional relationship between Serological Products Ltd., Immuno Ltd and Immuno AG in Vienna, Austria (please note that the***

companies are referred to below generally as "Immuno" unless otherwise specifically stated).

4.1 Serological Products Ltd was the initial company set up to distribute in the UK pharmaceutical and laboratory diagnostic products produced by IMMUNO AG. I think the company was set up in 1972 when the first staff were recruited. The company was started by Norman Berry who was Managing Director until 1984 when I took over the position and he became Executive Chairman. The name of the company was changed to Immuno Limited in 1976, I believe to fall in line with how other subsidiaries in the group were named. I think Immuno Limited was one of the smaller subsidiaries with a total staff of around 25 people including eight field staff.

4.2 During my time with the business the function of Serological Products Ltd and Immuno Limited was as a wholesaler and distributor for IMMUNO AG's pharmaceutical and diagnostic products and we held a pharmaceutical Wholesale Dealer's Licence issued by the Medicines Control Agency ("MCA"). To the best of my recollection I think at that time all non-UK based pharmaceutical companies had to have a UK based distributor as part of the product licence application.

4.3 As far as I recall the group's central production, research, clinical trials, regulatory affairs and marketing departments were not in the UK but based at IMMUNO AG in Vienna, Austria. In addition to commercial activities in the UK, Immuno Limited acted as a link between the IMMUNO AG Regulatory Affairs Department and the UK Licensing Authority and submitted product licence application files in the UK which were prepared by IMMUNO AG. The UK company also assisted IMMUNO AG in resolving UK regulatory questions.

4.4 I have not researched the corporate history of the companies but I think the UK company Immuno Limited was ultimately owned by an entity which I recall was named IMMUNO International and based in Zurich. You can see that the Immuno Limited company letter footnote includes a Swiss Director [see for example SHPL0000218_002.] I think that the

UK company may have been responsible financially to IMMUNO International; but on a day to day level Immuno Limited reported to IMMUNO AG in Vienna, Austria in respect of matters relating to products distributed in the UK. To the best of my knowledge, all products distributed in the UK were manufactured in Vienna, Austria by IMMUNO AG.

5. ***Please identify any senior colleagues at Immuno (whether in the UK or in Austria) 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.***

5.1 As far as I recall the joint Managing Directors at IMMUNO AG, were Dr H Eibl and Dr O Schwarz. I believe that they were the senior persons at the time within that company. I do not know what the decision making structure would have been or how decisions were made at IMMUNO AG.

5.2 Other senior colleagues I had regular contact with at IMMUNO AG included Mrs Diernhofer who headed the Regulatory Affairs Department.

5.3 As I have noted above the UK company was a distributor company, not a manufacturing company, so the kind of decisions that we were making in the UK related to the practical aspects of licensing, delivery and supply of products.

6. ***Please identify the various blood products which were supplied in the UK by Immuno in the 1970s and the 1980s, to the best of your knowledge.***

6.1 I cannot recall the exact timings of when different blood products were supplied in the UK but during my time with Serological Products Ltd and then Immuno Limited the blood products I dealt with that I can recall included: Human Albumin Solution 4.5% and Human Albumin Solution 20% which were albumin replacements, ie they were not coagulation

products. The main coagulation products were Feiba, Kryobulin and Prothromplex, and there were variations in terms of heat treatment processes.

6.2 Immuno Limited also supplied Endobulin, Gammabulin, Partobulin and Tetabulin which were all immunoglobulins. We supplied Heparin (low dose) which was an anti-coagulation product. We also sold Plasminogen in bulk form to Beecham which they combined with another product.

6.3 Immuno Limited supplied some other products on request to specific doctors for their named patients. These included Protein C and C1 Esterase Inhibitor which were highly specialised products for a handful of patients.

6.4 I also recall that the company sold approximately 150 non-therapeutic diagnostic products – reagents and kits for carrying out tests and assays in haematology, transfusion and biochemistry laboratories. Some of these non-therapeutic products were obtained from plasma but were not for administration to patients and only for laboratory use. I mention these products because the Inquiry has referenced some documents which are about these non-therapeutic products.

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

7.1 I have not been involved in or provided written or oral evidence in the circumstances stated.

Section 2: Knowledge of risk of blood products

8. ***During your time working at Serological Products Ltd. in the 1970s and Immuno in the 1980s, what was your knowledge and understanding of:***

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

(b) ***The risks of transmission of hepatitis (including HBV and Non-A Non-B Hepatitis ("HCV")); and***

(c) ***The nature and severity of the risks of these infections?***

What were the sources of your knowledge? How, if at all, did they change over time?

8.1 I came to the business from a medical-scientific background and I had trained and practised as a pharmacist. Though it was not formally within my role I had a general familiarity with the science that related to the company's products. I think that some of the risks of virus infection associated with using factor concentrates or other donated blood products were known generally when I joined the business.

8.2 Again, from memory, I think I was aware that IMMUNO AG tested donors, donations and pools for HBV. This would have been from the time the first products were licensed in the UK, which I think were Human Albumin Solution and Kryobulin in the early or mid-1970s.

8.3 I cannot remember discussions on Non-A Non-B Hepatitis in the 1970's. At some point I became aware of hepatitis which was not A or B and was designated non-A non-B. I see now from the document noting the discussions in January 1983 [see document RFLT0000050] that IMMUNO AG were looking at the issue of Non-A and Non-B Hepatitis, however I have no personal recollection of that meeting or attending it. I do remember clinicians discussing that some patients seemed to develop a mild form of hepatitis when they were given factor concentrates but the doctors were not sure what it indicated. I do not recall when or where I had such conversations but I cannot remember

any specific reports to me that this occurred with Immuno Limited's products in the UK.

9. ***The enclosed letter from Norman Berry, Managing Director of Serological Products Ltd., to J.D. Corden Esq. of Derbyshire Royal Infirmary, dated 01 August 1974, notes that Kryobulin has an 'excellent record.... as far as Serum Hepatitis is concerned' [UHDB0000020]. To the best of your knowledge:***

(a) ***What was the basis of Serological Products Ltd's knowledge of the risk of serum hepatitis? How was this record maintained?***

9.1 I have noted my observations about the basis of my knowledge regarding Serum Hepatitis (HBV). All I can say on the subject is that I think, at the time of the first licences in the UK which was around 1973, the donors, donations and pools were all screened and tested.

(b) ***What is your understanding of the statement that Kryobulin had an "excellent record" ? On the basis of what evidence was such a statement made, to the best of your knowledge? In answering this question, you may be assisted by the documents enclosed at MHRA0033323_001, SHPL0000071_170, MHRA0033322_009 and MHRA0033322_008.***

9.2 This is not a letter I wrote. I assume Norman Berry would have been referring to HBV – serum hepatitis in the letter. What he means by "excellent record" I do not know. I do not recognise the phrase.

(c) ***The letter further refers to "reconstitution of the material". To the best of your knowledge, what changes were made to the product and why were they made?***

9.3 In the early months of my time with the company I recall that a few hospitals felt that Kryobulin did not dissolve quickly. In most cases I think it was resolved by reviewing the reconstitution

method they were using. I cannot remember what changes were made to the product beyond those mentioned in the letter but I do not recall that there were further problems.

(d) ***As a medical representative, what did your role entail in relation to blood products? Did it involve informing buyers of the risk? How would you represent the product to obtain a sale?***

9.4 As noted above, my recollection was that Immuno Limited was fulfilling a contract of supply with the Department of Health as regards Factor VIII. I do not think there was marketing material. The official Data Sheet which was approved as part of the product licence was what we used to communicate information. I remember the company approach was that a Data Sheet had to be given to the doctor as part of any discussion.

(e) ***How did other blood products, such as Factor Eight Inhibitor Bypass Activity ("Feiba") compare to this 'excellent record'? Please see SHPL0000218_002.***

9.5 I am unable to comment on the 'excellent record' statement as I am not sure what Norman Berry had in mind.

10. ***To the best of your knowledge, what was the state of knowledge within Immuno more generally in the 1970s and 1980s about the risks of infection associated with blood and/or blood products?***

10.1 I have tried to answer this question in relation to hepatitis see question 8 above. It is hard to recollect with accuracy what I and colleagues in the UK knew and when we knew it in relation to matters that took place at least three decades ago.

11. ***Please consider the cover letter SBTS0000315_088 and Summary of Discussions RFLT0000050, which summarises a meeting at the Excelsior Hotel, Heathrow Airport held with Immuno on 24 January 1983. You are not noted to have been in attendance at this meeting, but are referred to in a handwritten note on the top right hand of the cover letter which says***

"Peter, we need to talk about this". To the best of your knowledge and recollection please address the following:

(a) ***Do you recall the discussion referred to in the handwritten note? If so, please explain with whom it took place and the content of that discussion.***

11.1 I cannot remember being at the meeting or the topic of the meeting. I also cannot recollect any discussions with Norman Berry following the meeting.

(b) ***To the extent that you are able to recollect, please explain:***

(i) ***Who was in attendance at the meeting at the Excelsior Hotel?***

11.2 I can only reflect on the contents of the document as I have no recollection of the events it describes. From the note of the meeting it would appear that a significant number of haemophilia centre directors were invited.

(ii) ***How did Immuno utilise either of Dr. Eibl's methods to reduce or remove Non-A Non-B Hepatitis? How were Dr. Eibl's studies and trials initiated and funded?***

11.3 I have no recollection of these inactivation methods. I am also reasonably certain that no clinical trials in relation to these methods took place in the UK, as I think I would have been aware of them if they had taken place.

(iii) ***It is stated that adult haemophiliacs would not benefit from the trial but would be 'sufficiently public spirited to agree to these materials being used on them'. Did you agree? In your view, did the public benefit outweigh the risk to those individuals?***

11.4 See my comments above. I cannot recall any trials of this kind in the UK. I am unable to comment on this point from my own knowledge and experience.

(iv) ***In the summary, it is stated that 'all batches of NHS and US commercial concentrates had been shown capable of transmitting Non A Non B Hepatitis' but that there was only a 'one in fifty chance of transmission from cryoprecipitate'. To the best of your knowledge, when, in your view, did Immuno become aware of this information?***

11.5 I do not recollect anything about this meeting and I cannot remember being made aware of this specific observation.

(v) ***On page 2, point 7 it is stated that the removal of Hepatitis Non-A Non-B, Hepatitis B and other viruses would be tested for the effect of the method on their clearance 'later on'? To the best of your knowledge, how did Immuno prioritise this?***

11.6 As I have noted already I have no recollection about this meeting.

12. ***To the best of your knowledge, what advisory or decision-making structures were in place at Immuno to assess the risks of infection associated with the use of blood and/or blood products?***

12.1 Please refer to my answer to question 5 above.

13. ***When did you become aware of the risk of hepatitis in products produced by Serological Products Ltd. and by Immuno specifically?***

13.1 I cannot remember being aware of the risk of hepatitis specifically associated with IMMUNO AG's products. I cannot remember receiving any reports in the UK from hospitals. Prior to 1984 this would have been my predecessor's responsibility, but I think that I would have been made aware of any reports. As I have already noted, I think I can remember at some point clinicians saying that some patients had a mild form of hepatitis after using factor concentrates. I am not sure exactly where or

when I was aware of this fact and I do not think it was a comment made in relation to an IMMUNO AG product specifically.

14. ***To the best of your knowledge, what was your understanding of the effect, if any, of studies and articles carried out and written in the 1980's by writers such as Manucci, on Immuno's knowledge of hepatitis?***

14.1 I cannot remember the articles in the 1980's by writers such as Manucci. I do not recall having any contemporary knowledge of the detail of such studies and articles.

14.2 On the basis of the documents given to me to read I can see Mrs Kunschak from IMMUNO AG reported on studies with steam/vapour treated products during the meeting at NIBSC on 30 March 1988. [Reference CBLA0002406 page 5.] On the basis of this document rather than my own personal recollection I see that she reported 0/97 seroconversions with anti-HIV, 0/65 cases of Non A Non B (using ALT) and 4/37 seroconversions with Hepatitis B (HBV). The HBV cases were thought to be related to the fact that HBV was endemic in the area of the trial in Italy. When products from the same batches were then tested on laboratory animals at IMMUNO AG there was no evidence that the animals contracted HBV.

15. ***Insofar as you are able to do so, please provide a chronological account of the steps taken by Immuno during your employment to reduce the risk of people being infected with hepatitis (in particular Non-A Non-B Hepatitis) in consequence of treatment with Immuno products. Please consider the following document to assist you in your response DHSC0003896_158.***

15.1 I do not have the specific knowledge to be able to answer this question. Please note that the reference DHSC0003896_158 in this question relates to diagnostic products for laboratory use and not to therapeutic pharmaceutical products for use in patients. I do not think the document referenced has relevance to the question asked. However, as noted above, when I started working for Serological Products Ltd I was aware

of protocols for testing donors, donations and pools, which I think evolved as testing procedures were developed.

16. ***What if any steps were taken by you and, in so far as you recall, by Immuno more generally, to ensure that:***

(a) ***NHS bodies and/or clinicians purchasing and/or using Immuno products were made aware of the risks of hepatitis?***

(b) ***Patients treated with Immuno products were made aware of the risks of hepatitis?***

16.1 The Data Sheet was the key document that we used in our discussions with doctors. Any contraindications and warnings would form part of the Data Sheet and Pack Insert. I include an example of a Data Sheet as **[Exhibit SHPL0000067_009].**

16.2 These documents had to be agreed between the company and the MCA as part of the product licence. We had no direct contact with patients.

HIV and AIDS

17. ***Please refer to the summary of discussions of a meeting held at Excelsior Hotel, Heathrow Airport on 24 January 1983, at question 11 above. Representatives of Immuno were present and it is noted that it was stated that 'the possibility of reducing the risk of AIDS was not known at this stage. In any case it is not known if AIDS is caused by a virus or an attacker inimical to T cells' RFLT0000050, pp 2-4. To the best of your knowledge:***

17.1 I cannot remember being at the meeting at the Excelsior Hotel meeting on 24 January 1983 or remember any of the topics noted so I have no direct personal recollections of the discussions.

(a) ***What was your initial knowledge and understanding of HIV (previously known as HTLV-III) and AIDS? How and when did you***

first become aware that there might be an association between AIDS and the use of blood products?

17.2 I cannot remember what my initial understanding of HIV was beyond what was generally known and in the public domain or when I was aware of the association of HIV infection and blood products. Looking at the documents the Inquiry has asked me to review I note that the cause was not understood in January 1983 [See RFL 00000050]. Then there was a later realisation that there might be a connection to blood products but I cannot specify when I knew that.

(b) ***When did you become aware of the risk of HIV and AIDS in Immuno products specifically?***

17.3 I cannot remember being aware about HIV being related specifically to IMMUNO AG's products but I do recall an effort by the industry and the Department of Health to attempt to address HIV transmission in factor concentrate products by heat treatment [See documents SHPL 000000067_028 and IPSN0000376_004].

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

17.4 See my answer to (a) above.

18. ***To your knowledge, what enquiries and/or investigations did Immuno 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 wish to consider DHSC0003896_158 when answering this question.***

18.1 Please note that the reference to DHSC0003896_158 refers to Immuno AG's diagnostic reagents for laboratory use and not to therapeutic pharmaceutical products. These diagnostic products would not be used by patients or used in any treatment. I think that at that time there was a concern regarding possible HIV transmission through the mere handling of the reagents.

18.2 In terms of what enquiries or investigations were undertaken, I do not have the knowledge to be able to answer the question.

19. ***To the best of your recollection, what were the early steps taken by Immuno in response to the concerns about AIDS and blood products? You may wish to consider PARA0000001 and IPSN0000246_003 when answering this question.***

19.1 I cannot recollect this information, please see my answer to 18 above. Again please note that the reference IPSN0000246_003 associated with this question refers to IMMUNO AG's diagnostic products for laboratory use and not to therapeutic pharmaceutical products for patient use.

20. ***Insofar as you are able to do so, please provide a chronological account of the steps taken by Immuno during your employment to reduce the risk of people being infected with HTLV-III, HIV and/or AIDS as a consequence of treatment with Immuno products.***

20.1 Please remember that Immuno Limited was a distributor of products and so I had no involvement in the detail of product research and development and so I do not have the specific knowledge to be able to answer this question. Please note my comments above in answer to question 17.

21. ***Please refer to the internal Immuno telex dated 15 December 1986 SHPL0000162_142 which notes that you and Mr Norman Berry require proof that the product, Gammabulin does not transmit AIDS in order for it to be sold after 31 December 1986. Please explain, to the extent that you can recall:***

21.1 I do not recall the telex and I see it was sent by Norman Berry.

(a) ***Why could the product not be sold after this date?***

21.2 I cannot recall why there was a suggestion that Gammabulin could not be sold after 31 December 1986. This product is normal intramuscular immunoglobulin and part of the immunoglobulin group of products. I am

not aware that it was implicated in HIV infection. My understanding was that the immunoglobulins were separated later in the fractionation process and that the effect of the procedures used in the process would inactivate any virus but I was not involved in the development or design of the production process. I am not sure how the request made was satisfied but I do not remember Immuno Limited ever having to stop selling the product. I think BPL also continued to supply a similar product.

(b) ***What was the process for the sale of products proved to be incapable of transmitting AIDS prior to this date?***

21.3 I am sorry but I do not understand this question.

22. ***What, if any, steps were taken by you and/or by Immuno more generally to ensure that:***

(a) ***NHS bodies and/or clinicians purchasing and/or using Immuno products were made aware of the risks of HTLV-III, HIV and/or AIDS?***

(b) ***Patients treated with Immuno products were made aware of the risks of HTLV-III, HIV and/or AIDS?***

22.1 See my response to Question 16. I think NHS bodies, clinicians and directors of the haemophilia centres in particular were knowledgeable about the science and our discussions with them about products would be based around the product Data Sheet, an example of which I include as **[Exhibit SHPL0000067_009]**

Section 3: Blood supply, donors and screening

23. ***To the best of your knowledge, where and from whom did Immuno obtain source plasma and how did this change over time? Please provide details and identities of sources where you are able to. You may be assisted in your response to these questions by the documents enclosed at MHRA0033321_085, PARA0000001 and SHPL0000067_057.***

23.1 To the best of my recollection initially plasma came from IMMUNO AG plasmapheresis centres in Austria and Germany. At a later date IMMUNO AG also processed plasma from FDA licensed plasmapheresis centres in USA. I am not sure whether these were IMMUNO group managed centres or were run by other companies. My understanding was that all plasma sources met the same IMMUNO specifications and similar tests were carried out on donors and plasma. Certainly in the late 1980's I was aware of the IMMUNO group owning their own plasmapheresis stations in the Mid-West USA and were opening up new stations.

Please explain:

(a) ***How was the risk of using source plasma from the United States (i.e. paid donor), weighed against the benefit of its lower price? What weight was given to each factor, and what if any other factors were considered in the decision making?***

23.2 At the time Immuno Ltd started supplying Kryobulin made from USA sourced plasma, it was my understanding that IMMUNO AG did not perceive that there was any difference in quality between their European and USA sourced plasma. However there was a significant difference in price between the Factor VIII products which were made from the two sources. Once Kryobulin made from US sourced plasma was made available in the UK, it quickly outsold the Kryobulin product sourced from European plasma though both were available in the UK.

(b) ***The Inquiry understands that packaging of Immuno's blood products was made distinguishable by colour depending on the source. Why was this felt to be necessary? Would you agree that the differentiation of the colour of packaging equated to an acknowledgement of risk? Was it clear to the consumer what the difference in colour denoted? Please be advised that the following document is of poor quality, however it may assist by way of reference SHPL0000071_066.***

23.3 I think it was only Kryobulin which had different colour packs and I do not recall being involved in the decision making concerning the different colour of the packs. I do not recollect that there was ever any intention to denote a difference in quality. I don't recall that Immuno Limited ever promoted advantages of European plasma over US Plasma. The difference in colour packs was as far as I recall simply to clearly identify the packs and batches in house and for customer Haemophilia centres, which had been supplied with Factor VIII derived from European plasma, and who wanted to remain with the product they were familiar with. When Factor VIII products derived from USA sourced plasma became available Immuno UK Limited differentiated the packaging of the products. The UK Licensing Authority agreed to this identification. The product licence for Kryobulin in the UK was the same licence for both European and American derived Factor VIII.

(c) ***Was US and European source plasma combined for some products? Was this considered to increase risk? The document enclosed at SHPL0000010_062 may assist in your response.***

23.4 I am not sure whether European and USA plasma was combined in IMMUNO AG products supplied to the UK market.

23.5 I note during the hearings relating to Immuno, on Friday 24 September 2021, that Counsel to the Inquiry referred to a memo written by Dr Jones document PJON0000055_001. I have now been provided with a copy of this document. The memo records the suggestion that Immuno AG were using US sourced plasma in the Kryobulin which was made from European sourced plasma. Reference to this suggestion reminded me that I was made aware in around 1979 that a comment had been made to one of our field staff, that our 'Red' Kryobulin sourced from European plasma, actually included US sourced plasma. I knew this was wrong but did not know where the idea had come from and I recall specifically discussing this comment, which had been

picked up in the field, with Dr Schwarz at Immuno AG who categorically confirmed to me that only European sourced plasma was used in the 'Red' Kryobulin.

24. ***Please set out your understanding of Immuno's use of pooled plasma in its factor concentrate products.***

24.1 Please note my comments above. Beyond the answers already provided I do not have the knowledge or expertise to answer in more detail.

25. ***Please set out your understanding of Immuno's assessment of the link between the number of donors and the level of risk of transmission. Please also set out your understanding of the infection risk a single donation, when pooled, could pose to an eventual recipient. Please consider these documents to assist you in your assessment: SHPL0000008_086 and SHPL0000008_037.***

25.1 Please note my comments above. Beyond the answers already provided I do not have the knowledge or expertise to answer in more detail.

26. ***Please set out your understanding of Immuno's donor testing and screening policies from the years 1970 to 1990, having regard to reducing the risk of transmission of HBV, HCV and HIV. Was there a difference in testing depending on location/source? Please consider the following documents to assist you in answering this question: SHPL0000065_004,SHPL0000008_048-p.3, SHPL0000012_007-p.3, SHPL0000311_053, regarding US and Austria and SHPL0000005_002, p.4 regarding West Germany.***

26.1 I no longer have the knowledge to be able to answer this question. My understanding was that all testing of donors and products was equivalent whether made from US or European plasma, though I see, from document SHPL0000311_053 which I wrote in July 1990 based on information from colleagues in Austria, that at least in 1990 there were some restrictions under FDA rules which applied to testing.

Section 4: Reduction of Risk including viral inactivation and heat treatment

27. ***To the best of your knowledge what methods of testing were used on Immuno products and how did these change over time?***

27.1 Please note my answers given above. In the UK we were the distributor not the manufacturer so my knowledge is limited.

ALT Testing

Please set out your understanding of Immuno's policies regarding ALT testing as a measure to reduce the risk of HCV. You may wish to consider the following telex communication of 24 February 1986, regarding your recent visit SHPL0000065_037.

27.2 I cannot recall the visit that is referred to in this document. From memory I do recall that raised ALT levels might have indicated a variety of conditions. I think donors were removed from donor panels if ALT levels were above a certain value though I am not sure what the levels were. ALT testing may have been referenced in our early Data Sheets. I am not sure if ALT testing was noted in our product licences. This information about ALT testing would probably be included in the product licence files which may still be held by the MHRA.

Heat Treatment

Early Efforts

28. ***To the best of your knowledge please outline what efforts were made by Immuno in the early 1970s and 1980s to prevent transmission of HBV, HCV and HIV viruses, including any major trials or studies with which it was involved.***

28.1 Again given that I worked for the distributor not the manufacturer my knowledge in this area is limited. I do not recall being aware of major trials or studies in the UK involving IMMUNO AG's products. I think most clinical data from trials would probably come from other countries.

29. ***According to a letter from Mr Norman Berry, the Managing Director of Immuno to Professor Bloom BPLL0001351_119 dated 20 June 1983, it appears that Immuno continued to progress with the method of reducing transmission of Non-A Non-B Hepatitis outlined in the discussions held on 24 January 1983 RFLT0000050. To the best of your knowledge:***

(a) ***What were the inactivation methods referred to as generation one and generation two?***

(b) ***Why was the 'first generation' heat treatment method only focused on removing Non-A Non-B Hepatitis? Please see RFLT0000050 p. 3 paragraph 7.***

(c) ***Were these efforts to reduce the risk of Non-A Non-B Hepatitis transmission successful?***

29.1 I have already noted in answer to earlier questions about this meeting and the notes of the discussions, that I have no recollection of attending the meeting or knowledge of these discussions and therefore I am unable to comment. I have no recollection or understanding of what is meant by the 'generation' 1 and 2 inactivation methods mentioned.

Dry Heat Treatment

30. ***The UK Licensing Authority advised Immuno Ltd on 26 November 1984 that dry heat treatment methods should be implemented for blood products [SHPL0000067_028]. You then corresponded with the Licensing Authority [SHPL0000271_021] at the beginning of 1985 regarding the decision to introduce heat-treated fractionated products. To the best of your knowledge:***

(a) ***When was dry heat treatment first implemented and marketed by Immuno?***

30.1 From the reference documents provided by the Inquiry it would appear that Immuno Limited submitted a product licence amendment for Kryobulin in December 1984 in the UK and it was

approved on 7 February 1985. Looking at document SHPL00000670_011 I think that Kryobulin dry heat treated was supplied unlicensed from December 1984. I think that UK licensed stock would have been available possibly as early as March or April 1985.

(b) ***If a first generation heat treatment method was available in June 1983 BPLL0001351_119, why were applications to change product licences to include heat treatment only submitted in 1984? You may wish to consider SHPL0000377 and MHRA0033320_066 in respect of Prothromplex and Kryobulin respectively, when answering this question.***

30.2 I do not remember being aware of the 'first-generation' heat treatment method or the other ideas for virus inactivation which were discussed.

(c) ***The document enclosed at SHPL0000048_026 at p.1 paragraph 2 refers to the unofficial judgment that the information submitted by Immuno in respect of Kryobulin for a product licence modification was most inadequate and but for the panic situation to get everyone on to heat treated material as quickly as possible, it would not have been granted. Do you recall this situation? How would you describe the panic situation? What was your understanding at the time of its implications for the safety of products which were approved during this period? Do you agree that it led to the approval of inadequately inactivated products?***

30.3 I cannot remember reporting that the company had been told that the submission was inadequate but, having read document SHP0000048_026, I must have been aware of this.

30.4 I think the 'panic situation' referred to the desire by the Department of Health for all companies to heat treat their products and file for licence amendments as soon as possible to enable these viral inactivated products to be widely available.

(d) ***If not directed otherwise, what is your view as to whether Immuno would have chosen a different heat treatment method such as wet heat?***

30.5 Again, given my role, I regret that I do not have the knowledge to answer this question. IMMUNO AG did switch most production to steam heat treatment by 1986.

(e) ***If Immuno had not followed the Licensing Authority's advice, would there have been any repercussions for the company? How, if at all, did this weigh in the company's decision making regarding this issue?***

30.6 I do not know what the repercussions would have been if we had not followed the Licensing Authority's advice. I do not recall what IMMUNO AG's considerations were. I think the concern in the UK was to have heat treated product available to patients as soon as possible. I am not sure how much evidence of HIV inactivation was initially submitted and I cannot remember what claims were made with the initial dry heat products.

31. ***In your opinion, how confident was Immuno that the dry heat treatment method used on Kryobulin and other products effectively removed HIV and/or HBV and/or HCV infections? Was one particular virus the focus of Immuno's risk reduction efforts in the early/mid 1980's? What relative importance was given to the reduction of risk of transmission of HIV? Please refer to these documents to assist you in your response: IPSN0000376_004, and IPSN0000246_003.***

31.1 I regret that I do not have the knowledge or expertise to answer this question.

32. ***In your experience whilst employed at Immuno, what was the process for 'returns' of blood products being used or reused when 'updated' heat treated alternatives were available? You may be assisted in your response by the documents enclosed at SHPL0000067_030 and SHPL0000068_035.***

32.1 Once a new or amended licence is granted then the old product cannot be sold. As far as hospitals were concerned, from memory, our approach was to exchange old licensed stock for new licensed stock. I do not know what IMMUNO AG did with returned products.

Steam/Vapour Heat Treatment

33. ***Please consider the Immuno telefax from yourself to Mr Norman Berry dated October 1985 enclosed at SHPL0000050_013. It appears that Immuno had discovered that steam treatment was 'superior' to heat treatment and there was interest in replacing that method with the steam treated product. Please answer to the best of your knowledge:***

(a) ***Was the superiority of steam treated products proven? You may wish to consider SHPL0000050_011.***

33.1 Steam treatment was an IMMUNO AG method. I recall that it was patented in some countries. I cannot remember details of the inactivation data produced for steam treated products compared with dry heated products. Steam treatment had been licensed in many countries where IMMUNO AG supplied factor concentrate except the UK.

33.2 As most other markets which IMMUNO AG supplied had changed to steam treated products, IMMUNO AG no longer wished to produce dry heated just for the UK.

(b) ***Following the implementation of steam treatment, in light of the Licensing Authority continuing to consider dry heated applications, when were (dry) heat treated products removed from the market? Did you consider, or were you aware that it was considered more generally, that there was an increase in risk in relation to dry heated products? You may wish to consider the following documents: MHRA0033319_001 and SHPL0000313_066.***

33.3 By the time dry heat treatment was licensed in the UK in 1985 Immuno Limited was only selling small quantities of Factor VIII and was not a

major supplier in the UK. As I have said before, I think that IMMUNO AG also wanted one product, Kryobulin STIM3, for all countries and so Immuno Limited stopped selling Kryobulin TIM2. Immuno Limited tried to licence Kryobulin STIM3 in the UK but there were difficulties with meeting the Department of Health's requirements as I think were noted in minutes of a meeting from 3 November 1987 [SHPL0000008_108].

33.4 There was limited demand for Prothromplex as BPL was generally self-sufficient in their equivalent product. I think Prothromplex TIM4 heat treated and then steam treated versions may have been sold unlicensed in small quantities for a short time when BPL did not have stocks of an inactivated product.

(c) ***Why did Feiba only become available as a steam heated product in July 1986? You may wish to consider SBTS0000330_115.***

(i) ***What impact would this have had on the competition and estimated sales?***

33.5 I am afraid I do not understand the question regarding timing and availability. The change to steam treated Feiba appears to be consistent with availability in other countries.

34. ***To the best of your ability, please provide an explanation for the suffix after the name of Immuno products e.g. 'TIM 2', 'TIM 3'. Please see the Telex from you to Mrs Diernhoffer and Mrs Henniger dated October 1985 to assist you SHPL0000050_012.***

34.1 I remember that the terminology used for the various treatments was very confusing and did change. From memory I think TIM stands for 'thermal inactivation method'. TIM2 was dry heated 'method 2' which I think was the first heat treated version of Kryobulin licensed in the UK. I am not aware of a dry heat TIM3 Kryobulin product in UK. Feiba and Prothromplex used a TIM4 dry heat at a higher temperature.

34.2 STIM 'steam thermal inactivation method' was a steam treatment. I think Immuno Limited only sold the Kryobulin STIM3 as an unlicensed

product for use on a doctor and named patient basis for a short period and then STIM4 for Feiba and Prothromplex again as unlicenced products for the reasons explained above.

35. ***Please outline to the best of your knowledge the difference between 'moist heat treatment', 'steam heat treatment' and 'vapour heat treatment'. Please consider these documents to assist with your answer: SHPL0000008_108, MHRA0033320_032 and SHPL0000176_007.***

When responding please consider:

(a) ***How did these methods differ (if at all) in terms of risk?***

(b) ***What was 'unique' about Immuno's vapour heat treatment method? See SHPL0000176_007.***

35.1 I am not aware of the term moist heat but steam treated and vapour treated were the same. I think the UK authorities did not like the name vapour heated and wanted the name changed to steam treated. The name vapour heated was used in other countries. I think the method may have been a unique IMMUNO AG method and as noted above I think it was patented by the company.

36. ***In your opinion, how effective was the steam/vapour treatment and how confident was Immuno, that steam treatment and/or vapour treatment reduced the risk of HIV and/or HBV and/or HCV infections? Please consider the following documents ranging from the mid 1980's to the early 1990's to assist with your response SHPL0000050_011, DHSC0003896_158 and SHPL0000008_086.***

When responding please answer the following:

(a) ***How, if in any way, did confidence in this inactivation method impact progress on other methods, such as testing?***

(b) ***What, if any, further studies were undertaken by Immuno to ensure the reduction of risk and how much discretion did Immuno have when choosing their studies?***

36.1 For the reasons I have already stated I do not have the relevant knowledge or memory to answer this question.

37. ***Please consider the enclosed letter dated 31 July 1991 from you to Dr Schwarz SHPL0000106_094, p. 1 and the Minutes of a Meeting between Immuno and the Medicines Control Agency ("MCA") held on 08 October 1991 SHPL0000106_080 where you discuss the serious problem Immuno is having with Kryobulin Vapour Heated and that it would be unable to show significant improvement from dry heat. To the best of your ability, please explain:***

(a) ***Why were there issues with vapour heat treatment in 1991?***

(b) ***As the vapour heat treatment process was previously described as unique, in your opinion why was the MCA unhappy with the method?***

(c) ***Why had the vapour heat inactivation method not improved further than dry heat treatment which was developed earlier?***

(d) ***In your opinion, should Immuno have been developing 'new generation products'?***

37.1 I can remember very little about the various discussions on IMMUNO AG inactivation methods and other issues with the UK Licensing Authority. Whilst I did attend some meetings with or without regulatory staff from IMMUNO AG, I cannot recall any context for those meetings or any details. I am also aware that with the passage of time I no longer have the technical knowledge I once had to be able to fully understand these issues now. It appears from the documents referenced that some information had not been made clear in the application. I recall that sometimes we had to wait for IMMUNO AG to compile data specific for the UK and quite often when the data initially requested came it was no longer sufficient for the UK authorities and we needed to go back to IMMUNO AG to obtain additional data. We seemed to be often trying to catch up with the Licensing Authority in the UK asking for more information from IMMUNO AG. I think I expressed concern about delays

in some of my correspondence. However the steam method had already been licensed in some European countries including Ireland and I think that steam treated Feiba was licensed in the USA by this time.

37.2 On the basis of the documents referenced I think we were starting with a new abridged application for Kryobulin steam treated. The data required and views of the UK Licensing Authority had changed since the original licence was granted for Kryobulin TIM2 and I think that all the requirements were not communicated to us until the application was submitted and reviewed. My recollection is that the UK Licensing Authority asked for additional data that was not needed for other markets which I recall would take considerable time to acquire and then present in a form to meet UK requirements.

38. ***Please outline to the best of your knowledge the challenges Immuno faced and its response regarding reducing the risk of transmission of hepatitis, particularly in light of the alleged seroconversions reported in various articles/journals from Immuno products. Please consider the following documents ranging from the mid 1980's to early 1990's to assist with your answer: SHPL0000065_037, SHPL0000141_131, SHPL0000014_001, CBLA0002406, SHPL0000102_117.***

38.1 I cannot recall the articles on seroconversions. It would appear from CBLA0002406 that Mrs Kunschak from IMMUNO AG Clinical Trial Department commented on these studies. Please see my comments made in response to Question 14.

Delay in Responding

39. ***Do you accept that there was a delay in obtaining viral inactivation data for Immuno products? If so, please explain to the best of your knowledge what effect, if any, this had on the safety, licensing, and sales of Immuno's blood products. Please consider the following documents from the late 1980's to assist in your response: SHPL0000141_097, SHPL0000141_086, SHPL0000010_005 and SHPL0000106_172.***

39.1 There was a delay in providing some data. In many cases whilst the data may have already existed in some form, it was a case of accessing it and organising it for submission to the UK Licensing Authority.

39.2 I recall that Immuno Limited's sales of Factor VIII had reduced significantly into the 1980's due to price competition and increased availability of BPL supplies. I refer to the telex of 8 October 1985 which notes the sales estimates I had provided for 1986 for Prothromplex and Kryobulin being 'very low' and records that I had suggested might 'even be reduced to zero'.

40. ***Please explain to the best of your ability the rationale for the Department of Health and Social Security ("DHSS")'s approval of Immuno's licence for a non-heat treated product and dry heated product between 1989 and 1991. Please consider these documents to assist you with your answer: [SHPL0000141_098], SHPL0000175_009, SHPL0000106_165, SHPL0000106_161, and SHPL0000311_014.***

Please consider:

(a) ***Whether in your opinion the licensing and/or attempt to license a non-heat treated product increased the risk of infection, particularly when heat treated products were readily available?***

(b) ***Was the DHSS aware of these products being marketed/licensed? If not, how and why did this occur?***

40.1 The referenced documents relate to Kryobulin, Prothomplex and Feiba licences. At this time Immuno Ltd was not supplying Prothromplex non-heat treated factor concentrates in UK and it was not available from Immuno AG. Looking at notes of a meeting I had in Vienna on 21 June 1988 [SHPL0000141_098] it looks like the intention was for Immuno Limited to apply to the UK Licensing Authority for renewal for Prothomplex on the basis that it would be submitting a variation to that licence to convert it to the STIM 4 product. This procedure was probably carried out so that a completely new application was not required and

the non-heat treated licence could be changed with a variation. I think that the licence for Prothomplex was later cancelled.

Adverse Reaction Reports

41. ***Please set out your understanding of Immuno's policies regarding adverse reaction reports of blood products and the requirements regarding these. Please consider these documents to assist you with your answer: SHPL0000005_086 and SHPL0000005_016.***

41.1 The requirements for adverse reactions reporting are stated in the product licence. There are general ADR 'adverse drug reaction' reporting requirements for all pharmaceuticals but new products when first licensed could have additional requirements specified by the Licensing Authority. The two referenced documents with this question refer to the supply of bulk Plasminogen Vapour Heated from IMMUNO AG to Beecham to incorporate into a formulation for one of their finished pharmaceuticals. There were obligations in the licence granted to Immuno Limited for ADR reporting. There was also ADR reporting requirements in the Beecham product licence for their finished product. Immuno Limited ensured in the contract with Beecham that any ADR's would be notified to each company. I am not aware of any ADR's being reported to Immuno Limited by Beecham or from Immuno Limited to Beecham.

Withdrawal/Surrender

42. ***Please consider the internal Immuno letter written by you SHPL0000148_001, dated 24 March 1992. Please explain to the best of your knowledge why you believed there was "no way" that Immuno could use these two blood products in the future, causing their licences to be surrendered in 1992?***

42.1 The Kryobulin licence was for a dry heat treated product and the Prothromplex licence was for a non-heat treated product. As noted

above, to the best of my recollection, we had not been selling these products for several years and they were really just redundant licences.

42.2 It would appear that there was a licence review and the licences would be cancelled. I think that IMMUNO AG had decided that they did not want to renew the licences in the UK for reasons I have already noted above.

43. ***Please provide a detailed chronology of any steps taken by Immuno in response to reports of seroconversion following treatment with blood products and of any withdrawals of any blood products in the UK. You may wish to consider the documents enclosed at BNOR0000368 and SCGV0000155_065.***

43.1 I cannot remember being involved in the recall of any products due to reports of seroconversions.

43.2 The documents referenced in this question relate to a German licensed plasmapheresis station. From memory there was an inspection by the authorities in Germany and a review of their procedures. The raw material plasma had been used in the manufacture of certain batches of Gammabulin and 4.5% Human Albumin Solution for the UK. These were both products that to my knowledge were not implicated in viral transmission. Batches had been tested by NIBSC before release on to the UK market. However, as a precaution, IMMUNO AG decided to recall all batches in the UK. We informed the MCA that we were carrying out a recall and detailed the steps being taken. We issued a recall notice to all customers and other interested organisations. As far as I can remember all stock recalled was returned to IMMUNO AG. The Immuno Limited batch retrieval system could trace where every delivery of the specific batches had been made. All customers were telephoned the same day and stock was replaced with new batches.

43.3 I cannot remember any other product recalls.

Section 5: Communication and notification of risk

44. ***Please explain to the best of your knowledge Immuno's efforts to communicate the risk of infection to patients, clinicians and other purchasers of blood products. How did this evolve over time? Please consider the enclosed document SHPL0000162_085 when responding to this question.***

44.1 Any precautions or warnings for Immuno Limited's products or which were required by the UK Licensing Authority would be included in the Data Sheet and the pack insert leaflet. The clinician would have the contact with the patient.

44.2 The document referenced in relation to this question is about Albumin product licences in Ireland. These products have always been pasteurised. It would appear that some companies were using albumin as an additive in other pharmaceutical preparations. The NDAB Licensing Department in Ireland were asking for confirmation that all our albumin sold in Ireland was pasteurised.

45. ***Please explain to the best of your knowledge Immuno's policies regarding communication of risk, including via warnings on packaging and data sheets.***

(a) ***How, if at all, did communication of risk change over time?***

45.1 Cautions and warnings were given on the Data Sheet and Pack Insert. These were updated as circumstances changed. This could be initiated by the company or Licensing Authority but all changes had to be approved by the Licensing Authority. I have already commented that the Data Sheet was the basis for our communications with clinicians.

(b) ***What was the difference between UK neutral and UK specific texts? Please consider SHPL0000066_001, at pages 4 and 27.***

45.2 UK specific text would have been text specifically produced for the UK as part of the product licence and approved by the UK Licensing Authority. 'Neutral' texts would be the standard text where a specific country document was not required. It would be the starting point for UK

texts but would have to be adapted to meet UK requirements and layouts.

(c) ***How much was the UK Licensing Authority involved in these decisions and what would have been the repercussions of a failure to comply with its views? You may wish to consider the following documents: SHPL0000665_092, SHPL0000271_021 and SHPL0000163_017.***

45.3 To the best of my recollection, the UK Licensing Authority had complete authority to ask the company to alter or change the pack insert and Data Sheet. If we did not comply then they would not issue a licence or renew an existing licence.

(d) ***What were Immuno's processes to ensure warnings were updated and were these efficient? What factors or entities may have contributed to these delays? Please see SHPL0000075_020.***

45.4 I am not sure what is meant by reference to delays in this context as the document referenced is not about warnings specifically.

46. ***Please consider this memo of a discussion on 17 October 1985 at which you were present SHPL0000050_011. With regards to a clinical trial certificate for Prothromplex TIM 4, steam treated, the memo states 'for this Product, we may claim that it does not transmit non-A/non-B hepatitis'. Please explain this remark. Did you consider that it was factually correct at the time?***

46.1 The note of the discussion I see was prepared by Mrs Diernhofer. I am not aware of such an absolute claim or the underlying rationale for it. As far as I am aware we did not apply for a Clinical Trial Certificate in the UK.

47. ***Please consider this letter from you to Mrs Diernhofer at Immuno AG dated 25 November 1987 in which you express concern due to a contradiction included in the warning statement which states the product is 'safe' with regard to transmission of HIV SHPL0000008_097. To the***

best of your knowledge, did the warnings/statements included on or with Immuno products of viral transmission accurately reflect the level of risk?

47.1 This letter relates to bulk Plasminogen Vapour treated for Beecham. It would appear from the letter I wrote that we sent Beecham a draft statement. I was pointing out the contradiction in the statement and giving my opinion on the use of language. I think that the UK Licensing Authority would have challenged such an absolute assertion even if there was supporting data.

48. ***Do you accept that some packaging was incorrect or made no claims regarding risk? If so, please explain why this occurred. You may find these documents can assist you in your response SHPL0000068_016 and SHPL0000354_056. Please also explain:***

48.1 After seeing my letter I have some recollection of this issue. I think that this was at a time where IMMUNO AG were supplying many countries with different heat/steam treated products. I think this was a supply chain error. There was a major effort to try and get inactivated products out to all companies and the wrong product and packaging were sent to the UK.

(a) ***Whether this was a regular occurrence?***

48.2 I do not recognise this situation occurring on a regular basis at all. To the best of my recollection this was a very unusual situation.

(b) ***In your opinion, how, if in any way, could these omissions and mistakes have led to an increased risk of transmission?***

48.3 Based on my experience these supply errors would not have led to any increased risk of viral transmission. This is because all products coming into the UK, both licensed and unlicensed, are quarantined. They are only released for sale following an internal batch release by the Qualified Person. This check ensures that the batch meets all aspects of the product licence and the batch protocol. Also the batch, if licensed,

has an NIBSC batch release. Packaging is also checked. Knowing this process I feel confident to assume that the issues identified in the letter would have been discovered during this process.

(c) ***Why did you suggest the deletion of references to source material in package inserts?***

48.4 I can't recall why I raised this question. Some of our products were from European plasma and some from USA plasma. My understanding was that both were equivalent.

48.5 Please note that the second half of the telex SHPL0000068_016 refers to diagnostic plasmas for use in assays in laboratories and not for therapeutic use in patients.

49. ***Please explain to the best of your ability and recollection what external policies, guidance and/or obligations were placed on Immuno to provide information about the risk posed by products relating to HCV, HIV and other infections to:***

(a) ***The licensing authorities;***

(b) ***Clinicians and other purchasers of blood products; and***

(c) ***Patients.***

How, if in any way, did these change over time?

49.1 I cannot recall what external guidance and obligations were placed on Immuno Limited to specifically provide information about the risk posed by products relating to HCV, HIV and other infections other than what was required to be provided in the product Data Sheet. I was not a lawyer so I didn't have detailed knowledge of any legal requirements beyond the requirements related to licensing.

50. ***Do you recall any instances of research relevant to the risks of HCV, HIV and other infections posed by Immuno products, or knowledge of risk more generally, which were known to Immuno or to yourself but not***

widely published or disseminated? If so, why were these not widely published or disseminated?

50.1 I do not recall instances of research relating to the risks of HCV, HIV or other infections. Most research work relating to IMMUNO AG's products was carried out in Austria, Germany, Italy or the USA. Conducting or managing research was not part of Immuno Limited's remit. I was appointed Managing Director of Immuno Limited in 1984 and during that time I was not aware of any research on IMMUNO AG's coagulation concentrates in the UK.

Section 6: Interactions with External Bodies: the DHSS, Haemophilia Centres, UKHCDO and the Haemophilia Society

51. ***Please describe, in so far as you are able to, Immuno's relationship with the Department of Health and Social Security ("DHSS") including the Central Blood Laboratories Authority ("CBLA") during the period in which you were employed by Immuno and how, if at all, it changed over time. Please consider the following documents to assist your response: DHSC0002412_010 and SHPL0000067_004.***

51.1 We had a good professional working relationship with the DHSS. Both with the UK Licensing Authority for our product licences and the Medicines Inspectorate for inspection of our premises and systems. There were also visits by the Medicines Inspectorate to IMMUNO AG in Vienna.

51.2 We also had a good relationship with BPL (which I recall was under the authority of the CBLA) despite being a competitor. At times they would notify us about shortages if we were the only company that could supply the shortfall.

(a) ***In your opinion, was Immuno's perception of the DHSS as one of the most stringent licensing authorities for blood products correct? How did this affect Immuno's relationship with the DHSS? Please consider the document enclosed at SHPL0000008_108, p.1 in your response.***

51.3 I think it is fair to say that IMMUNO AG considered the UK Licensing Authority required more detail and sometimes different information in the applications than other countries. It was more difficult to obtain a licence in the UK compared to other countries. However I think having a UK licence for a product was valued by IMMUNO AG. The company usually did all it could to supply the information required.

(b) ***Were there particular individuals with whom Immuno had relationships at the DHSS which would have an impact upon Immuno's applications? See SHPL0000141_143.***

51.4 There was a small group of people dealing with licence applications for blood products at the MCA. We would usually deal with the same people each time. In my experience they were approachable and helpful.

52. ***Please set out your recollection of any specific interactions or meetings with the DHSS in which you were involved during the 1970s or 1980s (and in particular any interactions or meetings in which issues relating to the safety of blood products generally or Immuno products in particular, or where licensing processes or risks relating to hepatitis or HIV were considered). You may wish to consider the following documents: SHPL0000048_026 and SHPL0000075_020.***

52.1 I do not recall having any meetings at the DHSS in the 1970's. I did attend some meetings probably from mid to late 1980's when I started to become more involved in liaising on regulatory issues relevant to IMMUNO products. I do not have any memory of the content of the meetings. The central Regulatory Affairs department was based at IMMUNO AG in Vienna. They prepared all initial licence applications and variations. At Immuno Limited we submitted the data on their behalf and fed back any questions from the UK Licensing Authority. We would then submit the answers from IMMUNO AG back to the Licensing Authority. On occasions we had meetings with licensing staff to try and get a clearer picture of any additional data required so we could explain

any concerns to IMMUNO AG. For important meetings we would also have regulatory staff attending from IMMUNO AG.

53. ***Please describe, in so far as you are able to, Immuno's relationship with other pharmaceutical companies during the period in which you were employed by Immuno and how, if at all, it changed over time. You may wish to consider the following documents: IPSN0000376_004, SHPL0000010_056, SHPL0000313_028, DHSC0002412_012, BART0000566 and DHSC0002412_007.***

In particular, please explain to the best of your ability:

(a) ***What was the nature of Immuno's relationship with Beecham Pharmaceuticals and Bio/Blood Products Laboratories?***

(b) ***How much knowledge was shared between these companies?***

53.1 We had a relationship with Beecham as IMMUNO AG supplied them with bulk Plasminogen on a commercial contract between Immuno Limited and Beecham. Beecham used the Plasminogen as a component in one of their products. IMMUNO AG shared information on the manufacturing process with Beecham so that Beecham could licence their own finished product.

53.2 I am not aware of any relationship with BPL. There were discussions with BPL on possible collaborations but I do not think that these happened.

54. ***Please describe, in so far as you are able to, Immuno's relationship with clinicians and hospitals during the period in which you were employed by Immuno and how, if at all, it changed over time. You may wish to consider the following documents: SHPL0000068_035 and NHBT0096602_072.***

(a) ***In particular, what is your view regarding how Immuno considered complaints received from hospitals and notifications that the product was out of stock?***

54.1 Immuno Limited had field staff visiting, doctors, pharmacists and technical staff in relation to the range of pharmaceutical and diagnostic products supplied. I do not believe that the relationship changed over time. In my opinion Immuno Limited always operated in an ethical manner. All complaints were dealt with promptly by the appropriate person depending on the nature of the complaint. Any adverse reactions to products would be reported to the relevant authority. If there were any stock supply issues relating to a product then all customers would be notified.

55. ***Please describe, in so far as you are able to, Immuno's relationship with the Haemophilia Society in the UK during the period in which you were employed by Immuno, particularly any specific interactions or meetings, and how, if at all, the relationship changed over time. Please consider the following documents: HSOC0023097 and HSOC0012356.***

55.1 I think the Haemophilia Society asked Immuno Limited for an annual donation each year. I cannot remember how much was paid. I believe that all pharmaceutical companies donated in order to help fund the society and provide help and assistance to patients. Immuno Limited was pleased to do this.

55.2 Over the years there may have been the odd additional request for financial help for a specific project or for a local group event. We would respond to any requests for information. I did meet the Secretary of the Society at international haemophilia meetings. This relationship remained much the same over time.

56. ***Please:***

(a) ***Describe, in broad terms, Immuno's relationship with the UK Haemophilia Centre Directors Organisation ("UKHCDO") including Immuno's sales/marketing policies or strategies with regard to UK haemophilia centers/directors during the 1970s and 1980s. Please include a description of any arrangements which Immuno had for visiting centres/directors and any financial or non-financial***

assistance or incentives provided to centres and directors. You may wish to refer to the following documents SHPL0000141_097, SHPL0000141_086, SHPL0000010_005, and SHPL0000068_046;

56.1 Immuno Limited had no particular relationship with UKHCDO. I think the only contact we had was in relation to their annual conference and AGM when I recall that they asked all UK companies to provide some sponsorship to cover the costs of their meeting. The companies were not allowed to attend the actual meeting but were invited to attend the educational presentations. The companies were allowed to put up a promotional display stand at the meeting.

56.2 I note that some haemophilia directors attended the meeting in January 1983 as already discussed above, but I have no recollection of that meeting myself. As far as licensed coagulation concentrates are concerned, in the 1970's and 1980's our field staff would have visited haemophilia centres or their directors and other relevant departments, depending who was involved in the purchase of products.

56.3 We had a wide range of pharmaceutical products and we visited clinicians and technicians in many areas of the hospital. Haemophilia involved just one group of clinicians applicable to our range of pharmaceutical and diagnostic products.

56.4 Prices in the UK were generally lower than the rest of Europe and it was therefore difficult for Immuno Limited to compete on certain products. Stock was budgeted a year in advance so quite often too much success in selling a product would be met with problems in obtaining additional supplies. Albumin solutions were probably our main licensed sales products in the 1970's and 1980's.

56.5 I am not aware of any incentive arrangements at Immuno Limited or IMMUNO AG with clinicians or haemophilia centres either

financial or non-financial. Very occasionally we would consider a request for a contribution for assistance to travel to a congress, usually the World Haemophilia Conference which took place every two years. We had a general policy at Immuno Limited of not actively offering or promoting financial assistance. Any assistance granted did not relate in any way to current or potential sales. Any payments would be made to a hospital fund.

(b) ***Identify any particular haemophilia centre directors in the UK with whom Immuno had a close relationship, sought advice, provided consultancy advice to Immuno or who undertook research for or with Immuno in the 1970s and 1980s. Please provide details of those individuals, insofar as you are able to do so.***

56.6 We tended to keep the commercial aspects of the business separate from research which was managed by IMMUNO AG in Austria. My predecessor who started the business would be the contact in most cases between IMMUNO AG and any UK contacts and opinion leaders to discuss projects or obtain advice on topics which were of interest to IMMUNO AG. He would set up any meeting requested by IMMUNO AG. He continued this function when he became Chairman following my appointment as Managing Director. The only paid consultancy of which I was aware was arranged by my predecessor and that was with Professor Preston at Sheffield who gave advice on haemophilia, thrombosis and related diagnostic issues to Immuno Limited and IMMUNO AG. I think this arrangement was requested by IMMUNO AG so that they had the views of an opinion leader in UK. I had no involvement in this arrangement and I think it was terminated at some stage before I left the company. I was not aware or cannot remember of any significant research projects in the UK during my time as Managing Director.

Section 7: Licensing

57. ***Please explain to the best of your recollection whether it was common practice at Immuno to base UK product licence applications on***

information/studies used in other international markets. The following documents may be of assistance to you: SHPL0000008_068 and SHPL0000008_051.

57.1 Yes, I think it was. IMMUNO AG would include clinical data from products used in other countries as a basis for a product licence application. The two documents referenced relating to this question concern the commercial arrangement to supply bulk Plasminogen to Beecham for further processing into their final product. I think this was a steam treated product and licensed in the UK

58. ***To the best of your knowledge, what was the effect on Immuno of the EEC Directive, mentioned in Immuno correspondence in 1989, SHPL0000141_041 which brought blood products into the mainstream? Did it affect testing requirements in the UK? Please see the following documents which refer to the NDAB in Dublin, Ireland SHPL0000240_085 and SHPL0000119_026 and how this may bear on licensing within the UK in your response.***

58.1 Austria was not in the EU initially and therefore imports from IMMUNO AG based in Vienna were affected by the new directive. Products had to be tested and batch released by the country of first import. NIBSC testing qualified as the testing laboratory for batch testing. Both myself and Norman Berry had the status of 'Qualified Person' for Immuno Limited and would batch release products when they arrived in the UK. These procedures were accepted by the Medicines Inspectorate when they carried out their regular inspections in relation to our Pharmaceutical Wholesale Dealer's Licence. The Medicines Inspectorate also inspected IMMUNO AG as the manufacturer of the products. I cannot remember the issues raised in the documents from the NDAB in Ireland.

Unlicensed Products

59. ***Please set out your understanding of the processes in place at Immuno when products were supplied on an unlicensed or named patient basis.***

You may wish to consider the following documents when providing your response: SHPL0000218_002, SHPL0000078_010, SHPL0000067_030, SHPL0000067_026, SHPL0000141_097 and SHPL0000670_011.

When responding please consider:

(a) ***Why was this process used and how long would a product be unlicensed for?***

59.1 During my career and my time at Immuno Limited, the option of an unlicensed supply of a pharmaceutical product had always been available in the UK in that a doctor was able to prescribe any pharmaceutical for his patient. If the product was unlicensed then the clinician took responsibility for the treatment and it was ordered on a doctor and named patient basis. This means for a specific patient for use by a specific doctor. A product may be unlicensed because a licence application has not as yet been submitted, an application is in progress, or the company may not want to apply for a licence because sales in a country are extremely low. There may also have been exceptional circumstances where a product was supplied unlicensed because no equivalent licensed product was available, possibly due to a national stock shortage as I think happened in respect of Prothomplex. An unlicensed product supplied to the UK was usually licensed in other countries. A doctor may have heard about a product in a clinical paper or at an international medical meeting. I recall that it was not permitted to promote unlicensed products and field staff could not give out any literature. In my experience Immuno Limited always did everything it could to comply with the legal framework for the supply of unlicensed products. We kept records of all supplies on a doctor named patient basis and the names were entered on the invoice and delivery note to the customer. Internal systems for their supply were checked by the Medicines Inspectorate on regular inspections.

(b) ***In your view, how safe were unlicensed blood products in comparison to licensed blood products?***

59.2 Usually the products which were unlicensed in the UK were licensed in other countries and the reasons for not licensing in the UK were usually to do with volume of sales not issues of the quality of the product.

(c) ***What, if any, restrictions were imposed on Immuno by the Licensing Authority?***

59.3 A supply could be made direct from IMMUNO AG to the hospital at the request of a specific doctor for his patient. However if we wanted to hold stock of the product in the UK for potential orders then we had to obtain permission to import. I recall that the regulations, at least during some of my time at Immuno Limited, were that Department of Health required the company to give advanced written notice to them of the importation of products to be held in stock. I think they restricted the quantity to a certain number of treatment courses over a certain period. When the request was approved in writing to us we were able to import the stock and supply to a named doctor for his named patient.

(d) ***How did the use of this process affect Immuno's relationships with other organisations, referred to above?***

59.4 To the best of my knowledge it did not really affect Immuno Limited's relationships.

(e) ***To the best of your knowledge, were products sold unlicensed after being refused a licence on safety grounds? Please consider the document enclosed at SHPL0000106_094 to assist you in your response.***

59.5 I am not aware of products being sold on an unlicensed basis if the product licence had been turned down on 'safety grounds'. I think the licences referred to in the documents referenced in this question refer to variations to existing licences. However, to the best of my recollection, I do not think either Kryobulin or Prothromplex were being supplied on the UK market at this time.

60. ***Please provide your recollection of whether all blood products were sent to NIBSC for testing prior to their distribution? Did this apply to unlicensed products? The following documents may assist you in providing a response SHPL0000068_046 and SHPL0000085_027.***

60.1 Samples of every licensed blood product for UK and Ireland went to NIBSC for batch testing. We could only import and sell the batch once we received a batch pass certificate. NIBSC would not test unlicensed products as they did not have a final licence specification to test against.

61. ***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.***

61.1 I am not aware of any further matters that would be of relevance to the Infected Blood Inquiry.

Statement of Truth

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

Signed: GRO-C

Dated: 15th March 2022

Table of exhibits:

Date	Notes/Description	Exhibit number
March 1985	DATA SHEET re KRYOBULIN HEAT TERATED Dried Factor VIII Fraction B.P.	SHPL0000067_009

Witness Name: Mr Peter Coombes

Statement No. : WITN6409001

Dated: 15 March 2022

INFECTED BLOOD INQUIRY

EXHIBIT SHPL0000067_009 TO WRITTEN STATEMENT OF PETER COOMBES

Treatment of overdosage
No specific side effects have been reported following overdosage with Kryobulin (Factor VIII-activity above 120%). The half life of about 12 hours will rapidly normalise Factor VIII-activity in the patient.

pharmaceutical precautions: Kryobulin must be stored between +2°C and +6°C, and protected from the light. It then has a shelf-life of two years. When stored between +20°C and +30°C it has a life of six months.

legal category: P.O.M.

package quantity: **KRYOBULIN HOME TREATMENT PACK**
Each pack contains:
1 rubber capped vial containing 250 or 500 i.u. Dried Factor VIII Fraction B.P.
1 rubber capped vial containing Water for Injections BP.
This pack also contains a syringe, I/V needles, winged adaptor needle, filter needle, venting needle and swabs.

KRYOBULIN HOSPITAL PACK
Each pack contains:
1 rubber capped vial containing 1,000 i.u. Dried Factor VIII Fraction B.P.
1 rubber capped vial containing Water for Injections BP.
The pack also contains a filter needle and venting needle.

further information: Kryobulin is especially suitable for Home Treatment. Packs contain all requirements and can be stored in a domestic refrigerator for two years and for up to six months at room temperatures not exceeding 30°C.

Effect on laboratory tests
Laboratory tests influenced in patients treated with Kryobulin are: Factor VIII assays; activated PTT; Fibrinogen determination according to Clauss.

product licence number, name and address:
Product Licence Number:
0215/0003

Product Licence Holder:
Immuno Limited,
Arctic House, Rye Lane, Dunton Green,
Nr Sevenoaks, Kent TN14 5HB
Tel. No: Sevenoaks (0732) 458101
Telex No: 95413

date of preparation: March 1985

Kryobulin is a registered trade mark.

Heat Treated
Dried Factor VIII Fraction B.P.

Immuno Ltd

DATA SHEET

name of product: KRYOBULIN™ HEAT TREATED
Dried Factor VIII Fraction B.P.

presentation: Dried Factor VIII Fraction B.P. is a white to yellowish amorphous powder or friable solid without any characteristic odour.

It is prepared from the plasma of suitable human donors† whose donations are shown by R.I.A. to be free from HB_sAg. Pooled plasma and the final product are also tested for freedom from HB_sAg.

The product has been heated at 60°C for 10 hours. This step has been introduced to reduce the risk of transmission of infectious agents.

It is packed in vials each containing approximately 250, 500 or 1000 International Units of Factor VIII. Separate vials of Water for Injections B.P. are provided for reconstitution.

1 International Unit is the amount of Factor VIII activity contained in 12.745 mg of the 2nd International Standard for Blood Coagulation Factor VIII Human. It is approximately equivalent to the Factor VIII activity in 1 ml of average normal plasma.

uses: Kryobulin corrects Factor VIII deficiency, and is used in the treatment of bleeding due to such deficiency in:
Haemophilia A
von Willebrand's disease
Haemophilia complicated by Factor VIII inhibitors

dosage and administration: Frequent tests of the patient's plasma level of Factor VIII must be made to allow correction of the deficiency by administration of Kryobulin but for guidance an estimation of the required dosage can be made by the following calculation:

To achieve an increase of Factor VIII concentration of 1% it is necessary to administer 1 i.u. of Kryobulin per kg bodyweight, both for adults and children.

Initial treatment requires doses to be given at shorter intervals than in maintenance therapy, to provide an initial high level of activity and to replenish the extravascular compartment.

† Human donors as described in the British Pharmacopoeia 1980 Vol II under Albumin

Bleeding from skin, nose and oral mucous membrane:
Initial dose should be 10 i.u./kg at intervals of 6 to 12 hours.

Haemarthrosis:
The initial dose should be approximately 10 i.u./kg and the maintenance dose 5 to 10 i.u. per kg at intervals of 6 to 12 hours. Combined with immobilisation of the affected joint for several days, the treatment should be sufficient to restore function.

Bruising:
In most cases a single dose of 10 i.u./kg is sufficient. For widespread bruising, repeated administration of 5 to 10 i.u./kg at intervals of 6 to 12 hours may be required.

Heavy bleeding into muscles:
Immediate treatment is required to prevent permanent deformity and loss of function, and initial immobilisation of the affected area is important. An initial dose of 15 to 20 i.u./kg should be given, the maintenance dose to be 10 i.u./kg at intervals of 6 hours from the first to the second day, and at intervals of 12 hours from the third to the fifth day.

Haematuria:
The initial dose should be 15 to 20 i.u./kg, and the maintenance dose 10 i.u./kg at intervals of 12 hours.

Major surgery on haemophilic patients:
The initial dose should be at least 25 to 50 i.u./kg, and the maintenance dose 20 to 40 i.u./kg at intervals of 4 hours from the first to the fourth day, of 8 hours from the fifth to the eighth day, and of 12 hours until all wounds are healed.

The effect of treatment must be checked daily. Factor VIII activity should not be allowed to fall below 50% of the normal 100% average value. It is important that treatment be continued until all wounds have healed completely, as the risk of haemorrhage persists till then.

In addition to monitoring Factor VIII activity, tests for the development of Factor VIII inhibitors should also be made.

Dental extractions:
The required dosage depends on the number and type of teeth to be extracted, and on the severity of the haemophilia. If **one or two teeth** are to be extracted from a patient with severe haemophilia, an initial dose of 10 to 20 i.u./kg should be given. Maintenance treatment with this dosage at intervals of 6 hours from the first to the third day, and 8 hours from the fourth to the eighth day after extraction, should be given. If **more than two teeth are to be extracted from patients with severe haemophilia** a minimum initial dose of 20 to 30 i.u./kg should be given, and a maintenance dose of 10-20 i.u./kg at intervals of 6 hours from the first to the third day, and of 8 hours for twelve more days. The plasma concentration of Factor VIII should not be allowed to fall below 10% of the normal 100% average value.

Factor VIII assays should be used to monitor the effectiveness of treatment, as partial thromboplastin time gives a less accurate value when large quantities of Kryobulin are being used.

Solutions of Kryobulin must be administered intravenously, at a rate not exceeding 10 ml in 3 minutes.

Use in the elderly

No specific precautions or side effects have to be taken into account in the elderly.

Use in pregnancy

The use of Kryobulin need not be restricted during pregnancy.

contra-indications warnings, etc.:

Although the danger of volume overload is small with Kryobulin, during major surgery monitoring of the patient's central venous pressure and blood pressure, and serial chest X-rays, may be advisable.

In disseminated intravascular coagulation associated with low Factor VIII levels Heparin should be given to interrupt intravascular coagulation before therapy with Kryobulin is started.

A low incidence of adverse reactions is experienced with Kryobulin, but the following may occur:

1 All forms of allergic reaction from mild and transient urticaria to severe anaphylactic shock are possible when human plasma derivatives are administered. If such reactions occur, treatment with Kryobulin must be interrupted at once. Allergic reactions should be controlled with antihistamines and routine treatment given for anaphylactic shock. Monitoring of pulse rate and blood pressure is essential. If the pulse rate increases and/or blood pressure falls transfusion of 5% Dextrose should be started.

2 Despite the measures taken to reduce the risk, the transmission of viral hepatitis or other viral infections cannot be ruled out.

3 The appearance of a circulating Factor VIII inhibitor is possible. Its appearance cannot be predicted as it does not relate to the amount of Kryobulin administered, nor to the frequency of administration. As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

GRO-C