Witness Name: David Ian Bell
Statement No.: WITN4514001
Exhibits:
Dated:

INFECTED BLOOD INQUIRY

ADDITIONAL WRITTEN STATEMENT OF DAVID IAN BELL

I provide this additional statement in response to the request under Rule 9 of the Inquiry Rules 2006 dated 13 April 2021.

I, **DAVID IAN BELL**, will say as follows: -

1. As indicated in my previously delivered Statement of 2 February 2021, I was employed by Alpha Therapeutic Corporation for approximately two and a half years beginning in October 2000. While employed, I was the General Counsel and had, at various times during this period, oversight responsibility for Regulatory Affairs and other corporate support functions. Prior to my direct employment by Alpha, I was a partner in a Los Angeles law firm and acted as lead outside litigation counsel for Alpha in litigation beginning in 1981, including, among other claims, litigation arising out of the transmission of HIV through factor concentrates. The information included in my Statement was based upon my best recollection without review of any specific documents.
2. My original Statement included information that I can specifically recall and there are certainly numerous other matters of relevance that are not within my personal recollection. However, based upon your specific questions in your correspondence of 13 April 2021, I can provide you with responses to some of your questions based upon my general recollection, but without reference to any specific documents.
3. Referring to your questions that I can answer:

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e. Paragraph 6: Please provide, insofar as you can recall:
i. Any dates of and/or further detail about the reports of hepatitis;
ii. How and when Alpha told clinicians 'to weigh the benefits of concentrate therapy with the potential risk of hepatitis exposure' ;
iii. How and when clinicians told Alpha that the 'benefits of concentrate therapy outweighed the potential risk of hepatitis exposure…' ; and
iv. Please outline the basis of your knowledge on these matters, providing copies of any relevant document(s).

Alpha Therapeutic Corporation issued Package Inserts approved by the United States Food and Drug Administration identifying statements that were approved by FDA after submission and review by the relevant government regulator. Alpha included as a warning that the risk of viral hepatitis was present in its factor concentrates from the late 1970s; that the risks of hepatitis should be weighed by the patient's physician against the benefit of concentrate therapy and specifically stated that patients with mild disease should use single donor products whenever possible. Alpha could not deviate from the language approved by FDA and FDA's regulatory authority and oversight pre-empted any independent action by Alpha.

g. Paragraphs 8 - 9: Please outline the basis of your knowledge on these matters, providing copies of any relevant document(s). Please also comment on the following, insofar as you are able to do so:
i. Why did Alpha begin a heat treatment programme, and why, specifically, did it do so in 1982?
ii. How were decisions reached within Alpha on which research and development projects would be undertaken? In particular, how was the decision to begin a heat treatment programme taken, and who was responsible for it? How was the programme funded?
iii. Given that heat treatment was well-established as a method of viral inactivation, why was a heat treatment programme for Factor VIII not introduced before 1982?
h. It was argued during the course of previous litigation that by the mid-1970s, fractionators were aware both of the risk of hepatitis B virus infection and of relevant methods of viral inactivation (such as heat treatment, detergent treatment and lipid solvent treatment). It has been suggested that had a "reasonable research effort" taken place in the mid-1970s, then this would

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have established methods of inactivating hepatitis B virus and, consequently, hepatitis C virus and HIV [see document with Unique Relativity Reference number: CGRA0000621, para. 33]. How do you respond to this argument, insofar as it may be made against Alpha?

Alpha began its research program for factor concentrates prior to the initial reports of HIV. The program was in response to the potential risks of hepatitis and was undertaken by senior Alpha scientists including Martha Heinski and Charles Heldebrant. Prior to the work initiated by Alpha and others in the late 1970s/early 1980s in response to the risk of Hepatitis, the scientific and clinical understanding was that, while heat treatment/pasteurization was utilized for viral inactivation in Albumin, it required the addition of specific stabilizers. As it related to heat treating factor concentrates, it was believed that the factor concentrates were very heat labile and, even in the presence of stabilizers, heat would denature the proteins creating neoantigens and rendering a patient untreatable. Even today, the creation of neoantigens (inhibitors) is one of the largest problems facing patients being treated for bleeding disorders. My current recollection is that this information was based upon scientific and clinical evidence as conducted by Charles Heldebrant in the laboratory of Ed Davis at the University of Washignton in the late 1970s where it was found that factor VIII was denatured by heat even in the presence of stabilizers and by clinical information provided by leading clinicians treating hemophilia, including Louis Aledort, who, along with recognition as one of the leading treaters of hemophilia, was also the Medical Director of the National Hemophilia Foundation.

j. Paragraphs 11 - 15: Please outline the basis of your knowledge on these matters, providing copies of any relevant document(s), particularly in relation to:

i. Alpha becoming aware of the MMWR report in July 1982;

ii. The establishment and operation of the AIDS Task Force along with its decisions;

iii. The donor screening programme Alpha implemented in December 1982; and

iv. Criticisms about/opposition to Alpha's donor screening programme.

My knowledge of these facts is based upon my own personal recollection and information conveyed directly to me by Clyde McAuley, Alpha's Medical Director.

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l. Did Alpha take any steps to close plasma collection centres in geographical areas known to have a high prevalence of HIV?

Yes. My recollection is that Alpha stopped collecting plasma from certain identified "hotspots" for AIDS including Los Angeles, San Francisco and Houston.

m. What steps did Alpha take to test their donor exclusion policy? For example, what work was done to examine whether donors, particularly paid donors, were answering the donor screening questions honestly?

Despite criticism from others, Alpha required donors to attest, in writing prior to each donation, to specific questions relating to then known risk factors for AIDS. Additionally, Alpha medical personnel at the plasma centers performed medical and physical examinations of donors to exclude those at risk for HIV infection.

q. Please provide the Inquiry with the names of the members of the Alpha AIDS Task Force, and identify, to the best of your knowledge, which members are still alive.

My recollection of the members of Alpha's AIDS Task Force included, at various times, Bill Hartin, Clyde McAuley, Dave Gury, Edward "Bud" Mealey, Marietta "Penny" Carr, Martha Heinski, Edward Colton, Charlene Wisdom and Charles Heldebrant. I have not had contact with any of these individuals for approximately twenty years, however, I understand that Penny Carr, Bud Mealey and Clyde McAuley are deceased. I do not know the status of the others, though they must all be quite aged if they are still alive.

Statement of Truth

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

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Signed: _____

Dated: 6July 2021

Statement of David Bell Before the UK Infected Blood Inquiry

The following statement by David Bell is based upon information and belief and to the best of my knowledge is true and correct. I first became involved with Alpha Therapeutic Corporation (Alpha) in 1981, providing services as an external advisor. Among my responsibilities was the lead counsel role for Alpha in litigation arising out of the transmission of HIV to persons with Hemophilia using factor replacement therapy processed from Human Source Plasma and advice relating to regulatory activities. In 2000, I became employed directly by Alpha as its General Counsel and in a nonlegal role with certain responsibilities and oversight for Regulatory Affairs and other corporate functions. This statement contains non-confidential information in the public domain, including that made public by Alpha, the U.S. Food and Drug Administration or other third parties. It does not include any confidential information or any facts, information, data, conclusions, recommendations or opinions that are protected by the attorney client privilege. Notwithstanding this, the presentation of this statement as required by the UK Infected Blood Inquiry, shall not be construed as a waiver of any relevant privileges or protections.

Since it was first formed in August 1978, Alpha Therapeutic Corporation had a leadership role in the donor screening of plasma and the processing of safe and effective plasma derivatives. As a result of the purchase of certain assets of Abbott Laboratories' Scientific Products Division, Alpha was formed with a central group of research scientists experienced in coagulation chemistry and the early development of factor concentrates for use in the treatment of hemophilia.

Beginning in 1965, when Judith Poole discovered and published her observations that cryoprecipitate derived from fresh frozen plasma contained clotting Factor VIII, the treatment of hemophilia was forever altered. First, with the use of crude cryoprecipitate, ultimately leading to a licensed Factor VIII concentrate in 1966 and the later development of Factor IX concentrate, the treatment of individuals with hemophilia A and B was significantly improved. The advent of these two factor concentrates derived from human plasma also offered dramatic improvement in the quality of life of persons with hemophilia. Concentrates allowed patients to lead essentially normal lives and enjoy the benefits afforded by freedom from continual hospitalizations.

However, in spite of the advantages in managing bleeding disorders they afforded, plasma-derived cryoprecipitate and concentrates were ultimately associated with the risk of transmission of hepatitis. Following the discovery of the hepatitis B surface antigen (HbsAg) it was determined that many of the individuals treated with cryoprecipitate and concentrate had previously been exposed to hepatitis B. Based on this understanding, it was concluded that the incidence of hepatitis transmission through coagulation factors could be minimized if donors could be screened for hepatitis B surface antigen. As of January 1971, all of the plasmapheresis centers that were owned by Abbott Laboratories, the predecessor to Alpha, started routine screening of all plasma donation for hepatitis B surface antigen. Originally the screening was performed using the second generation counter immunoelectrophoresis technique (AUSTEC). However, Alpha had taken the initiative to start screening for hepatitis B antigen by this second generation method fully a year before it was mandated by the FDA inJuly 1972.

This is only one instance in which Alpha took quick action to protect persons with hemophilia from the unavoidable risks associated with factor replacement therapy. Shortly after the test was licensed in 1972, Alpha's predecessor implemented a third generation radioimmuno assay technique (Ausria I) for routine hepatitis B surface antigen testing. In

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1975, when Ausria II testing became available, it was instituted by Alpha's predecessor for donor screening. All donors and donations were tested, and donors were permanently rejected from donating if they were found to be hepatitis B surface antigen positive. With each successive improvement in donor testing, the level of confidence in processing hepatitis-safe concentrate increased.

In spite of these screening methods for hepatitis B, there were still occasional reports of a short incubation hepatitis in persons infusing factor concentrates. Since these cases were believed to be due to non-A, non-B hepatitis, Alpha advised physicians to weigh the benefits of concentrate therapy with the potential risk of hepatitis exposure. Physicians treating persons with hemophilia reported that, in their judgment, the benefits of concentrate therapy outweighed the potential risk of hepatitis exposure; the availability of concentrate allowed many patients to lead a more normal life, undergo surgery, live with less joint deformity, and ultimately resulted in prolonged lives.

Unfortunately, at that time it was not recognized that chronic hepatitis non-A, non-B would have the tremendous sequelae of which we are now aware-namely chronic persistent hepatitis, chronic active hepatitis, or hepatocellular carcinoma. The true impact of hepatitis on persons with hemophilia only became known with the increased life expectancy directly resulting from the use of concentrates. Early attitudes regarding the risk of hepatitis played a role in the treatment community's interpretation of the developing knowledge of AIDS. In the early years of factor replacement therapy, very few physicians and scientists realized the impact of chronic hepatitis on the hemophilia population; in the early 1980's, the same was true of what later became known as HIV infection.

In addition to the use of specific hepatitis testing for donor screening, Alpha adopted various manufacturing procedures in the late 1970's to increase the specific activity of Factor VIII in its concentrate. This was accomplished primarily by removing excess fibrinogen, which was felt to carry a large burden of the hepatitis virus. In 1981, Alpha received its license for a more highly purified concentrate incorporating polyethylene glycol fractionation. Alpha believed that concentrate purification would offer a greater degree of protection against hepatitis transmission as a result of viral partitioning and removal.

In early 1982, Alpha began an additional program to inactivate any residual hepatitis virus through heat, which culminated in a licensed product in February 1984. After evaluating various inactivation processes, researchers at Alpha concluded that heating the concentrate in a liquid solvent without added stabilizers might not have the undesirable effect of stabilizing any residual virus in addition to the Factor VIII protein. Unlike other entities who utilized "dry heat", Alpha developed a procedure using "wet heat" (a suspension in n-heptane). While this procedure reduced the final yield of Factor VIII and was costlier to implement, it provided, in Alpha's opinion, a more robust inactivation of viruses. (a simple analogy is dry heat is similar to placing your hand in an oven; wet heat is like placing your hand in a hot water bath – the transmission of heat in the bath is much greater.) Alpha's protocol for this additional processing step was established in the Fall of 1982 and submitted to the FDA.

Studies conducted pursuant to FDA licensure demonstrated that Alpha's heat treatment process inactivated significant quantities of marker virus, hepatitis B and non-A, non-B hepatitis. However. both the Bureau of Biologics of the FDA and the hemophilia treatment community raised concerns about the possibility of neoantigenicity related to heat treatment. This concern centered around researchers' and physicians' belief that heating the concentrate altered the molecular structure of the Factor VIII molecule, which could have a deleterious effect on persons using heat-treated concentrates; essentially making a treatable

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patient untreatable. Studies conducted by Alpha failed to show any evidence of neoantigenicity. However, the treatment community did not fully accept these results until the end of 1985. Until hemophilia treaters' concerns about neoantigenicity were allayed, non-heat treated concentrates continued to be prescribed and recommended by physicians as the principal treatment of choice.

AIDS

In July 1982, Alpha first became aware of the report in the Morbidity and Mortality Weekly Report (MMWR) that three hemophilia patients had developed Pneumocystis Carinii Pneumonia (PCP). Through continuing surveillance, Alpha followed the early, developing knowledge of AIDS. Alpha established its AIDS Task Force in December 1982 because of the possibility that this new pathogen might be transmitted by blood or blood products. In early December 1982 Alpha's Task Force met and determined that all plasma collected for use in coagulation products, including concentrates, would be screened through a process of direct donor questioning for affiliation with any of the groups then thought to be a high risk for AIDS. Initially, these high risk groups included homosexuals and bisexual persons who had sexual contact with persons in that high risk group, as well as intravenous drug users and persons from Haiti, a known "hotspot" for AIDS. At that moment in time, 75% of reported AIDS cases had occurred in homosexuals, 15% in intravenous drug users and 5% in Haitians.

Under the screening program Alpha adopted, donors were also educated through a series of materials which explained the information then known about AIDS and advised that if donors were members of a high risk group, they should exclude themselves from donating plasma. In addition to implementing these new donor screening procedures in its own plasmapheresis centers, Alpha refused to accept plasma purchased for use in processing concentrates if that plasma had not been certified in writing as meeting these strict donor exclusion requirements. At the time these policies were implemented, Alpha's procedures were criticized as being discriminatory, overreactive and inappropriate; later, they were embraced as innovative and responsible.

In addition to implementing strict donor screening procedures, Alpha's AIDS Task Force considered other options in response to the developing knowledge concerning AIDS. These options included:

1. Possible ways to diagnose AIDS, study the epidemiology of the disease and establish safeguards for recipients of Alpha concentrates;
2. Safety recommendations for donor center personnel and plant workers;
3. Development of possible laboratory tests for use as a preliminary screen for potential donors at risk for AIDS;
4. Consideration of the possible use of Interferon as a prophylactic or treatment of patients at risk for AIDS;
5. Suggestions for animal models to find the then-unknown causative agent for AIDS;
6. Research to determine whether any viruses were not killed by pasteurization of blood products;
7. Possible ways of speeding up the approval process for Alpha's n-heptane heat treatment through the FDA; and
8. Analyzing the potential of lyophilized cryoprecipitate processing as an alternative treatment for hemophilia.

Before guidelines were issued by the Public Health Service, Alpha's Donor History and Physical form were revised to include not only the high risk group questionnaire, but also to include a physical examination specific for signs and symptoms suggestive of AIDS,

such as night sweats, unexplained fever; weight loss, lymphadenopathy, or the red, black, or dark spots on the skin suggestive of Kaposi's Sarcoma. Detailed instructions on how to handle and dispose of plasma thought to be infected where instituted. Communication methods were established between donor centers in the same locale to make sure that there was a comprehensive Permanent Reject List of High Risk Donors. These changes were incorporated into the Alpha Standard Operating Procedure and Training Manual, which formed the basis for its Source Plasma License.

On January 4, 1983, at a joint meeting between CDC and the FDA, an Alpha representative announced that Alpha had already instituted direct donor questioning designed to exclude individuals in high risk groups. This announcement was met with a great deal of opposition from many groups, including the volunteer blood banks and the Gay community. Those groups took the position that donor confidentiality and sexual preference was a private matter, and that the questionnaire was an invasion of privacy. Additionally, Alpha took the position at the January meeting that AIDS should be a reportable disease, similar to syphilis and other sexually transmitted diseases, in order to assist in donor screening.

During this time frame, there was close interaction between Alpha and others involved in the hemophilia community. Researchers and officials from Alpha were in constant contact with the FDA discussing the status of license amendments designed to increase product safety and labeling changes reflecting the developing knowledge of AIDS. The National Hemophilia Foundation was in constant contact with the CDC, obtaining and releasing up to date information to the entire hemophilia community. Physicians treating hemophilia were networked through the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation. The scientific and lay press continuously reported on the often conflicting developments regarding the possible relationship between AIDS and blood. These conflicting developments contributed to a time of general uncertainty, but nonetheless all information was widely disseminated in real time through scientific and medical experts, Government scientists and regulators as well as the popular press, without discrimination to all interested parties as soon as it became known; there was no withholding of information relating to the etiology, sequelae or transmissibility of AIDS/HIV.

In the face of this uncertainty, and as part of Alpha's effort to investigate all potential methods of improving factor concentrate safety, on March 15, 1983, a request was sent to the Director of National Center for Drugs and Biologics of the FDA. This request sought approval to develop a pilot program of donor exclusion based upon the use of plasma tested and found to be negative for hepatitis B core antibody, which some had suggested as a possible surrogate test for AIDS.

Alpha's pilot program proposed that donors found to be positive for anti-HBc would be permanently rejected as plasma donors. Alpha did not request any promotional labeling claims for anti-HBc negative AHF, other than, for full transparency, an indication that it was derived from donors tested for the presence of anti-HBc. At the same time, Alpha advised the FDA of its intention to revise its labeling for all Antihemophilic Factor (Human) to include a cautionary statement regarding potential transmission of AIDS. Under the regulatory scheme adopted for biologics, neither of these steps could be taken without prior FDA approval.

On May 3, 1983, Alpha received a letter from the Office of Biologics denying both requests. The FDA advised that it did not feel that Alpha could make the requested labeling change, including the proposed warning, in the absence of additional data. The FDA also suggested that screening out all core antibody might selectively remove protective

antibodies, such as those for anti-HBs against hepatitis B.

HTLVIII ANTIBODY TESTING

Prior to the discovery and reporting of the isolation of the HTLV-III virus in April of 1984, multiple theories were proposed regarding the possible etiology of AIDS. Many researchers thought that AIDS resulted from reactivation of a previous infection with cytomegalovirus or Epstein Barr virus. Other scientists felt that AIDS was related to antigen overload with the loss of immunologic competence. The fact that the syndrome occurred so frequently in the Haitian population created further confusion. With specific regard to patients with hemophilia, physicians and regulatory officials questioned why so few hemophiliacs at the time had developed the syndrome if, as hypothesized, the transmission vector for AIDS was similar to that for hepatitis. To many researchers, this fact suggested that the syndrome seen in the hemophilia population was different than AIDS seen in the homosexual and intravenous drug abuser population. It was not until April of 1984, when scientists in the United States and France announced the discovery of the virus believed to be responsible for AIDS that the exact etiology became readily apparent. Only then did the medical community reach a full consensus that AIDS could be transmissible by blood.

Following this discovery, an enzyme-linked immunosorbent assay (ELISA) test was developed to detect antibodies to HTLV-ill. The ELISA test was licensed by the FDA in March of 1985, and thereafter it was made available for commercial use in screening blood and plasma. Alpha participated in the original studies of plasma donor testing for the HTLVIII antibody and helped in the development of the subsequent test kits. The ELISA test was implemented in March of 1985, and all of Alpha's plasmapheresis donor centers immediately began testing donations for HTLVIII antibody. All donations collected after this time, whether at centers owned by Alpha or from which Alpha purchased plasma, were tested by the ELISA methodology. Donors who tested positive were permanently excluded from donating plasma.

The period from 1982 through 1986 was an extremely difficult period of time for all interested and concerned parties, including the entire hemophilia community: hemophilia patients, physician-treaters, governmental entities, the National Hemophilia Foundation, along with the processors of factor concentrate. It was a time marked by difficult decisions in the face of uncertainty about a new and insidious disease process with many variables; a time during which the etiology of that disease was a matter of intense debate and constant discussion. It was said by the World's leading experts that HIV was not just an unknown virus, but an unknowable virus; it could not be foreseen as an infective pathogen in humans. In the beginning, it was not known how to destroy HIV without affecting the efficacy and safety of Factor Concentrates. However, it was ultimately understood that HIV could be destroyed with relative ease, and with the advent of heat treatment, solvent detergent and other pathogen safety procedures, AIDS was essentially eradicated as a risk associated with continued concentrate therapy. Unfortunately, through retrospective studies of the hemophilia population, we now know that the majority of individuals were exposed to the virus responsible for AIDS before AIDS was identified as a risk to persons with hemophilia.

While the search for an individual or entity to blame for the epidemic of AIDS amongst a naive population may be part of human nature, an objective evaluation of the facts demonstrates that Alpha always attempted to act in good faith based upon the facts known at the time, taking into account the risks known or perceived and the benefits identified by key medical opinion leaders, expert scientists, governmental researchers, regulators and

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persons with hemophilia. The availability of a safe and effective treatment for hemophilia was always Alpha's paramount concern.

Alpha considered itself a leader in the processing of safe and effective therapies for use in the treatment of hemophilia. It was also an innovator in donor screening practices and surveillance for hepatitis and HIV, as well as the development of human derived, high purity coagulation factor replacements.

In 2003 Alpha divested certain of its assets to Baxter Healthcare and Probitas Pharma, however, Alpha maintained its corporate identity as an independent entity at that time.

Dated: 2 February 2021

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David Ian Bell