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INFECTED BLOOD INQUIRY

FIRST WRITTEN STATEMENT OF PROFESSOR ROBERT ANTHONY WEISS

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I, Professor Robin Weiss, will say as follows: -

Section 0: Opening Comments

0.1. At the outset of this statement, I wish to express my deepest sympathies to those who have suffered directly or indirectly as a result of the events that the Inquiry is exploring. In preparing this statement I have reflected on my involvement and understanding at the time, in so far as I can now remember matters going back nearly 40 years, since my powers of recall are no longer what they were. However, I have used the documents which I have been able to access to assist my memory of events with the intention of providing accurate information on the early days of HIV/AIDS to the Inquiry.

0.2. During the greater part of the period the Inquiry asks me to comment upon I held the role of Director at the Institute of Cancer Research (University of London), which I will refer to as the ICR, based at the Royal Marsden Hospital in London. I held this post between 1980 and 1989.

0.3. In trying to assist the Inquiry I have endeavoured to refresh my memory using relevant documentation and research although I am not sure that I have reviewed all of the relevant documents. My ability to take in and re-analyse their contents is not as sharp as it used to be. As I would hope the Inquiry is aware, it is challenging to recreate the depth and extent of the contemporaneous knowledge within such a limited time and at my age. For the above reasons and limitations, I am conscious that my evidence will not be as detailed as I would otherwise wish. I have tried my best to answer the questions asked of me.

0.4. In writing this statement the answers I have given are entirely my own words and thoughts, and the scientific opinions are also my own. In answering the questions, I have mainly focussed my review of documents to those which I

was personally aware of rather than those which I would not have seen at the time although, where necessary, some reference is made to such documents.

Section 1: Introduction

Personal Background

1.0. My name is Robert Anthony Weiss, known personally and professionally as Robin Weiss. My date of birth is GRO-C 1940 and I hold a BSc, PhD, FRCPath, FMedSci and FRS. My address is known to the Inquiry.

Employment History

1.1. I am asked about my employment history and the roles and responsibilities I have held throughout my career. The following table outlines my employment history which I have filled in as fully as possible. I have provided approximate dates where I have no recollection or record as to the exact months in which I took up and left the relevant roles.

Table 1 – Employment History

October 1961 to September 1963	Research Assistant: Medical Research Council Experimental Genetics Unit. In this role I was involved in assisting in field work and the genetic analysis of black rats living in an environment of high natural radiation, Kerala, India with follow-up studies in London.
October 1963 to September 1964	Full time PhD student University College London.
October 1964 to October 1970	Assistant Lecturer/Lecturer: University College London. In this role I taught and was engaged in research. I took a period of sabbatical leave from August to December 1969 where I conducted research at the Institute of Molecular Genetics, Czechoslovak National Academy of Sciences, Prague, Czechoslovakia.

October 1970 to July 1972	Eleanor Roosevelt International Fellow of the American Cancer Society: University of Washington, Seattle and then University of Southern California, Los Angeles, USA.
August 1972 to April 1980	Head of Laboratory of Viral Oncology: Imperial Cancer Research Fund (now Cancer Research UK). I led a team of five to six scientists and research students investigating leukaemia and sarcoma viruses of chickens as models for cancer.
May 1980 to November 1989	Director: Institute of Cancer Research (University of London) at the Royal Marsden Hospital, London and Surrey. I managed around 600 staff and led a small team of four to five staff in 1984-1985 in studying human retroviruses including HIV.
December 1989 to December 1998	Professor of Viral Oncology: Institute of Cancer Research, London. I continued research on retroviruses and on Kaposi's sarcoma herpesvirus. From 1990 to 1995, I served part-time as director of research, helping to co-ordinate internal research activities on behalf of the Chief Executive.
January 1999 to December 2014	Professor of Viral Oncology: University College London. I worked full time to September 2007 and part time thereafter. I held emeritus status from 2010.
1985 to 2019	Honorary Professor: London School of Hygiene and Tropical Medicine. I taught on a post-graduate medical virology course and on AIDS modules.
January 2015 to present	Emeritus Professor: University College London: I teach voluntarily but do not run a laboratory. Prior to COVID-19 lock down in March 2020, I would give a series of 3-5 lectures or seminars on "*Cancer causing viruses*" and on "*AIDS-associated cancers*" to post-graduate (MSc) students in the UCL Cancer Institute and to undergraduate science and medical students in the UCL Division of Infection & Immunity on "*Oncogenic viruses*" and "*Introduction to HIV/AIDS*". I would also mark examination papers. I currently give two Zoom-type talks each year to UCL medical students on "*HIV*" and on "*Emerging Infections*". I also present a series of six adult education seminars at the University of the Third Age (U3A) in London, most recently on "*A Germ's Eye View of History: Pandemics Past and Present*" and "*Natural History: Aristotle to Attenborough*".

Membership of Committees and other groups

1.2. The following table outlines the details of my memberships of committees or other groups relevant to the Inquiry's terms of reference. Again, where it is not possible to provide exact dates, on account of poor recollection and lack of records I have given approximated dates:

Table 2 – Membership of Committees and other groups

1983 to 1994	Member of the National Biological Standards Board, UK.
October 1983 to late 1986	Member, Medical Research Council Working Party on AIDS
January 1985 to December 1986	Member of the DHSS Expert Advisory Group on Aids ('EAGA').
1986 to 1991	Participant of the All-Party Parliamentary Group on HIV/AIDS.
1992 to 1993	Chair of the Committee on HIV Vaccines, WHO Global Program on Aids, Geneva, Switzerland.
1999 to 2003	Member of the Physiological Medicine and Infection Board, Medical Research Council.
2005 to 2007	Member of the Life Sciences Committee, Health Protection Agency.
2005 to 2007	Member of the Scientific Council, Institut Pasteur, Paris, France.
2006 to 2009	President of the Microbiology Society. I occasionally presented the Society's view on threats from infectious diseases to the Government or to Parliament.
2013 to 2017	Chair of the Scientific Committee and Board Member, International AIDS Vaccine Initiative, New York, USA.

Section 2: Previous statements and evidence

Written statement and oral evidence given to the Penrose Inquiry

2.1. The Inquiry refers me to a letter I wrote to the Penrose Inquiry dated 12 September 2011 **[PRSE0001039].** The Inquiry asks me to reflect upon that document and a transcript of the oral evidence I gave to the Penrose Inquiry on 27 September 2011 **[PRSE0006048]**. I am asked whether that evidence is, to the best of my knowledge and belief, true and accurate. The Inquiry will, of course, be aware that I gave the Penrose Inquiry an affirmation before presenting my oral evidence. I also confirmed that since I was without contemporaneous records, I was not confident that I could respond with wholesale accuracy.

2.2. I believe that the evidence I gave to the Penrose Inquiry was at the time it was given true and accurate, with the caveat that I then explained not everything could be said with certainty. I have noticed a minor transcriptional error on pages 166 and 167 in the transcript of my oral evidence. I had been discussing cellular antigens called 'MHC Class II' but these were incorrectly noted as 'MAT Class II'. However, this does not have a material bearing on the substance of the evidence I gave.

2.3. Nevertheless, given the general limitations which I have raised at the beginning of this statement, it would greatly assist me if the Inquiry is aware of, or has reason to believe, any specific areas of my written and oral evidence that do not appear to be true and accurate or are now inconsistent, that these could be raised with me and the opportunity to clarify and/or explain further. I would be very happy to assist the Inquiry with any further queries or clarifications.

2.4. I can confirm that I am not aware of any other evidence that I gave to the Penrose Inquiry which this Inquiry has not listed.

Evidence given to other inquiries or courts or regulatory bodies

2.5. To the best of my recollection, I have not given evidence on these subjects in any other formal inquiry, investigation or litigation concerning infected blood. In August 1989, I was invited to be an expert witness by a representative of the litigants suing the Department of Health concerning HIV infection; despite my sympathy for their situation, I declined to do so because I did not consider that I was sufficiently expert on the issues to be addressed. In November 1989, I was invited by Dr Rejman to assist the DHSS in the same litigation, and I similarly declined.

2.6. I have on occasion provided an 'expert' view in responding to *ad hoc* inquiries about the safety of processing potentially infected cells for diagnoses of non-infectious conditions such as chromosome anomalies. Dr Peter Lister on behalf of the Advisory Committee on Dangerous Pathogens asked me to comment on the risk of HIV infection to laboratory staff working in NHS cytogenetics laboratories on how to handle short-term culture of lymphocytes from patients not screened for HIV **[WITN6868002]**.

2.7. I have provided commentary on the potential dangers of infections from animals via medical procedures. The most pertinent were oral presentations and provision of research papers in 1997 to the US Food & Drug Administration (FDA), to the DHSS Advisory Committee on the Ethics of Xenotransplantation (the Kennedy Report 1997), and to the DHSS Xenotransplantation Interim Regulatory Authority (UKXIRA) in 1997. We initiated studies of pig retroviruses owing to my concern that such viruses might be transmitted to recipients of porcine organs or tissues in xenotransplantation (the transfer or infusion of animal cells into humans or exposure to live animal tissue *ex vivo*). We published two research papers **[WITN6868003; WITN6868004]** on the nature

of porcine retroviruses and on the susceptibility of human cells in culture to infection. It was in large part our papers that led the FDA to increase its regulatory oversight of xenotransplantation and, following the Kennedy Report, of the DHSS to establish the UKXIRA. I recently reviewed these issues and remain wary of the possibility of iatrogenic transmission to human transplant recipients by viruses in animal sources.

Section 3: Knowledge of Risks

Understanding of risks of infection

3.1. I have been asked to comment on the extent to which I was aware of the risks of infection associated with blood products when I joined the ICR and how this developed over time.

3.2. I should, however, clarify at the outset that the correct name and abbreviation of the academic institution where I worked during the 1980s and 1990s is called the Institute of Cancer Research and is abbreviated 'ICR' and not 'CRI' as the Inquiry refers to. The ICR was a component party of the British Postgraduate Medical Federation ('BPMF') of the University of London and BPMF Institutes were affiliated to specialist hospitals. The ICR was the academic partner of the Royal Marsden Hospital ('RMH') which was and continues to be a specialist cancer hospital based in South Kensington, London and at Banstead, Sutton, Surrey. The ICR constituted research laboratories in the hospital buildings and in adjacent buildings of its own. The building that contained my office and laboratory was situated on Fulham Road in South Kensington SW7 and was called the Chester Beatty Laboratories ('CBL'). Accordingly, to avoid further confusion, where the terms CRI or CBRI have been used, for the purposes of this statement I have taken them to mean the ICR.

3.3. I joined the ICR in May 1980. At that time, I had little professional knowledge of the risks of infection associated with blood and/or blood products. I had been a volunteer blood donor and carried an organ donor card since 1958 and therefore held a limited awareness of the danger of passing on blood-borne infections. This was reinforced by the fact that when I returned from field work on rats in India in 1961-1962, I was disqualified from donating blood for six months in case I was carrying an infection acquired in India. Therefore, in 1982 when I commenced work on investigating human viruses in the laboratory, I decided to stop being a donor on the basis that, if I inadvertently picked up a laboratory infection, I might be a potential risk to recipients.

3.4. Whilst I am not a medical doctor, as a non-medical virologist I had a good understanding of how infections can spread, but I had no special training or interest in blood-borne infections. Moreover, my research on joining ICR was focused on cancer-causing retroviruses in chickens (which are not infectious to humans) as a model for understanding mechanisms of how cancer develops, such as oncogenes that were first identified in these viruses. In 1980, the first human oncogenic retrovirus was identified by Robert C. Gallo and colleagues at the National Institutes of Health in the USA and was named human T-cell leukaemia virus (HTLV). In 1981, a similar virus named ATLV was shown by Isao Miyoshi and colleagues to be linked to a particular form of adult T-cell leukaemia that was prevalent in South-West Japan. In 1982, a related yet distinct retrovirus was identified, also by Robert Gallo's team. The two viruses were then designated HTLV-I and HTLV-II. Early in 1982, I decided to switch my research from chicken retroviruses to human ones.

3.5. As a result of starting to investigate human retroviruses, my knowledge of human blood-borne infections expanded quickly, and I began to keep abreast of current medical literature in the field. By 1982, it became apparent that ATLV in Japan could be spread via whole blood transfusion, but further evidence indicated that ATLV was not transmitted by cell-free blood products.

3.6. When I started to collaborate with Dr Richard Tedder at the Middlesex Hospital Medical School ('MHMS') on HTLV-I in 1983, my knowledge of blood-borne infections greatly increased because he was an experienced clinical virologist and was already an expert on Hepatitis B Virus infection. Our joint research at ICR and MHMS certainly enhanced my understanding of blood-borne infections by retroviruses.

3.7. I also gained valuable knowledge of infectious diseases caused by viruses, especially AIDS, from other collaborators including Dr Antony Pinching and Dr Jonathan Weber, St Mary's Hospital Medical School, and Dr Charles Farthing and Dr David Shanson at St Stephen's Hospital, Chelsea. This is clear from, for example, minutes of a meeting of the Medical Research Council (MRC) Working Party on AIDS dated 10 October 1983 of which I was a member as was Dr Pinching **[CBLA0001749]**. At paragraph 3 of these minutes, it is recorded that:

> "*the Working Party reviewed the present position on AIDS, assuming that most of the major literature was known to members in advance…*".

Moreover, these minutes record a proposal of mine which would enable me to:

> "*…collaborate with several groups in research on HTLV and other retroviruses".*

In turn, our own findings contributed to the overall state of knowledge in the field during the period 1983-1985 as is clear from, for example, the Lancet article dated 1 September 1984 to which I refer below in paragraphs 3.23, 0, 4.6 and 5.34 **[NHBT0000068_015]**.

Awareness of AIDS

3.8. The Inquiry has asked me to comment on when I first became aware of AIDS; the association between AIDS and blood products; and when I first considered that AIDS might be caused by a virus.

3.9. I first became aware of AIDS in 1982, although I cannot recall the exact date. I say this because I recall that on a visit to ICR during Spring or early Summer, Sir Anthony Epstein alerted me to this strange new disease emerging among homosexual men. Not long after this I remember Dr Pinching of St Mary's Hospital Medical School gave a talk to the Oncology Club (which was an informal group of medical oncologists in London that used to meet at the ICR). He presented a case history of one of the first AIDS patients seen in London who presented with Kaposi's sarcoma. I recall subsequently reading up on it and noting what had been published on AIDS at that time.

3.10. In terms of when I became aware of the possible association between AIDS and blood/blood products, it happened incrementally. The starting point for the recognition of AIDS as a novel disease was the publication of two notes in May and June 1981 in Mortality & Morbidity Weekly Report ('MMWR'), published by the Centres for Disease Control & Prevention ('CDC') in USA, which described that clusters of homosexual men were developing *Pneumocystis carinii* pneumonia and/or Kaposi's sarcoma. These were rare diseases in young men and were indicative of an underlying defect of the immune system. They appeared to be newly acquired hence the eventual name given to the condition, *Acquired* Immune Deficiency Syndrome (AIDS).

3.11. In December 1981, Henry Masur and colleagues reported that seven injecting drug users had developed AIDS **[WITN6868005]** This was not proof of transmission via blood but was suggestive of it. Then, on 16 July 1982, *MMWR* published a report on three cases of Pneumocystis carinii pneumonia in persons with Haemophilia A (Factor VIII deficiency) who had been treated with pooled clotting factors **[PRSE0000523]**. The editorial note at the end of the report stated:

> *"Although the cause of the severe immune dysfunction is unknown, the occurrence among the three haemophiliac cases suggests the possible transmission of an agent through blood products…CDC has notified Directors of Hemophilia Centres about these cases and, with the*

National Hemophilia Foundation, has initiated collaborative surveillance. A Public Health Service advisory committee is being formed to consider the implication of these findings."

3.12. That report in July 1982 coincided with my developing an interest in AIDS; it indicated to me the strong likelihood of an association between AIDS and the administration of contaminated blood products.

3.13. I first became aware that AIDS might be caused by a virus when I learnt of AIDS as a mysterious new disease as I mention above. The MMWR reports in July 1982 that AIDS occurred in three people with haemophilia (referred to in paragraph 3.12) also indicated to me that AIDS was most likely to be caused by a virus. This was because it seemed less likely that other infectious agents such as bacteria or fungi would be present in plasma fractions or clotting factor concentrates. Among various kinds of infectious agents under consideration between July 1982 and May 1983 were retroviruses related to HTLV-I, suggested by Robert Gallo at NIH and also by Myron (Max) Essex at the Harvard School of Public Health.

3.14. However, at that time, I personally thought that a small, non-enveloped virus, such as a parvovirus, would be more likely to survive the processing of clotting factors. In fact, that guess turned out to be incorrect as I had wrongly assumed that making cryo-precipitates of clotting factors would inactivate a delicate, enveloped virus such as a retrovirus. I also learned in a conversation in October 1982 with Prof Yorio Hinuma, an eminent colleague in Japan, that while HTLV-I (called ATLV in Japan) was frequently transmitted from infected persons via whole blood transfusions, no cases on infection had been observed after transfusion of plasma or cryoprecipitates of clotting factors (his data were later published in *Vox Sanguinis* in 1984) **[WITN6868006]**. Thus, I was sceptical that a virus closely related to HTLV-I would be the causative agent.

3.15. In May 1983, Barré-Sinoussi, Montagnier *et al* published their first paper on 'LAV' (Lymphadenopathy virus) isolated from a homosexual man with lymphadenopathy (swollen lymph glands, sometimes a precursor of AIDS) **[PRSE0004469]**. LAV was associated with reverse transcriptase activity (a hallmark of retroviruses). It was an interesting candidate although I remained sceptical that it was the genuine cause rather than a co-incidental, opportunistic infection, partly because the electron micrographs of budding viruses presented in that paper did not look at all typical of retroviruses, but more like arenaviruses (e.g. Lassa disease virus).

3.16. I became more convinced that LAV was the leading suspect in September 1983, when Luc Montagnier showed me new unpublished electron microscope images of the virus from two further patients with AIDS which he called 'IDAV' (Immune Deficiency Associated Virus). Further, in September 1983, Luc Montagnier presented his new results to a meeting on human retroviruses at Cold Spring Harbor Laboratory in USA attended by representatives of many of the teams investigating human retroviruses in USA, Europe and Japan.

3.17. New evidence claiming to be independent from the French group appeared when Robert Gallo and colleagues published four papers in May 1984 on what looked very similar to LAV/IDAV (but which Gallo called HTLV-III). The key paper described the isolation and propagation of HTLV-III: Gallo RC, Salahuddin SZ, Popovic M *et al*. Frequent Detection and Isolation of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and at Risk for AIDS. *Science* 1984; 224 (4648) 500-503. **[WITN6868007]** I, like many virologists, then became convinced that this retrovirus was indeed the culprit, I pointed out that the French and NIH isolates had more similarities than differences in my commentary in *Nature* on 3 May 1984 **[BAYP0000026_107]**. In particular, in that article I stated the following:

> "*…the two groups are using three different names for what I believe will turn out to be the same virus…the similarities between HTLV-3 and LAV are more remarkable than the discrepancies… The relationship of HTLV-3 and LAV could be rapidly resolved by an exchange of reagents between the two laboratories".*

Knowledge of AIDS between 1983 and 1984

3.18. As I have mentioned above, my knowledge about AIDS and the conclusive identification of HIV as its cause was incremental. It is like assembling a jigsaw puzzle in which certain pieces suddenly help to make the overall picture clearer. The really key pieces in this process were the report by Barré-Sinoussi *et al* in May 1983, and Dr Gallo's key paper a year later. My knowledge of human retroviruses developed between 1982 when I started to study HTLV-I and HTLV-II, and when I later explored AIDS candidates in 1983/84.

3.19. Being a cancer researcher, I was not initially inclined to become involved in AIDS research. However, in August 1983 Dr David Tyrrell FRS persuaded me to take an interest and to contact Luc Montagnier with a view to study his virus, LAV. Dr Tyrrell was Director of the MRC Common Cold Research Unit on Salisbury Plain, and he also chaired the UK Advisory Committee on Dangerous Pathogens. With Dr June Almeida, Dr Tyrrell had discovered the first human coronavirus and coined the name 'Coronavirus' in 1967. I had a great respect for Dr Tyrrell and agreed to his suggestion. I already knew Luc Montagnier and therefore I contacted him knowing that we would both be attending a Human Retrovirus workshop the following month at Cold Spring Harbor Laboratory, USA, that I described in paragraph 3.16. However, I had to depart before the last session of the workshop when he was due to speak and that is why he privately showed me his data before my departure. I suggested that my laboratory might be able to propagate LAV in leukaemic T-cell lines.

3.20. Luc Montagnier kindly provided LAV to us in October 1983, but we were not able to propagate this isolate in T-cell lines. We wondered whether the virus had died during transport as it was left at room temperature over the weekend before delivery to the ICR. However, in retrospect I think that the main reason for the failure to propagate the first French sample only became fully apparent 13 years later in 1996. Only around 7% HIV isolates can use a co-receptor (CXCR4) for virus entry into cells that is present on permanently growing T-cell lines, whereas the usual co-receptor in the body and in primary cultures of lymphocytes is CCR5. Dr Montagnier provided a second sample of virus on 29 February 1984 that we found would grow rapidly and to high levels in the CEM T-cell line. We now know that this sample was LAV LAI which can utilise the CXCR4 co-receptor. Luc Montagnier and his colleague Jean-Claude Chermann were excited by our observation because they had not themselves been able to obtain high yields of the virus. They requested a sample of the infected CEM cells which we provided in late April 1984.

3.21. As a result of this work and that of other scientists in the field, my knowledge of AIDS accelerated rapidly in 1984. Of course, this knowledge did not mainly emanate from our own research in the articles produced in the period in 1984 and 1985, but to the huge interest in and expansion of HIV research internationally following its discovery and preliminary characterisation. Our research reports revealed the prevalence of HIV infection in the UK.

3.22. The Inquiry refers me to a study that I carried out with Dr Tedder, Dr Shanson, Prof Jeffries, and others dated 21 July 1984 entitled '*Low prevalence in the UK of HTLV-I and HTLV-II infection in subjects with AIDS, with extended lymphadenopathy, and at risk of AIDS'* **[SHTM0000569]**. This study was initiated before we obtained HIV and it demonstrated that HTLV-I or a closely related virus, while present at low frequency in some risk groups for AIDS, seemed unlikely to be a cause, contrary to what was being postulated by Robert Gallo in the USA. As the discussion section of this study noted:

> *"the isolation of HTLV-1 from ELAS* [extended lymphadenopathy syndrome] *and AIDS patients raised the possibility of a causal relation between HTLV-1 and AIDS. However, our data, that HTLV-1 infection is rare in subjects at risk of AIDS, do not support this notion".*

In this study we described a novel RIA assay for antibodies to HTLV-I which we used as a basis to develop an RIA for HIV antibodies.

3.23. The Inquiry also refers me to an article in the Lancet dated 1 September 1984 titled 'Prevalence of antibody to human T-Lymphotrophic Virus Type III in AIDS and AIDS-risk patients in Britain' **[NHBT0000068_015]**. I was corresponding author for this study which included many AIDS immunologists and virologists. This study was our major contribution to understanding the UK situation in 1984 and in particular to draw more concrete links between HTLV-III/LAV and AIDS:

> "*We detected antibodies to HTLV-III in all but one of our AIDS patients, which strengthens the evidence that HTLV-III is aetiologically related to AIDS…. The great majority of the PGL patients were seropositive for HTLV-III, despite the non-specific definition of this syndrome. This finding confirms the notion that HTLV-III is not only the cause of AIDS but is also the cause of PGL…*".

3.24. This study was significant for two main reasons: first because it constituted the largest population conducted so far; and second because it was the first survey to be published of the frequency of HIV infection in the UK among blood donors and known risk groups for AIDS. Our findings revealed that while the prevalence of HIV among blood donors was negligible at the time, it occurred in about 8% of promiscuous homosexuals and in 34% haemophilia patients who had received treatment with Factor VIII concentrates. I address this article in more detail below at paragraph 4.5.

3.25. The other papers referred to me by the Inquiry represent sub-studies. For example, one such paper is also dated 1 September 1984 titled 'Clinical findings and serological evidence of HTLV-III infection in homosexual contacts of patients with AIDS and Persistent Generalised Lymphadenopathy in London' **[PRSE0002140]**. This paper reported HIV prevalence in one major GUM clinic (St Stephen's Hospital) in London, led by Dr Brian Gazzard and ascertained networks of HIV infection among homosexual men:

> "*The pattern of sexual contact and spread of disease suggests that there were two clusters of homosexuals among whom AIDS and PGL were most likely to be spreading…Several of our findings are consistent with the hypothesis that HTLV-III is the sexually transmitted agent responsible for both AIDS and PGL"*.

3.26. Another study relevant to the Inquiry is the Lancet paper titled 'Human T-Lymphotropic Virus Type III (HTLV-III) infection in seronegative haemophiliacs after transfusion of Factor VIII' published on 3 August 1985 **[HSOC0002656]**. This was published in collaboration with Drs McClelland and Ludlam in Scotland; and whilst the date of this paper is outside of the 1984 time period, it relates to a batch of Factor VIII given to haemophiliac patients and the subsequent development of antibodies to HTLV-III during 1984. What was interesting about this study, in particular, was that:

> "*If it is true that all but one of our seropositive patients developed anti-HTLV-III as a result of the transfusion of a single contaminated batch of factor VIII, it is interesting that only half the patients who received batch of factor VIII concentrate acquired the antibody".*

3.27. In other words, by testing serial blood samples taken at different time points from the same patients, we could track when HIV entered a Scottish clotting factor pool, probably from a single donor. Most of the infections occurred in late 1983 and early 1984. It also showed that British supplies of Factor VIII were now a risk to recipients, though perhaps not as great as the risk posed by US commercial sources.

3.28. I should clarify that, contrary to the Inquiry's suggestion that I co-authored the article in the Lancet dated 9 February 1985 and titled '*Seroconversion for HTLV-III since 1980 in British haemophiliacs*' **[PRSE0001758]**, in fact I did not co-author this study. It was carried out by Dr S Machin, Dr B McVerry, Dr R Cheingsong-Popov (who was a member of my laboratory) and Dr Tedder. In any event, in this study my colleagues noted that:

> "*three UK cases of acquired immunodeficiency syndrome (AIDS) in haemophiliac patients and several reports of a pre-AIDS-like syndrome have been recorded".*

Accordingly, this study revealed the increasing prevalence of HIV infection from 1982 to late 1984 among persons in England with haemophilia. Thus, the study of English patients mentioned here, and the Scottish patients mentioned in the previous paragraph showed us that haemophilia patients in the UK were at risk of HIV infection from both imported and from British sources of Factor VIII.

3.29. Finally, the Inquiry will also be aware that I co-authored, with Angus Dalgleish and others, a further article titled '*The CD4 (T4) antigen is an essential component of the receptor for the AIDS retrovirus*' **[WITN0684025]**, which was published in *Nature on* 27 December 1984 alongside one with a similar finding by David Klatzmann and colleagues in Paris. In summary, this article demonstrated that HIV specifically binds to the CD4 molecule on the cell surface as a receptor, which helped to explain why this particular subset of T-lymphocytes is selectively lost from the blood of patients with AIDS. It is again illustrative of how our knowledge of AIDS grew incrementally yet rapidly during this period.

Article in *Nature*: "Retroviruses Linked with AIDS"

3.30. I have been asked to comment on an article that I wrote in *Nature* published on 3 May 1984 with the title "*Retroviruses Linked with AIDS*" **[BAYP0000026_107]**. I have been asked to focus on issues relating to rivalry

and lack of cooperation between public health institutions and why blood banks might require ELISA rather than RIA tests.

3.31. I should clarify that this article did not represent my own laboratory's research findings, rather it was an invited short review for *Nature's* 'News & Views' column on the state of knowledge of recently isolated retroviruses from AIDS patients and those at risk of AIDS. Scientists normally distinguish between papers detailing their own novel data and "opinion/editorials" which are reviews or commentaries on a rapidly developing field. Discovery papers undergo peer review whereas short reviews often do not, although the person editing the piece (in this case at *Nature*) might suggest changes to improve its clarity or to fit it into the space available.

3.32. The first paragraph of this article referred to various rivalries between: (a) two different institutes, the National Cancer Institute ('NCI'), being Robert Gallo's lab and the National Institute of Allergy and Infectious Disease ('NIAID'), being Tony Fauci's lab at the National Institutes of Health (NIH) near Washington DC; (b) between the NCI and the Centers for Disease Control and Prevention ('CDC'), i.e. Don Francis' lab in Atlanta, Georgia; and (c) between the NCI and the Institut Pasteur (Dr Luc Montagnier's group) in Paris. In other words, there were institutional rivalries both within the USA and internationally. Investigators in each of these institutions were trying to identify the true cause of AIDS (CDC in collaboration with Luc Montagnier at Institut Pasteur).

3.33. My reference to the rivalries specifically concerned what I considered to be the unnecessary confusion in various press releases and claims for being 'The Discoverer' of the AIDS virus, called LAV and IDAV in Paris and HTLV-III at NCI. Clearly there was a 'rush' to claim credit for the discovery of the cause of AIDS which had resulted in this regrettable situation. In fact, the CDC scientists were already collaborating with Montagnier's group to study the French isolate, LAV. At the time, I criticised the lack of any mention of the French discovery of LAV (that had been reported one year earlier) in the News Conference and

press release announcing the 'discovery' of the AIDS virus by the U.S. Secretary of State for Human Health and Welfare, Margaret Heckler. As I stated in that article, Luc Montagnier's group had "*published first but with skimpy data*". On reflection, the phrase 'skimpy data' could be interpreted as a derogatory term, and I would have been wiser to use the term 'preliminary data'. However, Dr Montagnier did not take offence, rather he was pleased that his pioneering research was noted.

3.34. Whilst I do not believe that these rivalries had more than a minor impact on understanding the aetiology of AIDS, they were unhelpful concerning patent claims. In my experience, scientific research is a curious mixture of cooperation and competition. It is sometimes the case that competition stimulates faster gain of knowledge and understanding whereas at other times it acts as an impediment. In this case I think it was a bit of both: an impediment to exchanging virus samples and a gain in stimulating the field and the development of independent diagnostic tests. In any event, I recall that any negative impact on our knowledge and understanding of the virus was short-lived; I recall that better cooperation between the various research groups did develop soon after, and I would like to think that my article in some small way helped to bring minds together. Moreover, as the article demonstrates, I strongly emphasised the similarity between the NCI and French isolates, despite the different names and interpretations of the findings.

3.35. As to why I suggested in this article that ELISA screening tests for blood banks are urgently required, it was already the case in 1984 that ELISA tests were becoming the routine method for large scale testing and screening in most biomedical applications, including diagnosis of other viruses. ELISA stands for Enzyme-linked 22immunosorbent assay, giving a colour read-out marker (like the colour band of COVID-19 lateral flow tests today) whereas the RIA depended on a radio-activity read-out. RIA screening tests like the one we used were undoubtedly useful for pilot research but, in terms of their application to large-scale screening exercises of this type, they involved radioactive isotopes

that were more expensive and more dangerous to handle in non-research laboratories. It is in this context, therefore, that I mentioned ELISA. Had I had more space, I could have expanded on the importance and usefulness of developing secondary, confirmatory tests using a different technique or format to check out the reliability of a result. Such results can have an impact on the patient or donor providing the sample, especially if the result is based on what we call a 'false positive' reading. I discuss this further in Sections 4 and 5 below.

Section 4: HIV Testing

Testing of two thousand Londoners and results

4.1. The Inquiry refers to the fact that our study **[NHBT0000068_015]** included testing approximately two thousand Londoners including unselected sequential blood donors and the results of these tests were published in the Lancet on 1 September 1984. I am asked to comment on my conclusions in relation to various findings from these tests.

4.2. It is worth setting out that this study was significant as it included a larger data set on blood donors and recipients of blood products than previously published reports from any country. It also represented the first survey to be published of HIV infection rates among blood donors, blood product recipients and known AIDS risk groups in the UK.

4.3. This testing has been referenced in *"Science Fictions: A scientific mystery, a massive cover-up, and the dark legacy of Robert Gallo"* at pages 188 and 189 **[PRSE0002948]**. John Crewdson wrote:

> *"In fact, there was a British AIDS test. Months before, Robin Weiss had developed a laboratory ELISA and used it to test nearly two thousand Londoners, including a thousand randomly selected blood donors, for*

> *Weiss's Lancet paper concluding that LAV and HTLV 3B were both the cause of AIDS. That none of the randomly selected blood donors had been positive suggested that there wasn't much AIDS virus circulating in England. But the National Health Service, hoping to head off what might be an incipient epidemic, wanted to begin precautionary screening of donated blood at a few of its Regional Transfusion Centres".*

4.4. The testing is also referenced in the transcript of the oral evidence that I gave to the Penrose Inquiry on 27 September 2011 at pages 151-162 **[PRSE0006048]**. I note that on page 151 I gave evidence to the Inquiry that, with reference to pages 188-189 of John Crewdson's book:

> "*… I would say everything, including these two pages, that he has in double quotes is meticulously quoted. Where he is not quite correct is that he attributes emotions to the people he is speaking about".*

For example, on page 189 Crewdson writes that:

> "*An angry Robin Weiss responded to the American rebuff by "putting more effort into growing our own isolates"*.

I don't remember being angry at all. It was not surprising that a virus isolate provided to us for research purposes was not deemed to be available for the scale up of routine diagnostic tests. In addition, throughout his book, Crewdson often got details of the science wrong as he did on pages 188-189: He tends to attribute all discoveries to a single person (except when he attacks Gallo for not allowing his colleagues credit for discovery). He mistakenly writes here that "*Robin Weiss developed an ELISA*" whereas it was really my colleague Richard Tedder at MHMS who deserves the main credit for developing it; but more importantly he confuses an ELISA for our RIA test.

4.5. The results of this study were set out in an article in The Lancet on 1 September 1984 **[NHBT0000068_015]**. The study found antibodies to HTLV-III/LAV in 0 of 1,042 "*unselected blood donors*", 41 of 69 "*symptomatic homosexuals*", 53 of 308 "*homosexuals at risk*" and in 0 of 35 "*heterosexuals at genito-urinary*

clinics". In terms of these findings, the results published indicated that antibodies to HIV in the general population of blood donors in 1984 in North London was less than 0.1%. We therefore concluded that current blood donors posed a low risk of HIV infection to recipients. However, the tests found antibodies in approximately 59% of homosexuals suspected of having AIDS-like or pre-AIDS-like symptoms and 17% of non-symptomatic homosexuals attending a GUM clinic for other sexually transmitted diseases. We concluded at the time of the study that gay men in London who attended GUM clinics had a much higher risk of acquiring HIV infection than heterosexuals attending GUM clinics, and healthy unselected blood donors.

4.6. This article found antibodies to HTLV-III in 63 of 184 "*haemophiliacs who have received pooled clotting factors"* **[NHBT0000068_015]**. It was noted in this study that one of the groups being studied were:

> "*Haemophiliacs undergoing regular clotting factor replacement therapy, sometimes with American commercial factor VIII".*

In relation to this finding, we found that infection rates in persons with haemophilia who had received pooled clotting factors was about 1 in 3. Clearly, this meant that there was a high risk of HIV infection from treatment with pooled clotting factors (which included clotting factors imported from the USA). My reaction at the time was one of shock and alarm at the high prevalence of HIV infection in patients with haemophilia.

4.7. In terms of the overall significance of these findings, our article included a larger data set on blood donors and on recipient of blood products than previously published reports from any country. Perhaps more important for this Inquiry, the study revealed the actual rates of HIV infection in North London for donors and for different 'risk groups' for AIDS and more broadly in the UK for patients with haemophilia. The findings indicated the urgent need for screening to detect HIV infection even though the infection rates in healthy donors was currently low.

Section 5: Development and introduction of screening tests for donors

Chronological account of involvement in development of screening tests for anti-HTLV-III in 1984-1985

5.1. The Inquiry asks me to give a chronological account of my involvement in the development of screening tests for anti-HTLV-III in 1984-1985. I should state that, while my laboratory and I were heavily involved in developing screening tests as a research tool, I was only peripherally involved in the further development of tests for routine screening. In other words, my laboratory mainly focussed on the research end of the Research and Development ('R&D') spectrum. My research did, however, contribute to practical aspects, such as early surveillance of HIV prevalence, and the isolation of HIV from patients who were resident in the UK. Apart from my own laboratory's activities, I served on and offered my views on various advisory committees, for instance to the Medical Research Council (MRC), and most notably, the DHSS Expert Advisory Group on AIDS (EAGA). I have attempted to give some clarity both on my research programme and on my advisory work, where I have sufficient knowledge and recall of events.

5.2. Concerning committee work, I was a member of the Medical Research Council Working Party on AIDS that met in October 1983 until early 1987 (I do not have a record of the precise date) **[CBLA0001749]**. This working party was set up to combine expertise in the United Kingdom to generate ideas to contribute to the understanding of AIDS. The initial terms of reference for the MRC Working Party were:

> *1. "To review scientific knowledge and research on AIDS in the UK and abroad.*
>
> *2. To encourage contact and co-operation between research workers in this*

3. To advise the Council on the current state of knowledge in the field and on topics for research."

5.3. The MRC Working Party was distinct from the Expert Advisory Group on AIDS at the Department of Health and Social Services (the MRC was funded by the UK Government through the Department of Education and Science). The two groups advised different bodies. The MRC wanted to encourage research on AIDS in the UK whereas EAGA was primarily concerned with advising the DHSS on how to manage public health in the face of this new epidemic. I do not recall more than one meeting of the MRC Working Party.

5.4. Reviewing the clinical position at that time, the MRC Working Party recorded:

"The laboratory markers for disease were well established for AIDS itself but their relevance in screening and in a possible precursor state was not established."

5.5. Regarding my view on screening for HIV infection, in my *Nature* article published on 3 May 1984 titled:

"Acquired Immune Deficiency Syndrome Retroviruses Linked with AIDS". I wrote: "*reliable ELISA screening tests for blood banks are urgently needed and might have to be used as routinely as tests for hepatitis B virus*". **[BAYP0000026_107]**.

5.6. This remark illustrates my thinking at the time that routine screening of blood donations should be developed as quickly as possible.

5.7. I have been referred to a DHSS internal memo titled "Acquired Immune Deficiency Syndrome AIDS Current Developments" on 27 July 1984 **[MACK0002588]**. It stated:

"The importance of a screening test for the UK National Blood Transfusion Service is paramount. Whilst the risk calculated so far of

AIDS being transmitted through ordinary blood transfusions is minimal, recipients of blood derivatives such as Factor VIII which are mainly extracted from large plasma pools are at greatly increased risk of having the disease transmitted".

5.8. It refers to collaboration between the USA, France and UK and the HIV isolates being provided to virologists at the ICR and MHMS and records the intention of isolating a similar agent in the UK. The paper also stated:

"*Using the USA agent they have been able to devise a test which uses a radio immunoassay technique to identify antibody to HTLV 3 virus in the blood of AIDS patients*".

5.9. In a letter from Dr M. Abrams (Senior Principal Medical Officer, DHSS) to Dr E. Brandt (Assistant Secretary for Health, USA), dated 10 August 1984 **[DHSC0000444]**, Dr Abrams stated:

"Dr R C Gallo of the National Cancer Institute sent Professor Robin Weiss of the Institute of Cancer Research here virus isolates of HTLV III in the usual way of exchange between research workers in the same field. Professor Weiss in the course of further investigation with co-workers has developed a radioimmunoassay for antibodies to HTLV III which appears to be specific and sensitive. The test has been used to examine the sera of patients with AIDS, patients with the extended lymphadenopathy syndrome, homosexuals attending clinics for sexually transmitted diseases, patients with haemophilia and normal blood donors"

Dr Brandt did not respond for several months and in November or early December I recall, although I no longer have any record of my letter, that I wrote to Dr Gallo to clarify our remit to use his HIV isolate (called HTLVIIIB). He replied on December 19 **[WITN6868008]**:

"I have just spoken to Dr Peter Fischinger. We are both in complete agreement that you are perfectly free to use H9 and H9/HTLV-III for any

non-commercial propose including testing of blood samples. Dr Harmison is now acting in Brandt's place since Brandt left December 1. Dr Fischinger is informing Dr Harmison of our position".

Obviously, the use of HTLVIIIB (in CEM cells, not in H9 cells) by Wellcome Diagnostics Ltd would be commercial. The scaling up for routine use of HTLVIIIB by BPL or another DHSS facility for mass screening that competed with tenders by commercial providers would arguably be regarded as commercial. After several months silence following Dr Abram's letter, the US Department of Health and Human Welfare declined to allow the use of this US isolate for the manufacture of British screening tests.

5.10. I have been referred to a paper titled, 'Proposed Working Group of the Advisory Committee on the National Blood Transfusion Services – Consequences to the NBTS of Screening for HTLV III,' dated 13 August 1984 **[PRSE0003109]**. It states:

"You will be aware of the recent development by Drs Weiss and Tedder of a radioimmunoassay for HTLV III antibody and the findings that the limited use of this test has revealed. It is proposed to extend the test to all blood donors at the North London Regional Transfusion Centre (NLRTC) for a period of at least 3 months. As the donor population for NLRTC is drawn from an area where the incidence of AIDS patients and possibly contacts is currently the highest in the UK, it is hoped to extend the screening test to at least two other Regional Transfusion Centres. This, of course, depends on our ability.to scale-up production of reagents for the test using either the virus isolate from Dr Gallo's laboratory or a UK isolate (yet to be achieved). The information collected from the use of a screening test in three centres will provide a basis on which to base policy decisions about extending the test more widely to the whole of the NBTS.

We would therefore be in a strong position to make decisions about the need to buy from one of the five US pharmaceutical companies who have been licenced to produce a screening test and are likely to wish to start marketing these tests in the UK in the next few months."

This note of the NBTS Advisory Committee seems to unaware of other tests being developed in USA and Europe.

5.11. I was copied into a letter written by Dr Tedder to the DHSS dated 18 December 1984 noting that we urgently need to upscale the RIA, developed by Middlesex Hospital Medical School and ICR **[PRSE0001117]**.

5.12. On 27 November 1984 I updated the Expert Working Group (which became EAGA) on Aids upon tests for HTLV III antibody **[WITN6868009]**. I do not now recall the detail of my briefing, however the minutes record **[PRSE0004191]**:

> *"Weiss has just isolated HTLV III from adult onset hypogamma treated with IgG (Plasma Rx not excluded)*
>
> *recombinant antigen is the chosen approach, but claims under-funded to do the work*
>
> *Weiss/Tedder/DHSS appear to be negotiating as follows: Wellcome ("interested") Celltech ("no interest") Unilever/Seward (?)"*

These excerpts from the minutes appear to be short notes rather than full minutes. The first item notes we had isolated HIV from a UK patient; the second item is inaccurate but makes reference to how one might wish to progress in the future; the third notes that negotiations were ongoing with diagnostic companies.

5.13. On 3 December 1984 I wrote to Dr Alison Smithies, at the Department of Health and Social Security, **[DHSC0002253_002]**:

> *"I am just writing to confirm that in view of (a) having a local, independent isolate of the AIDS retrovirus and (b) the requirement in Dr. Brandt's letter for the U.K. to negotiate with American commercial licensees, we should probably drop the use of any American reagents in scaling up our methods for serological screening and develop our own independently."*

5.14. I have seen a Note on Research and Development of AIDS (HTLV III Antibody Screening of Blood Donors in the British Transfusion Service) dated 2 January 1985, with letter attachment to Alison Smithies from Richard Tedder, in which he stated:

> *"plans are going ahead to scale up production of the test reagent and it is hoped that tests for blood donors could be ready to be used in the National Blood Transfusion Service in the early part of 1985"* **[PRSE0003287]**.

I think that Dr Tedder was referring to scale up of his RIA to encompass the North London Transfusion Service, not national screening. It details costing for two junior staff (secretary and technician) and items of equipment and consumables. It states that:

> *"Given funds are made available, it should be possible to start the pilot studies by June 1985"*.

5.15. I refer to a document **[OXUH0000392_002]** which is a letter from Dr John Craske and others including myself to haematologists who had kindly provided serum samples for our initial study **[NHBT0000068_015]**. It was part of a plan to conduct research into when recipients of blood and blood products became infected by HIV. In order to understand risks of infection better, we outlined what further studies could be achieved with their help in providing samples and notes of what kind of blood product patients had received.

5.16. I have now seen a memorandum from Dr A. Smithies to Dr Alderslade, dated 11 January 1985 **[DHSC0000562]**. In the annex to the memorandum to Ministers my work in respect of the antibody testing is referred to. It states that the Department were advised by the Expert Group on AIDS of the National Blood Transfusion Service that a screening test for HTLV III antibody should be introduced to all Regional Transfusion Centres (RTCs) as soon as possible. Pilot trials are needed before these tests can be introduced to all Centres.

5.17. The first meeting of the Expert Advisory Group on Aids ("**EAGA**") took place on 29 January 1985 **[PRSE0002734]**. The minutes record:

> *"18. Professor Weiss said that work was currently being carried out with Wellcome Diagnostics to develop a screening test, but there were still problems to be solved and he was not able to say when the test would become available. Professor Zuckerman said that tests were also being carried out at his laboratory and that the results of the American Dupont and Travenol tests might be available within a few months. Comparisons would be made with the test being developed by Professor Weiss and Dr Tedder.*
>
> *19. The Chairman reminded members that the November meeting of the BTS Advisory Group on AIDS had concluded that a screening test for all blood donors should be made available as soon as possible. He asked whether the EAGA endorsed this view.*
>
> *20. There was general support for the introduction of a test as soon as practicable.*
>
> *…*
>
> *23. A sub-group was set up comprising Drs Gunson, McLelland, Mortimer, Pinching, Rodin and Tedder to consider the various aspects of screening tests for AIDS, in particular the best way of introducing the Service when the tests become available. Dr Smithies would Chair this group."*

I was not a member of this sub-group.

I am not aware of the involvement of Dupont or Travenol at subsequent meetings. I am not aware that any comparisons between different tests as suggested by Prof Zuckerman were made until Dr Mortimer's evaluation studies were conducted.

5.18. There was an EAGA background paper marked 'confidential' dated January 1985 **[WITN6868010]** which stated:

"Development of Tests for HTLV III

Since the first isolation of HTLV III in 1984 numerous publications describing the prevalence of antibody in high risk groups have appeared. As far as the UK is concerned the study by the team led by Professor Weiss at the Chester Beatty Institute and Dr Richard Tedder at the Middlesex Hospital using a competitive radioimmunoassay (RIA) is of major interest. They reported:

'Two thousand person in the UK were examined for antibodies to HTLV III. Of patients with AIDS, 30/31 were sero-positive as were 89 per cent of patients with persistent generalised lymphadenopathy, 17 per cent symptomless homosexual men, 34 per cent haemophiliacs receiving pooled clotting factors and 1.5 per cent intravenous drug abusers. None of more than a thousand unselected blood donors was sero-positive.'

Since this study, further antibody tests have been undertaken mainly in haemophiliacs, recipients of whole blood and other blood products. Some population studies are being undertaken at PHLS.

Significance of the HTLV III Antibody Test

The test identifies antibody in an individual who has been exposed to the virus. A positive test is not diagnostic for AIDS since most people who sera covert will not necessarily develop the syndrome. Neither does a positive test necessarily indicate protection or exclude a carrier state, since the antibodies are not neutralizing. A viraemia is presumed to precede the development of antibody. It is not yet known how rapidly seroconversion occurs after infection.

Availability of HTLV III Antibody Test

The test is available in two centres at present namely the Middlesex Hospital and at the Central Public Health Laboratory Colindale. Commercial development of the test is underway and it is hoped that the test will be more widely available by the spring. The screening of blood donors by Regional Blood Transfusion Centres is seen as a priority."

5.19. On 22 April 1985 the screening sub-group of the Expert Advisory Group on AIDS reported there was a need to ensure that before screening was introduced that it was reliable, and that proper validation tests and arrangements were available. **[PRSE0001239]** I was not a member of this sub-group, but looking at this document now I would have endorsed its findings.

5.20. The minutes of the EAGA held its 5th meeting on 30 July 1985 **[PRSE0002628**

5.21. **]**. Evaluation of AIDS Screening Tests and Introduction of AIDS Screening tests was tabled and the following was minuted:

"Dr Gunson tabled an amendment to item 3 on page one of the report. The working party of the Regional Transfusion Directors Committee recognised the pressure to introduce routine screening in the BTS as soon as possible. Regional Transfusion Directors were therefore being advised to make arrangements with their respective RHAs for the introduction of routine screening and familiarising themselves with the kits recommended by the PHLS study, whilst the NBTS evaluation was proceeding. The evaluation within the BTS bad begun, 6000 specimens were being tested each in two centres, at the rate of 600 tests a day. An analysis should be available in September which would give estimates of the specificity of the kits and their ease of use. ***The working party considered it possible to commence screening of blood donations in October 1985 and recommended that the introduction of the tests should take place throughout the UK over the shortest period practicable.****" (my emphasis).*

5.22. The 6th EAGA meeting was held on 1st October **[MRCO0000001_068]**, but I was not in attendance.

5.23. The 7th meeting of the Expert Advisory Group was held on 26th November 1985 **[DHSC0002287_060]**. Dr Smithies explained that by 14 October the Regional Transfusion Centres were screening all blood donations.

5.24. If the Inquiry points to further matters concerning my involvement in the chronology of the development of screening tests, I shall try to answer them to the best of my ability.

Anti-HIV RIA development

5.25. I am asked about the development of the anti-HTLV-III RIA developed by me and colleagues at the Middlesex Hospital and Chester Beatty Laboratory. I am not sure exactly what the Inquiry means by a "*working RIA*". According to my memory, we had an RIA that seemed to perform reliably in preliminary tests in June 1984. By early July, it was working well enough as a research tool to screen approximately 2000 samples as reported in our Lancet paper **[NHBT0000068_015]**. However, to adapt the test for large scale routine screening while maintaining its 'working' properties, i.e., sensitivity, specificity, batch consistency, containment of HIV as a dangerous pathogen, containment of ^{125}Iodine as a hazardous isotope, was a major undertaking.

5.26. I do not know whether it was the first British anti-HTLV-III assay to be developed but it was likely that other British-based investigators would have been devising methods to study immune responses to HIV. I am not aware that any other British tests were in the public domain when we published our initial survey regarding the use of RIA on 1st September 1984 **[NHBT0000068_015]**.

5.27. In terms of the process adopted to develop the RIA and how it might have differed from the American method, our process was to prepare antigen from HIV-infected cells and to devise a competition format RIA whereby the sample to be tested would need to displace a radio-labelled standard anti-serum to yield a positive result. There was not a single American method because many laboratories were developing research tests for HIV antibodies, but I do not recall one using a competition format.

5.28. I am asked when it was first communicated to the DHSS that a working RIA had been developed. I have been referred to **[MACK0002588]**, being a DHSS internal memorandum dated 27 July 1984 and **[DHSC0000444]** being a letter dated 10 August 1984. However, I do not recall having seen these two documents prior to the Inquiry's communication with me on 22 February 2022.

5.29. I note some inaccuracies in the DHSS internal memorandum dated 27 July 1984 **[MACK0002588]**: Dr Montagnier's group in France published their discovery of LAV (HIV) in May 1983, not in late 1983 as stated, whereas there was no report of HTLV-III from America until May 1984, although there were reports in May 1983 of the presence of HTLV-I in some AIDS patients. This DHSS internal memorandum quite understandably confuses HTLV-I and HTLV-III since the nomenclature and indeed characterisation and understanding of the different viruses was opaque at this time. As stated, in our hands, the French isolate that we obtained on 29 February 1984 (though not the one obtained in October 1983) was just as easy to propagate to high levels as the American one that we received from Dr Gallo three months later. It was pure chance that we used HTLV-IIIB as antigen in our survey.

5.30. I did not have any direct contact with DHSS before November 1984 when I attended an informal advisory committee on AIDS, which I think officially became EAGA in January 1985.

5.31. With respect to the receipt of funding which facilitated the development of the RIA up to this point, unfortunately I no longer have written records of the funding to my laboratory. My core funding supported two researchers (research assistant Paul Clapham and post-doctoral scientist Rachanee Cheingsong-Popov). This funding came from the Joint Committee for the Institute of Cancer Research of the Cancer Research Campaign ('CRC', now part of Cancer Research UK) and the Medical Research Council ('MRC'). CRC funds derived from charitable donations, and MRC was funded by the UK Government through the Department of Education and Science and not the DHSS. I think that we received a supplementary grant from the MRC following the meeting of the MRC Advisory Group on AIDS in October 1983 to fund one research assistant specifically to study the possible association of retroviruses with AIDS. At that time, 1983/4, we also had a small grant for one technician from the Leukaemia Research Fund (LRF, now called Bloodwise) to study HTLV-I. When we switched much of our research effort from human leukaemia viruses to HIV in March 1984, I remember being concerned that the CRC and LRF might consider it inappropriate for us to divert funds to study a non-malignant disease such as AIDS. I therefore sought and gained permission to do so, but I do not have a record of this matter.

5.32. There were two people working in my laboratory who, as far as I can recall, were funded by their own fellowships; one was a clinical research fellow, Dr Angus Dalgleish and the other was a visiting scientist, Dr Karoly Nagy, from the Semmelweis Medical University in Budapest whose fellowship was funded from Hungary. They participated in our human retrovirus studies including early stages of HIV research that contributed to the RIA test and their laboratory costs were covered by my CRC/MRC research consumables budget.

5.33. From late 1984 to 1986, we found ourselves serving as a training laboratory for scientists employed by other institutions to acquire skills in handling and propagating HIV. We took this on because it was urgent to build up broader experience and expertise on HIV in the UK. Virologists and immunologists

came from Oxford, University College London, St Mary's Hospital Medical School, Middlesex Hospital Medical School and St Stephen's Hospital (Chelsea & Westminster Hospital Medical School). We provided them with the virus for non-commercial purposes through materials transfer agreements after seeking approval from either Dr Gallo or Dr Montagnier, provided they had HSE-approved Category III containment facilities to handle the virus. Those who did not yet have containment facilities handled the infectious part of their work in our laboratory. I remember that one virologist was seconded from the Central PHLS in Colindale for 3 months in 1985, but I don't think that we received any funding for the laboratory reagents that he used. In 1986, a technical assistant came from Beecham Laboratories (later part of GSK), which wished to test the potential of their candidate anti-herpesvirus drugs to inhibit HIV infection; we received funding for consumables and overheads for the costs of his work.

5.34. I am asked to explain the use of a "*membrane immunofluorescence assay ('IFA')* and a radioimmunoassay ('RIA')." I am referred to Lancet article I co-wrote which was published on 1st September 1984 **[NHBT0000068_015]**. In terms of how the IFA worked and its role, in IFA, an antibody specific to HIV could be detected by exposing it to a 2nd antibody specific to human antibodies that was tagged with a fluorescent marker. The fluorescent label emits visible green light under ultra-violet (UV) light. If the anti-viral antibody attached to HIV envelope antigen on the surface of HIV-infected cells, then the cells would glow green under UV illumination, indicating the presence of virus. It is a standard method called 'indirect IFA' for detecting antigens in infected cells, and antibodies in sera (i.e. blood fluids).

5.35. The Inquiry refers me to page 3 of the same document in which I state that both assays are "*simple, reliable and specific".* Both the IFA test and the RIA assay were relatively simple and reliable in a research setting. We could use IFA as a confirmatory test for serum samples yielding a positive result by RIA. I did not consider the IFA to be suitable for scaling up for screening blood donations. It was too labour-intensive; it involved using live cells producing HIV and therefore

needed to be conducted in a higher-level bio-security laboratory. The main reason we used the IFA in that study was to determine whether the American and French isolates were the same kind of virus, as I had suggested in my *Nature* News & Views article in May 1984 **[BAYP0000026_107]**. By absorbing out a high dilution of antibody on LAV-infected cells, there was no remaining immunofluorescence on HTLV-III infected cells. Thus, we concluded that the two viruses represented one and the same kind of virus. In other words, we performed a comparison that the discoverers of the two isolates had declined to do during the short period of claims and counterclaims.

5.36. I had no view at the time of the cost-effectiveness of IFA versus RIA because I did not regard IFA as suitable for large scale screening.

5.37. In relation to the question as to why an ELISA was not used to test the sera, Dr Richard Tedder had experience with RIA for Hepatitis B virus testing, and we had jointly set up an RIA for HTLV-I & -II testing for experimental research. Given the state of our art at that time, we thought we would make faster progress with the RIA for exploratory purposes than by learning the newer technique of ELISA on which we were less experienced. As expressed in my *Nature* News & Views commentary **[BAYP0000026_107]**, I envisaged that the ELISA technique would soon supersede RIA for scale up beyond a small research laboratory. Indeed, all the commercial screening tests for HIV that came on stream in 1985 used ELISA.

The findings of the radioimmunoassay HTLV III antibody test, communication to DHSS and subsequent scaling up.

5.38. The findings that the use of our test had revealed are set out in paragraphs 4.1 to 4.7, above. As I have stated, the findings concerning people who had received pooled clotting factors were something of a bombshell.

5.39. I personally had not communicated with the DHSS before publication, which occurred the day after the date on Dr Smithies' letter **[PRSE0003109]**, and neither did the DHSS communicate with me. Among our co-authors were John Craske of the Regional Virus Laboratory of the Public Health Laboratory in Manchester, and John Barbara of the North London Blood Transfusion Centre, Edgware. I expect that they informed their senior colleagues in advance of our paper appearing in print and I believe that Dr Richard Tedder was in contact with Haemophilia Centres. As Dr Smithies' letter makes it clear there had been communication with DHSS about our findings, but I do not know what the lines of communication were. Document **[MACK0002588]** indicates that the DHSS already knew of our findings by 27 July 1984.

5.40. I do not recall any specific plans that would involve my laboratory to scale up the production of sufficient reagents to carry out three month's testing of all blood donors at the North London on Regional Transfusion Centre. We had no further bio-security space to expand the effort. In fact, our Category III containment laboratory had been my office, and in 1983 I moved to a smaller office in order to convert the office suite into a containment laboratory. Dr Tedder, however, required a Category III containment laboratory and Dr Smithies may have been referring to his needs.

5.41. We were working flat out to exploit the RIA test to determine whether 'Slim' disease in Uganda and an 'aggressive' form of Kaposi's sarcoma (similar to that seen in gay men in the West) in Zambia were the result of HIV infection. Our 1985 papers in *The Lancet* revealed that the prevalence of HIV in healthy Ugandans employed by the Mulago Hospital in Kampala was around 10% - another shock to us. We were also seeking to isolate HIV from British patients. The African project, the search for British HIV isolates and our work on receptors and neutralizing (protective) antibodies fully occupied us.

Factors affecting the development of the test reagent

5.42. The Inquiry has referred me to a letter dated 19 October 1984 from Dr Smithies to Dr Alderslade **[DHSC0002323_009]**. This letter refers to the production of more of the test reagent and some of the factors delaying that production. I have been asked to set out the findings that the use of the test in our study had revealed, the information communicated between myself and DHSS regarding those results, and my plans for "scaling up" the production of reagents as at August 1984. I have addressed some of these points above.

5.43. As a starting point, I have only a hazy recollection of these discussions because I was not directly involved. Dr Tedder was interacting with the DHSS and kept me broadly informed. I agree with Dr Smithies' summary, with the sole reservation that when she referred to our research as "*only a pilot study*" she may not have fully appreciated what an achievement it was to test 1004 blood donors and a further 900 people in AIDS 'risk groups'. It represented a larger number of tests than the NIH and CDC in USA had conducted, and it was the largest surveillance study of HIV reported by that date. But Dr Smithies was correct in that it was a pilot study in terms of population screening.

5.44. As to whether it would be appropriate to develop further amounts of HIV antigen (the test reagent) without the agreement of US authorities, the situation was as follows: When I visited Dr Gallo at NIH at the end of May 1984, I asked him to provide us with the HTLV-IIIB isolate to conduct research. He promptly asked his colleague Dr Mika Popovic to give me a sample there and then which I brought back to London. There were no strings attached concerning our lines of research, but I signed a standard Materials Transfer Agreement (MTA) that the virus was provided for research purposes only and not for routine screening or for commercial development. It was therefore necessary either to gain permission from the USA to use the HTLVIIIB for routine screening, or to use a non-USA isolate of the virus for this purpose. Initially, seeking an agreement with the US seemed sensible.

5.45. I do not think that the lack of cooperation from the US Government significantly delayed the development of a British test. Regarding my involvement, if we had attempted to scale up production in our bio-security laboratory, it would have delayed our search for British HIV isolates. I would say that contrary to causing a delay, we made important progress on aspects of AIDS testing that fell within our competence. It is possible that the lack of response from the US Government might have delayed plans, if any, to scale-up elsewhere. If so, in my retrospective opinion, the DHSS could have anticipated the availability of a British isolate from British researchers, not necessarily in my laboratory, and made provision for it.

5.46. Naturally, we wished to conduct our research as safely as we could, but we simply did not know how dangerous it might be to handle the virus. One of the first things we did as soon as we had a rudimentary test was to test our own blood weekly. There was a case of laboratory acquired infection in USA in one of the contract laboratories producing Robert Gallo's isolate and I understand that this person died of AIDS some years later. Dr Tedder also tested the British nurse who had a needle-stick accident drawing blood from an HIV-infected patient and he recorded her seroconversion **[HCDO0000394_117]**. I think she also died eventually.

5.47. I thought then, and I still think now, that my colleagues and I willingly put ourselves at potential risk of infection in order to improve public health and to reduce the risks of HIV in recipients of blood and blood products.

5.48. Regarding the contributions to HIV test development from my laboratory, I don't think the requirements of Health & Safety Executive (HSE) and/or trade unions at ICR delayed the development of a test. I recall that we sought advice from and were inspected by the HSE, and we received co-operation of local officers representing each of the unions involved (technicians, scientists and medical).

Administrative staff and cleaners were not required to enter the Category III containment laboratory where we handled HIV.

Isolation of HIV from a British patient in 1984

5.49. The Inquiry has referred me to the isolation of the HTLV-III/LAV virus from a British patient in the Autumn of 1984 and document **[PRSE0004191]** on page 2 and raises a series of matters for me to address.

5.50. I do not have a record as to exactly when we were first able to isolate a virus from a patient in the UK (not necessarily a British citizen). I think it was during October 1984 although we had probably received the infected blood sample in September, most likely from the patient with hypo-gamma-globulinaemia who had presumably been infused with infected plasma. We did not 'receive' this isolate, we performed the isolation ourselves and began to study it immediately.

5.51. Many years later (1991) when DNA 'finger-printing' of individual isolates became possible, we realised that the CBL1 isolate was actually the French isolate LAI that had contaminated the culture. Indeed, LAI also had also spread within Institut Pasteur to the French isolate BRU, and in Dr Gallo's lab as HTLV-IIIB, at the CDC Atlanta, and probably elsewhere in the research world. In other words, LAI was like a 'laboratory equivalent' of the SARS-CoV-2 variant Omicron BA.2 in that it was extraordinarily transmissible - within Category III laboratories. We apologised to the Institut Pasteur at once. Since they in turn had adopted our CEM cell method for the ELAVIA test without honouring our MTA, ICR and Institut Pasteur came to an agreement not to challenge each other's transgressions of material property.

5.52. As to whether there were any licensing or other restrictions on this isolate, I doubt that, at the time of minute **[PRSE0004191]**, any companies, BPL or DHSS had access to the isolate because we would have needed to characterise it first.

Concerns over the development of an HIV test facility

5.53. The Inquiry has drawn my attention to the minutes of a meeting of the Advisory Group on AIDS dated 27 November 1984 **[PRSE0004191]** and the concerns that I raised according to those minutes regarding the development of an HTLV-III test facility. The Inquiry has asked me to address a number of matters arising from this note relating to the date of development of a cell line producing virus suitable for use as antigen in the diagnostic assay, whether funding was adequate, negotiations with biotech company third parties, the involvement of DHSS, and the provision of both clinical and laboratory facilities.

5.54. In terms of the date of development of a cell line producing virus suitable for assay, I no longer have my laboratory records, but I believe that by late November 1984, we felt confident that, provided the infected CEM cells could sustain virus production over a long period, the isolate we named CBL1 would yield sufficient viral antigens to be a suitable substrate for antibody assays, as communicated by me to Dr Smithies at DHSS on 3rd December 1984 **[DHSC0002253_002]**.

5.55. On the point relating to being under-funded, I note that the minute states:

> "*Weiss emphasises recombinant antigen is the chosen approach but claims under-funded to do the work*".

This note is inaccurate. My primary role at that *ad hoc* meeting and at subsequent EAGA meetings was to explain to DHSS the science and how it might progress, and only secondarily to speak about what was happening in my laboratory. The message I was trying to get across (perhaps unsuccessfully from reading this minute) was that ideally a recombinant HIV antigen would be a much better source of antigen to use in antibody assays and would not entail hazardous scale up of infected cells which could only be undertaken in a high bio-security laboratory. With a possible exception of Chiron Corp in Emeryville, California, which was examining Jay Levy's San Francisco HIV isolate ARV,

no-one worldwide had recombinant antigen at the time of this DHSS note in November 1984 because cloning and sequencing the HIV genome was not yet complete. Recombinant antigen, however, seemed to many scientists including me to be the obvious direction to go. With the benefit of hindsight, I consider that our judgement at the time was borne out because, within four years, all commercial HIV diagnostic and screening tests were based on recombinant antigen.

5.56. Regarding the funding available to my laboratory, as far as I can remember it had not changed between September (set out in para 5.68) and 27 November 1984. I did not regard my laboratory as "*under-funded*" and I did not seek further funding. Again, I suppose that the minute confuses a general comment by me on the costs involved with a personal plea for funding. In any case, my laboratory would not have been competent "*to do this work*" since we did not at that time have the technological know-how for gene cloning and protein production from recombinant DNA expression ('recombinant antigen').

5.57. I note that the minute mentions that "*Weiss/Tedder/DHSS" were negotiating with Wellcome, Celltech and Unilever/Seward"*. However, this statement is not strictly accurate, because it was our institutions and their business advisers who were negotiating with diagnostic companies. I was barely involved at all. Unfortunately, I did not know then and I do not know whether DHSS were involved in these negotiations, and I do not know why Celltech and Unilever were not interested. In fact, I did not even know that Unilever had been approached. Moreover, as far as I was aware, ICR did not contact other companies. ICR was advised by the British Technology Group (BTG) which was a government sponsored organisation set up to help universities seek commercial exploitation of inventions. The Prime Minister, herself a former chemist, was keen for universities and the MRC to form public-private partnerships citing the failure to develop and exploit the British invention of monoclonal antibodies. I am not aware whether the BTG contacted other organisations than those mentioned.

5.58. Turning to the issue of the clinical and laboratory facilities, and the minute's reference to a "*potential for a major impasse in the provision of both clinical and laboratory facilities"* (page 4), I have already described the facilities at the ICR, and I was not seeking to expand them. I suppose the potential impasse was to locate external facilities to produce sufficient reagents for a marketable test to supply the UK and Commonwealth countries in Africa. The Centre for Applied Microbiological Research (CAMR) at Porton Down had facilities for growing HIV-infected cells in bulk and was able to allot time and space to do so if funded for that purpose. To my recollection, the potential impasse was averted and there was not a significant delay.

Patent for the Isolate

5.59. The Inquiry has asked me when I obtained a patent for the isolate and refers me to document **[PRSE0004280]** which suggests this had been obtained by 22 January 1985. I note that this document, which is dated, erroneously, 28 January 1984 should, in fact, be dated 28 January 1985 states:

> "*Professor Weiss and Dr Tedder (who are not NHS employees), have patented the British isolate and certain aspects of their test method".*

5.60. I think that this document confuses filing a patent application with being granted a patent. Unfortunately, I no longer have the records of the application and approval of this patent. I recall that we would have filed a patent by 22 January 1985, probably by the end of December 1984, and that it is likely that it took at least one year for it to be approved. I cannot now be sure of these details, but it seems most unlikely that the patent had been approved and secured by 28 January 1985. This is supported by a memorandum from Mr Rogers to Mr Devereaux dated 13 February 1985, it refers to the fact that the:

> "*the Middlesex and Chester Beatty have jointly applied for a patent"* **[DHSC0002259_023]**.

This is further confirmed in a note produced by Dr Kennedy dated 4 January 1985 which mentions that:

> "*There has been a Patent application in the names of the Middlesex Hospital and Chester Beatty Laboratory, where Professor Weiss is based…".* **[DHSC0002255_039]**.

Moreover, the sponsorship agreement relating to research into diagnostic tests for the AIDS virus between Wellcome, ICR and the Middlesex Hospital Medical School dated 12 August 1985 suggests that, even by this date, it was still in the application stage:

> "*the U.K. Application" means the patent applied for in the United Kingdom under Patent Specification Number 8500918"***[UCLL0000001]**.

5.61. I remember that the main claims in the patent filing were on the competition format of the assay and on the use of CEM cells as a means of producing viral antigen. The use of the CBL1 virus isolate was a minor claim because it was not an invention, rather it was a proprietary material.

Development of an ELISA/RIA

5.62. I have been asked to comment on when Dr Tedder and I began to develop an ELISA rather than an RIA and the communications subsequently held with DHSS relating to this issue. I should clarify that we did not begin to develop an ELISA. Wellcome Diagnostics Ltd proposed to substitute ELISA for RIA in a screening test based on the competition format HIV antibody test that we had developed as a research tool, and Dr Tedder and I readily agreed. As can be seen in Dr Tedder's letter to DHSS **[PRSE0001117]**, he was asking DHSS for funding to his laboratory to scale up the RIA, not the ELISA, sufficient to introduce pilot testing at one Regional Transfusion Centre.

5.63. I do not recall having any communication with the DHSS on this issue, other than attending the advisory discussion on 27 November 1984 (my letter to Dr

Smithies dated 3 December 1984 **[DHSC0002253_002]** and then serving on EAGA from January 1985 to December 1986. The CMO asked me to join EAGA as an expert on HIV, not as a representative of Dr Tedder's and my collaborative research project. Contrary to what is stated in **[DHSC0000562]**, I had not recalled that the Medical Research Council had established an 'Expert Advisory Group', rather a working party, until 1987, when the MRC Directed Programme on AIDS started. Perhaps this note refers to EAGA which was a DHSS group.

Costs of tests

5.64. I have been referred to a DHSS memorandum/submission dated 11 January 1985 which states at paragraph 6 that:

> "*both American and British tests are still being developed but the likely cost will be between 75p and £2.00 for each donation. The British test is more sensitive… and is likely to be cheaper*" **[DHSC0000562]**.

5.65. Whilst I am asked to comment on the accuracy of these estimates, I had no knowledge about DHSS cost estimates, and I was not involved in any discussions about them. Moreover, as to whether the estimates were based on an RIA test rather than an ELISA and how those costs might differ, one can reasonably assume that there would be an initial capital cost to install ELISA plate readers in place of scintillation counters to measure radio-activity, and that thereafter ELISA tests would be less costly than RIA. I also note from the minutes of the 16th meeting of the Central Blood Laboratories Authority held on 1 February 1985 (which I did not attend) **[DHSC0002325_040]**, that the view was held that:

> "*if given the antibody BPL could produce a test as an alternative to the Chester Beatty's work in association with industry, at a much lower cost".*

Again, however, I simply cannot speculate on that statement for similar reasons. It is not clear to me what antibody the minute referred to and what the scientific basis for this assertion was.

CBLA/BPL access to an isolate to produce a RIA

5.66. The Inquiry has asked me a number of questions regarding the CBLA/BPL's potential to produce an RIA for mass use subject to access to an isolate. I am referred to document **[DHSC0002325_040]**.

5.67. I was made aware by Dr Tedder that CBLA/BPL were considering plans to develop their own anti-HTLV-III RIA and I do not remember being involved in any discussion as to whether CBLA/BPL had access to an isolate although it is possible that it was discussed in my presence at EAGA. Further, I was not involved in any discussion on this matter. Had CBLA or BPL requested an HIV isolate from me, I think that by February or March 1985 I would have been in a position to provide an isolate for research and standardisation purposes, but only if they had an HSE-approved Category III containment laboratory dedicated to propagating human retroviruses. It would be strictly against HSE regulations to distribute a dangerous pathogen to any organisation lacking an appropriate bio-safety facility.

5.68. I was and remain sceptical that CBLA/BPL would have been able to devise and to produce an anti-HTLV-III RIA for mass use without seeking collaboration because they did not have expertise in propagating retroviruses. I think they were adept at extracting Hepatitis B surface antigen from human plasma, but growing retroviruses in live cell lines involved quite a different technique. And if CBLA/BPL did have the skill, they surely had access to samples of infected blood and could have made their own British isolates. One should bear in mind, however, that only around 1 in 12 HIV isolates would grow in cell lines for the reason of cell receptor expression outlined in my response to Question 8 (Paragraph 3.20). Neither CBLA nor BPL requested us to train a virologist to work on HTLV-III. Later, we did accommodate trainees to gain experience in handling HTLV-III. They were Dr William Jesson, who was seconded from the Central PHLS, Colindale (October 1985 - April 1986), and Dr Dennis Aw, who

was seconded from the Scottish NBTS for 3 months in early 1986 **[PRSE0001171].** Overall, I consider that we pulled our weight whenever asked to help government-funded laboratories to acquire the necessary skills.

Requests for funding from DHSS/MRC

5.69. The Inquiry has raised a number of issues with me regarding requests for funding from the DHSS and the MRC in order to scale up the MHMS-ICR RIA for mass use and has asked me to consider a number of documents in this regard.

5.70. By way of a few introductory remarks, it is incorrect that at various times throughout 1984-85, I requested funding from the DHSS and the MRC in order to scale up the MHMS-ICR RIA for mass use. I don't recall requesting funds even once for this purpose. Dr David Tyrrell makes it clear in his letter to Dr Jane Cope **[MRCO0000541_033]** that I was not asking for further funding, although Dr Tedder was. In 1983, before the cause of AIDS was accepted, I had received a small supplementary MRC grant to our core grant in order to investigate retroviruses. The reason why I didn't ask for more funds during the period when we developed the RIA test was that I neither had the available space to establish a larger lab, especially Category III bio-containment space, nor had a wish to expand since my forte in research was to run a small team playing to our strengths. Besides, my 'day job' was to be head of the Institute of Cancer Research, and running my own lab was a secondary function. I therefore diverted funds from my existing project on human leukaemia retroviruses to study the more urgent problem of HIV.

5.71. In terms of the application process for applying for grants and funding from the DHSS, the MRC and other organisations during this time and the ease of that process, I cannot comment on applying for DHSS funding since I had not done so. Regarding applications to the MRC and to medical research charities, grant applications could be made with certain deadlines to meet the dates of grant

committees. Grant applications would go out for external peer-review and members of the grant committees would add their own views taking the comments of the specialist external reviewers into account. The committee would then draw up a priority list of the submitted applications for that grant period trying to balance the importance of the topic to that funding agency, the degree of innovation in the project, and the plausibility of making progress within the budget requested.

5.72. Winning grants was always difficult but proceeded along well understood lines. Apart from the intrinsic merit of your own application, you might be lucky or unlucky on your place on the priority list according to the quality of competing grants in different fields of research that came before the same committee with a fixed budget. Sometimes a successful application might be partially cut in budget, sometimes it was not successful although the granting agency would invite resubmission of a modified grant, and sometimes it was simply declined without the opportunity to resubmit. When you were unsuccessful, you tended to feel hard done by, but my view both as an applicant and at other times as a committee member, was that the process was on the whole fair. There were strict rules about declaring an interest and recusing yourself if an application competed directly with your own research, and you never sat in on discussion of your own application if it came before the same committee. During the period under discussion, I do not remember serving on any MRC committees other than the Working Party on AIDS, which did not review grant applications.

5.73. As to when I first approached these organisations for funding and the frequency of those requests, regarding my part of our joint research with Dr Tedder's lab on an RIA for HIV, I never applied for funding. We did it on the existing grants that included developing an RIA for the leukaemia viruses (HTLV-I & II) and for checking out retroviruses thought to be possibly linked to AIDS.

5.74. Given therefore, that I had not requested any extra funding the issue as to whether any of my requests for funding were granted is not applicable. The

mention of a need for extra funding mentioned in various DHSS internal notes may relate to Dr Tedder's part of the project.

5.75. In terms of the impact of a lack of funding on the timing of bringing a test to market, of course, bringing a test to market (i.e. development) is much more expensive than basic research, as pharmaceutical enterprises know all too well. That is why so many promising projects fall by the wayside during the development phase. I don't recall being present at the Haemophilia Reference Centre Directors Meeting of 10 December 1984 **[HCDO0000394_117]** or at any of their meetings. I don't think Dr Lane was realistic that he could produce a high-quality test as soon as and more cheaply than Wellcome Diagnostics. In 1985, the Centre for Applied Microbiology (CAMR) that was sub-contracted by Wellcome Diagnostics made excellent progress (after resolving some teething problems) in scaling up antigen production considering the complexity and safety concerns of propagating large amounts of HIV-infected cells.

5.76. As to other factors impacting on the progress of our work, looking back at our HIV research during 1984-85, I am surprised how much progress we made in our work. It was one of the most fruitful periods of research in my career. Perhaps the most important positive impact from pursuing our research, aside from funding, was the quality of young colleagues in our small lab, and our judicious (or lucky) choice of superb collaborators. They enabled us to progress as follows:

a) We identified the best substrate cell line (CEM) in which to propagate HIV; the big impact was fewer false positive results in tests for antibodies than in most of the American tests.

b) We revealed the true extent of HIV (and HTLV-I) infection in various AIDS risk group in the UK; the impact was seeing the grave situation among persons with haemophilia treated with pooled Factor VIII concentrates.

c) We demonstrated that 'Slim' disease and aggressive Kaposi's sarcoma in Africa were causally associated with HIV infection; the impact was the recognition of widespread HIV infection in sub-Saharan Africa.

d) We devised a 'pseudovirus' method as a surrogate HIV particle for tests of neutralising antibodies (see e) and of receptor discovery (see f) which allowed work to be carried out in a low containment laboratory, greatly speeding up the research as well as reducing its cost. The pseudovirus is a 'sheep in wolf's clothing' in that the spike proteins of HIV are assembled on a harmless virus-like particle. This technique and later variations on it proved to be a boon to vaccine research and development against other dangerous viruses such as Ebola filovirus and COVID-19 coronavirus.

e) We determined that most infected persons including those still in good health produced only low amounts of neutralising antibodies (i.e., the subset of antibodies that protect against infection); the impact was that developing an efficacious HIV vaccine was going to be far more problematic than previously thought.

f) We demonstrated that the CD4 protein on the surface of T-helper lymphocytes served as the binding receptor for HIV; this study became a paradigm for studying virus-cell surface interactions for many viral pathogens up to the COVID-19 virus.

5.77. Overall, our studies had a positive impact both on scientific understanding of HIV and on public health - of which a) and b) had an impact on infected blood. From the viewpoint of blood-borne infections, it could be argued that my decision to pursue African AIDS (project c), our investigation of neutralising antibodies and their relevance to vaccine development (projects d and e), and our research on the CD4 receptor (project f), diverted us from placing more effort on diagnostic tests, but these projects were exactly what CRC/MRC Committee for ICR, the main funder of our research, applauded when we sent in our progress report at the end of the grant period.

Middlesex Hospital and CRI contract with Wellcome

5.78. I have been asked a number of questions by the Inquiry in relation the Middlesex Hospital and CRI contract with Wellcome to develop an anti-HTLV-III assay suitable for large-scale production. These questions relate to whether these were the first contracts entered into and the respective assays used.

5.79. As to the issue of the contract, at the risk of appearing pedantic, I wish to restate that this contract with the Wellcome Foundation involved the Middlesex Hospital Medical School (MHMS) of the University of London, not the NHS Hospital with which it was associated; similarly, it involved the Institute of Cancer Research (ICR) see document **[UCLL0000001]**. As stated in this document, it was a contract of sponsorship of research over a 5-year period whereby Wellcome would support two post-doctoral scientists, one each at MHMS and at ICR, to assist the teams there to refine the antibody assay and to develop an *antigen* assay for HIV. The antigen assay would enable the detection of virus in newly infected people with a high virus load when the person would be at their most infectious to others. A modern version of an ELISA antigen test is the COVID-19 lateral flow test.

5.80. I am afraid that I no longer have records of previous agreements between ICR and Wellcome. I'm not sure that there was a formal contract, but there must have been a memorandum of understanding or at least a verbal agreement to explore and collaborate on test development as mentioned on page 1 of **[PRSE0004280]**. Such an understanding had advanced far enough for Wellcome to draft a subcontract for production of antigen from HIV-infected cells at CAMR. Since CAMR would have to plan well ahead to allocate category III containment space, these negotiations were important to make progress towards a diagnostic test for the NTBS and GUM clinics.

5.81. As to the issues raised in relation to the assays, our assay involved preparing antigen from HIV-infected CEM cells and devising a test to detect antibodies in

an infected person's serum specific to the virus. A positive test would indicate that the person being tested had contracted infection by HIV. It would not detect all infected people because it takes a few weeks following infection for antibodies to appear, and during this 'eclipse period', the person may already be infectious to others. The assay comprised a 'competition' format whereby the sample to be tested would need to displace a radio-labelled standard anti-serum to yield a positive result. Thus, the absence of a radioactive signal would indicate a positive result.

5.82. For initial research studies, our assay was an RIA and refinements and improvements included: (a) more efficient means of extracting viral antigen from the infected CEM cells; (b) studies to determine in scale-up whether the infected cells would maintain production of high levels of antigen; (c) determining whether people infected with variant HIV strains produced antibodies that reacted in the test; considering that HIV is 10x more variable than, say, the COVID-19 coronavirus, that was an important question; (d) comparing sensitivity of an ELISA read-out to the RIA read-out once Wellcome had accomplished the ELISA method.

5.83. It should be noted that this agreement between Wellcome and MHMS/ICR **[UCLL0000001]** was for sponsored research during the 5 years *following* the introduction of a commercial test, in order to improve it as well as to devise an antigen test, rather than to rest on our laurels.

5.84. As to the respective merits of an RIA or ELISA, the advantage of an ELISA format once established, was that it would be cheaper, less dangerous to produce and easier to handle than an RIA. The only advantage of an RIA was the short-term one that the NBTS was more familiar with RIA for other viruses. The diagnostic world, however, was moving away from RIA to ELISA on tests ranging from pregnancy to novel viruses.

5.85. Re-reading the minutes of the 1st meeting of EAGA on 29th January 1985 **[PRSE0002734]** reminds me that there were divergent opinions at that meeting on the relative merits of RIA and ELISA. Dr Harold Gunson favoured RIA while Prof Arie Zuckerman, who had much experience with hepatitis B virus, favoured ELISA. While I had no practical experience of large-scale screening myself, I agreed with Prof Zuckerman that the newer technique of ELISA was a distinct advance on RIA. I felt that RIA was backward looking while ELISA was forward looking. It is noteworthy that none of the HIV diagnostic assays that were marketed in 1985/86 used RIA. The 6 or 7 American tests and the 3 European tests all used some form of ELISA.

Announcement of Wellcozyme HTLV-III ELISA

5.86. Unfortunately, I regret that I do not recall the when and how of these events were announced and cannot further assist the Inquiry in this regard. I was not involved in the announcement or with the Health Authorities and Regional Transfusion Centres. My responsibility was to get on with the next stages of research.

Confirmatory testing procedure for positive Wellcozyme HTLV-III tests

5.87. Again, unfortunately I cannot assist the Inquiry in respect of this issue as I was not involved in confirmatory tests. IFA was one procedure (soon discarded), use of a non-competition ELISA test was another, and Western blotting (a different type of ELISA) was a third. I do not recall when they were introduced, and I had no preference between the latter two.

Wellcozyme HTLV-III test costs and British-made test equivalent costs.

5.88. I am asked about the costing of the Wellcozyme HTLV-III test and the equivalent costs of a British-made test and whether it would be cheaper.

However, I was neither consulted nor focussed on the costing of the Wellcozyme test. The only thing I recall is that Dr Richard Tedder and I requested that tests sold to Zambia and Uganda where we had conducted preliminary testing should be set at zero profit.

Involvement in HTLV-III evaluation programme for screening tests

5.89. The Inquiry has asked me to explain my involvement in the evaluation programme for HTLV-III screening tests and the decision-making processes amongst other issues. However, I took no part in the evaluation programme or in the decision-making processes. It might appear from Dr Kennedy's note **[DHSC0002255_039]** that there was a proposal from Dr Tedder and myself for funding to scale up testing and evaluation, but this was from Dr Tedder alone. In the same document, Dr Kennedy expressed concern on the introduction of commercial tests that "*It is likely that USA manufacturers will wish to use the UK as a proving ground for their products and thereby to gain support for performance submissions to the US Food and Drugs Administration. It is very important therefore to be able to assess these kits to ensure that the NHS can be told about unsatisfactory ones.*"

5.90. I did think and still think that an independent evaluation programme was essential to determine which tests performed to adequate sensitivity, specificity, and consistency. For instance, one of the first tests to be marketed, the Abbott test, turned out to be unreliable, as I detail below in paragraphs [5.101-5.106].

Delay of evaluation programme to include Wellcozyme HTLV-III test

5.91. As to the issue whether the evaluation programme was delayed in order to include the Wellcozyme HTLV-III test, to the best of my knowledge, except for an assertion made by Abbott Diagnostics, I do not recall any notion that the

evaluation programme of diagnostic tests for HIV might have been delayed in order to include the Wellcozyme test. However, I was not a member of the EAGA sub-group on screening, and I would have recused myself from any discussion on the Wellcozyme test at EAGA itself because I was an interested party. Incidentally, I never took any personal royalty income from the Wellcozyme test.

5.92. The minutes of the 15 February meeting of the EAGA sub-group on screening **[DHSC0000425]** may appear ambiguous on the availability of tests for evaluation. In my interpretation, where the minute states that five companies were licensed by the NIH to *develop* tests based on Dr Gallo's isolate, it means just that, a decision the NIH took in May or June 1984. It was nothing to do with the evaluation of tests or licensing tests for distribution or sale. So far as I can see, at the time of the EAGA meeting in February 1985, no tests were on sale even in USA, none had yet been approved by the FDA (Abbott was provisionally approved in March 1985), and none had been provided to the DHSS for evaluation.

5.93. Curiously, there was no mention in the minutes of 15 February meeting **[DHSC0000425]** of the test kit being developed in Europe by Organon-Teknika (Vironostika) or Pasteur Production, (ELAVIA) or of the USA West Coast effort to develop tests based on Jay Levy's HIV isolate (Chiron Corp). Moreover, according to Dr McClelland, the data on efficacy accrued by the companies using the Gallo isolate came from different blood samples so that one firm's product could not be closely compared with another.

5.94. DHSS officers proposed to agree a protocol for the PHLS to oversee the evaluation. It was stated that the Wellcozyme test might be available for evaluation in three months; I don't know who provided that time estimate although it turned out to be accurate. It is not evident to me that the Wellcozyme kit became available for evaluation any later than other kits.

5.95. Going forward to the minutes of the 10 June meeting of the Screening Sub-group **[DHSC0000551]**, it appears that Wellcozyme was among the first three tests to be provided to PHLS for evaluation. According to the minutes of the EAGA meeting on 30 July **[PRSE0002628]**, Dr Philip Mortimer of the PHLS reported that the Vironostika test (of Organon-Teknika) and the Wellcozyme test were particularly suitable for and easy to use in blood transfusion centres.

5.96. When Abbott Laboratories made assertions about the Wellcozyme test, it was picked up by the press, including the New Scientist **[WITN0684014]**. I would not lend any credence to Abbott's claim.

5.97. In conclusion, my view expressed here is a current one in the light of examining the documents received from the Inquiry. I remain unaware of any reliable evidence of a postulated delay in the evaluation programme. Neither am I aware of a delay to the roll-out of routine screening. I don't see any evidence in the documents supplied to me by the Inquiry that provision of Wellcozyme test kits was a significant factor in limiting the rate of progress or time of completion of the evaluation.

Other factors affecting the date on which routine anti-HTLV-III screening was introduced

5.98. I am asked by the Inquiry as to whether any other factors, other than those already addressed, affected the introduction date of anti-HTLV-III screening. I consider that two other factors may be pertinent: (a) there was a need for training to perform the test at screening centres in advance and (b) there was considerable concern that screening tests should be introduced simultaneously in blood donor centres and GUM clinics.

5.99. I recall that there was much discussion on EAGA of the importance of introducing testing to all RTCs simultaneously and also to GUM clinics. This was due to a concern that people who knew or suspected they were at risk of infection would volunteer to donate blood simply to obtain a test and might shop around different transfusion centres to find one running the tests. If there were an influx of high-risk donors, including high-risk persons in the eclipse stage of infection when they were highly infectious to others but did not yet have antibodies, it would increase the probability of contaminating the supply of blood and British blood products.

5.100. On the issue of the estimates of people who became infected with HIV owing to a postulated delay in evaluating or introducing screening tests, to my mind, there are four inadequately understood areas concerning the date of introduction of screening tests for HIV antibodies in the UK:

a. While there might have been a delay to the planned date for introducing universal blood screening, I do not consider there was a delay in completing the evaluation of tests. Perhaps the date set by DHSS to roll out screening was too optimistic, as reported to the EAGA Screening Sub-Committee on 10th June 1985 [**DHSC0000551 minute 9**]. Since the evaluation overseen by Dr Mortimer appears to have been completed by mid-July 1985 and published in October 1985, I doubt that the procurement and quality control of the test kits chosen could have been accomplished to commence screening before October 1985.

b. A similar point to consider (which I do not have the data for) is by what date each commercial diagnostic company tendering to the DHSS was genuinely able to supply enough tests, as recommended by the EAGA Screening Sub-Committee on 10th June 1985 [**DHSC0000551 minute 10**]. I vaguely recall press reports in the USA that the licensed diagnostic companies were struggling to supply sufficient tests for the whole of the US market, but I have not looked up any reports from this period.

c. If data are still available on seroconversions in donors during June-October 1985, the Inquiry could potentially ascertain the precise number

of new HIV infections transmitted by blood during this contentious period before screening was introduced.

d. I have considered whether purchasing the first test that became available in sufficient numbers, even if it turned out to be of inferior quality, would have resulted in HIV infection in fewer recipients of blood and blood products - or possibly increased contamination rates? If there were false negatives, it could have resulted in more cases of blood-borne infection; if there were too many false positives due to excess reactive host proteins such as DR4, many UK blood donations would have been discarded necessitating further importation of contaminated clotting factors. It might be useful for the Inquiry to commission a retrospective analysis using modern mathematical modelling like that used during the COVID-19 epidemic. The UK has much expertise in this area.

Extract from John Crewdson's book and comments from Angus Dalgleish

5.101. The Inquiry refers me to **[PRSE0002948]** which is an extract from a book by John Crewdson titled: "*Science Fictions - A scientific mystery, a massive cover-up, and the dark legacy of Robert Gallo*." At page 25 it is stated that my 'assistant', Angus Dalgleish, told the Daily Telegraph,

> *"We are prevented from using a perfectly good and reliable test because the Americans want to make money... The American test is worse than useless. It has produced false negative results and even false positives. It's not surprising that the American health department delayed giving it a license. Commercial considerations are absolutely hampering the containment of the disease in Britain. We've allowed AIDS to get a year's start*."

5.102. Gus Dalgleish worked in my lab from February 1984 until February 1986. I was academic advisor for his MD thesis, but I did not regard him as my 'assistant'. He was a clinical fellow in oncology and immunology equivalent to a specialist

senior registrar. I did not expect my colleagues to seek permission before speaking to the press about matters beyond our own unpublished research.

5.103. I do not recollect seeing Dr Dalgleish's comment in the Daily Telegraph when it appeared. I did see it on page 188 of John Crewdson's book, and I may have seen it before publication, because Mr Crewdson sent me a few chapters requesting scientific comment before final editing. I disagreed with Dr Dalgleish's comment about allowing AIDS to get a year's start because both the international research community and several independent diagnostic companies were working as fast as possible to design diagnostic methods to detect HIV infection. Yet I also thought there was a substantial kernel of truth buried in his colourful language.

5.104. My view of this hasn't changed over time except to become more cynical about the marketing policies of Abbott Diagnostics Division, the company selling the test to which Dalgleish was referring. My main concern was that the early (1985) batches of the Abbott HTLV-III ELISA test yielded some false negative results and far too many false positives. In other words, the tests did not have sufficient specificity.

5.105. Let us consider the situation where there is a constant rate of false positives of, say, 1%. That may seem acceptable when testing a population with a high rate of HIV infection, as in parts of Africa or among patients treated with clotting factors. But if the true rate of infection is low, such as less than 1 in a 1000 which we had found among North London blood donors, then the number of false positives would outnumber true positives by at least 10:1.

5.106. One of the reasons for false positives in tests using Dr Gallo's isolates was the presence of human proteins in the virus preparations used as antigen to detect the antibodies in the test. Too high a level of host antigens could mask detection of low levels of specific anti-HIV antibodies, resulting in false negative tests. On

the other hand, antibodies specific to host antigens in the cells used to grow HIV would result in false positive tests.

5.107. Let me describe one example of the unwitting false positive test results resulting from host antigens. A particular variant of a protein called major histocompatibility complex class II (MHC-II) generated some of the false positive readings. MHC-II proteins are polymorphic, that is, they are highly variable in the human population. They function in immune recognition and play a key role in the rejection of organ, tissue and bone marrow grafts. The variant in question is known as DR4 and it was expressed on the H9 cells producing HTLV-IIIB used to make the tests based on Dr Gallo's virus preparations. Thus, the human DR4 antigen 'contaminated' the Abbott HIV test and other tests based on Dr Gallo's virus. This came to light as Abbott testing gathered pace (analogous to side effects of novel drugs that only become apparent during Phase 3 large scale pharmaceutical trials). One study in Germany found that DR4-negative mothers of DR4 positive children (DR4 being inherited from their fathers) often make anti-DR4 antibodies after a second pregnancy with DR4 positive foetus. It was later confirmed among US donors. The maternal antibody reaction to DR4 resembles Rhesus blood group incompatibility, although the new-born children of DR4-negative mothers are usually healthy. This story can be read in Crewdson's book *Science Fictions*, except he erroneously wrote that the mothers were DR4 positive, whereas they were DR4-negative mothers with DR4 positive husbands.

5.108. The Wellcozyme test was not affected by DR4 for two reasons: First, we chose the CEM cell line to grow virus which does not express DR4 or any other MHC-II antigens; second, the competition format of our assay abrogates any antibody reaction with host antigens and is therefore more specific for HIV antibodies.

5.109. With hindsight, one could say that the DR4 problem was but one reason why several batches of the Abbott test did not pass quality control. There was a suspicion, although I am not aware of conclusive evidence, that Abbott was off-

loading 'dud' batches that would fail FDA quality control onto the European market. I think that may be what Dr Dalgleish referred to as 'worse than useless'. One consequence was that some long-term, regular donors were wrongly told that they had become infected by HIV.

Section 6: Other issues

Assertions made by Dr Karpas

6.1. I am asked to set out my views in response to the various assertions which have been made by Dr Abraham Karpas in his statements **[WITN0684001]** and **[WITN0684019]**. I have considered the witness statements and the 17 documents he provided to the Inquiry in order to respond to the questions asked of me. I have focused on the parts of those statements in which my name is referenced. The witness statements of Dr Karpas contain assertions that are simply not true. To take two minor points, it is not correct that I was included in the Queen's Award for Technology that was awarded to Wellcome Diagnostics for the Wellcozyme test or that my office used a Royal typewriter (it was an IBM "golf-ball" typewriter).

6.2. Dr Karpas's major charge is that a decision by the scientific journal *Nature* in 1983 to decline to publish a paper on the tropism of HIV only in CD4 cells by Dr Klatzmann *et al* in Paris was due to two negative peer reviews, both written by me, and that this rejection set back progress in AIDS research by a year.

6.3. I recall very clearly that when John Crewdson came to my office (from recollection some time in 1990 or 1991) while researching his book *Science Fictions* **[PRSE0002948]**, he surprised me by asking me specifically about a manuscript which had apparently been submitted by Dr Klatzmann *et al* in 1983 and he showed me a photocopy of the references **[WITN0684003]**. I had no recollection of them but, in case I had forgotten, we looked together through my

Nature files. My secretary had kept detailed files during 1983/1984 on any reviewing I did for scientific journals, which were well ordered and had not been weeded out during the 1980s. There was no record of a request for or execution of peer review for Dr Klatzmann's article.

6.4. I have now re-examined the two references claimed by Dr Karpas to be written by me **[WITN0684003]**. I did not write either of them. The first recommends declining the manuscript on the grounds that it might be a contaminating laboratory virus rather than a genuine human infection. The second reference is quite supportive, provided the authors could provide further data. As recorded by Mr Crewdson, I remarked that I might well have written something similar to the second reviewer (discussed further below). I continue to regard it as a perceptive review, although I have not seen the original manuscript submitted by Dr Klatzmann, only the version published almost one year later in *Science*. The two reviews are so different in tone that it seems doubtful to me that one person would have written both of them, something that I have never encountered in my career either as a scientist or later as an editor myself (*British Journal on Cancer*, Nature Publishing Group, 1996-2002). They might have been typed or retyped in the offices of *Nature*, for example, if one of them was dictated orally to *Nature* as a late response to a request to review the manuscript.

6.5. Contrary to Dr Karpas's claim **[WITN0684001** and **[WITN0684019]** that I exerted an enormous influence on publications in the field of AIDS, I do not recall reviewing any papers on the topic of HIV/AIDS that were submitted to *Nature* during the period 1983-1985. This was probably on account of a policy (long since abandoned) of the then editor, John Maddox, that scientists like me should not simultaneously serve as peer-reviewers and be invited to write opinion pieces for *Nature*'s "News & Views" columns. An example of the latter is my article dated 3 May 1984 entitled "*Acquired Immune Deficiency Syndrome: Retroviruses linked with AIDS*" **[BAYP0000026_107]**.

6.6. Concerning the claim by Dr Karpas that Dr Peter Newmark was dismissed as an editor of *Nature* because he 'mishandled' Dr Klatzmann's manuscript, I have no knowledge of it. According to an affiliation tag to Dr Newmark's 2015 review of a book on the history of the journal *Nature*, he joined *Nature* in 1974 as a Biology Editor and was promoted to Deputy Editor by the Editor, John Maddox. In 1989, six years after Klatzmann's paper had been submitted to *Nature*, Newmark left to become founding Editor of *Current Biology*. After leading this journal over the course of 12 years or so, Newmark moved to be Editorial Director of BioMed Central, a company pioneering electronic science publishing in the UK.

6.7. Dr Karpas has misinterpreted my statement quoted by Mr Crewdson in *Science Fictions* that said: "*I might well have written something like that*" regarding the second referee's report if I had been asked to review Dr Klatzmann's manuscript. This was not an admission that I had reviewed it, but rather a statement that I might have agreed with that reviewer that further experiments should be conducted, and quantitative data obtained, before the findings were accepted for publication.

6.8. I do not know if *Nature* rejected the article out of hand or requested further data before resubmission which Dr Klatzmann did not subsequently provide. One should bear in mind the context that *Nature* used to reject and still rejects at least 90% of manuscripts submitted to it. Seeking to publish research papers in top general science journals such as *Nature* and *Science* has long been a lottery. Dr Klatzmann could have submitted the study to a highly respected if less prominent journal much earlier if he felt that publication would change the course of progress in our understanding of AIDS.

6.9. In my opinion, a question arising from Dr Karpas's assertions is whether the decision by *Nature* not to publish Dr Klatzmann's paper (whoever had peer-reviewed it) was the root cause of a delay in the progress of HIV research. Dr Karpas claims in his witness statements that the decision against publication in

1983 impeded progress in HIV research for a year. I have re-read Dr Klatzmann's paper as eventually published in *Science*, which I consider to be an excellent analysis of the cells targeted by HIV as CD4 positive T-cell lymphocytes **[WITN6868011]**. The study confirmed, for cells in grown in culture, what had already been demonstrated by clinical immunologists in December 1981 for cells in the blood of symptomatic patients, that is, a selective deficiency of CD4-positive cells, and thus Klatzmann showed that the direct cytopathic effect of the virus played a role in the mechanism of pathogenesis.

6.10. I do not agree with the assertion by Dr Karpas that Dr Klatzmann's observation on the cellular tropism of LAV (HIV) was so pivotal that the delay in publication caused innumerable deaths from AIDS. Dr Karpas stresses that Dr Klatzmann also importantly characterised the morphology of LAV by electron microscopy. On re-reading the paper, I note that Klatzmann characterised the electron micrographs of LAV as resembling beta-retroviruses ('D-type particles') cited as causing immunodeficiency in macaques held at the California Regional Primate Center and the New England Regional Primate Center. Since the discovery of these simian viruses had not yet been reported at the time Dr Klatzmann's manuscript was submitted to *Nature*, in May 1983, it was an interpretation that could not have been included in the original version. Dr Klatzmann had quite properly brought his manuscript up to date and had added new data in the interval between its initial submission to *Nature* and its later submission to *Science*. Actually, the apparent relationship to a beta-retrovirus was inaccurate, because a few months earlier, Dr Montagnier had published an article with the electron-microscopist, Charles Dauguet, indicating that LAV more closely resembled a Lentivirus called equine infectious anaemia virus **[WITN6868012]** (which Klatzmann also cited) and that observation turned out to be correct. Beta-retroviruses have spherical cores as seen by electron-microscopy whereas Lentiviruses have cone shaped cores. However, if the topology of the electron microscope cuts directly across the cone, it will look like a circular section. These details illustrate again how pieces of the HIV jigsaw took time and several steps to reveal an accurate picture.

6.11. Early in 1984, Dr Montagnier's team had also published a letter in The Lancet **[WITN6868013]** on the culture of further virus isolates from AIDS patients which they named IDAV (Immune Deficiency Associated Virus), and an isolate from a patient with haemophilia. Neither this paper nor Montagnier and Dauguet's morphology paper were co-authored by Dr Klatzmann. These important findings further strengthened the indication that LAV/IDAV was the cause of AIDS, not simply an opportunistic infection. Dr Montagnier had presented preliminary versions of these findings at the international workshop on human retroviruses held in USA in September 1983 (see my answer to Question 8) at which many of the major players in the field of human retroviruses were present. Thus, incremental data were already in the public domain from Montagnier's laboratory which strengthened the evidence that LAV/IDAV was the cause of AIDS. What was missing was confirmation of Montagnier's findings independently of his group, which came in May 1984 from Robert Gallo in NIH and in August 1984 from Jay Levy at the University of California in San Francisco.

6.12. I regard Dr Klatzmann's paper as important for showing that HIV directly kills CD4+ cells in culture. While I can appreciate and empathise with Dr Klatzmann's frustration, I doubt that the delay in formal publication significantly affected the overall pace of advances in our understanding of AIDS and its cause. Dr Karpas entitled his 2019 paper: *How the 1983 seminal French manuscript with the evidence that their HIV was the cause of AIDS was deliberately blocked, resulting in hundreds of thousands of infections and deaths worldwide* [**WITN0684026]**. In my opinion, this conclusion is wrong for the reason discussed above, namely that other papers from Dr Montagnier's group already demonstrated LAV to be a leading candidate as the cause of AIDS, although that was not yet confirmed by other, independent researchers.

6.13. With regard to Dr Karpas's second witness statement and the suggestion that that I had a monopoly control of funding and publishing on UK AIDS research

[WITN0684019], I should state that during the 1980s I neither acted as a peer reviewer for research papers nor sat on grant committees that reviewed grant applications for the Medical Research Council concerning HIV/AIDS.

6.14. Dr Karpas claims that several HIV investigators were close friends, namely Dr Gallo, Dr Mortimer and myself. However, this was not true at that time. I became friendly with Philip Mortimer a few years later when we realised that he and my wife shared the same violin teacher; my friendship (like that of so many others) with Robert Gallo tended to be on-off, although we acted cordially, e.g. Dr Gallo provided us with his HIV isolate HTLVIIIB. I am not aware whether Dr Mortimer and Dr Gallo knew each other at all. In my view, when scientists interact- as in other professions - personal friendship is not as relevant as professional trust and respect. I also regard Dr Tedder's letter to Dr Karpas **[WITN0684006]** in which he declines to establish a collaboration with Dr Karpas as a polite and reasonable response.

6.15. Dr Karpas appears to base his evidence for my being 'very close' to Dr Gallo on one paper on which we were co-authors, published in 1975 eight years before the discovery of HIV **[WITN0684005]**. To my recollection there is not a single publication where Dr Gallo and I were co-authors on an HIV study from 1983 to the present day. There were, however, two HIV papers in the 1988 which I co-authored with Dr Montagnier **[WITN6868014; WITN6868015]**, and Dr Klatzmann was senior author on one of them. Moreover, in 1992 I spent a sabbatical period in Dr Montagnier's department in Paris. It is difficult to reconcile Dr Karpas's account of my relationships with these facts.

6.16. I have no recollection of meeting Dr Nigel Byrom as suggested in the letter dated 31 May 1991 that Dr Karpas refers to **[WITN0684001]** but I have never spoken in that way to a young scientist. In fact, the MRC Working Party on AIDS (on which I sat but which did not evaluate grant applications) was trying to diversify its AIDS research portfolio and to encourage new people into the field. I did meet fairly frequently with his senior colleague Dr Farthing and Dr Byrom

may well have accompanied him on one occasion when I may have pointed out that I was not in a position to help with funding. I note that Dr Nigel Byron (spelled like the poet and having the same hospital affiliation as Dr Byrom) has co-authored two papers with Dr Karpas **[WITN6868016; WITN6868017]**, so it seems possible that Dr Byrom's name is mis-spelled in the copy of the letter submitted by Dr Karpas.

6.17. Dr Farthing was a dermatologist and a pioneer of AIDS research with Dr Brian Gazzard who ran the GUM clinic at St Stephen's Hospital. The hospital (now Chelsea and Westminster Hospital) was only 12 minutes' walk from my office at ICR and I was fortunate to learn a lot about the clinical aspects of AIDS from Dr Farthing and from the consultant clinical virologist to the clinic, Dr David Shanson. Dr Farthing and I were on good terms. I was a co-author on two of Drs Farthing and Shanson's papers to which the Inquiry referred me in respect of question 8, above **[NHBT0000068_015]** and **[PRSE0002140]**.

6.18. I remained in occasional contact with Dr Farthing after he moved to the USA in 1988 and later when he returned to his native New Zealand. Sadly, he died in 2014. In the mid-1980s Dr Farthing chaired the All-Party Parliamentary Group on AIDS and invited me to join it.

Other matters relevant to the Inquiry

6.19. I have been asked to set out any further matters that might be pertinent to the Inquiry's terms of reference and list of issues. I consider the following points may be of relevance, which may or may not have been considered.

Contaminated clotting factor preparations and virus inactivation

6.20. The reliance in England and Wales on imported concentrates of clotting factors pooled from large numbers of donors can be considered separately from the British blood donor population which had a lower prevalence and was more

often used for individual transfusions (except Scotland). I note from the minutes of the meeting of Haemophilia Directors on 10 December 1984 that there was an extended discussion about heat treatment of clotting factor concentrates, particularly Factor VIII to inactivate viruses **[CBLA0001948]**.

6.21. The Haemophilia Centres never contacted me directly, although they kindly provided Dr Tedder with serum samples. Looking back, I could have been pro-active in proposing and conducting experiments with haemophilia centres on HIV inactivation in clotting factor concentrates. By April 1984, we were able to propagate the HIV strain LAV obtained from Montagnier and to titrate it. We could therefore have spiked samples of Factor VIII concentrates with LAV and measured the reduction in virus titre by heat treatment and by ultra-filtration in relation to reduction of clotting factor. Such data might have helped to informed Haemophilia Centres how to proceed to manage the narrow margin between inactivating the virus and inactivating the clotting properties of the concentrate. Of course, by 1985, other virological laboratories in Europe and the USA were conducting research along these lines, including a detailed and quantitative study of heat inactivation by Jim McDougal and colleagues at the CDC published in August 1985, so whether it would have made a difference I cannot say. In 1986, my assistant, Paul Clapham did help with a similar evaluation of heat and chemical inactivation of HIV added to Factor VIII.

Difference in approach between the Blood Products Laboratory and the Protein Fractionation Laboratory

6.22. I expect that the Inquiry has considered why the Blood Products Laboratory ('BPL') in England lagged behind the Protein Fractionation Laboratory ('PFL') in Scotland in becoming self-sufficient in producing clotting factor concentrates.

6.23. One Scottish pool became contaminated with HIV during the second half of 1984 which unfortunately infected about 50% of the patients with haemophilia

A who were recipients of Factor VIII concentrate. None who received Factor IX were infected. **[HSOC0002656]**.

Non-US sources of concentrates

6.24. The USA commercial clotting factors were of high risk of carrying viruses because donors were paid for donations and thereby attracted donors in AIDS risk groups, such as addicted users of injected drugs and very poor Haitians. It might be useful for the Inquiry to ask whether non-US sources of concentrates were considered and were available.

Conclusion

6.25. The iatrogenic infections suffered by recipients of tainted blood and blood products and the impact on their families is profound and appalling. I wish to reiterate my sincere sympathies to all of those who have suffered.

6.26. I have tried to give my recollections and views of events concerning HIV as accurately and fully as I can but I'm all too aware that with the passage of time and concomitant loss of written records, not to say my waning mental acuity, my evidence is not as precise and detailed as I would wish.

Statement of Truth

I believe t s statement are true.

Signed GRO-C

Dated 23/06/2022